TURNING COMPLEX DIAGNOSTIC CHALLENGES INTO SIMPLE SOLUTIONS

STRATEGY 2015-2020
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Diagnosis is a complex word, from a simple root: to seek knowledge. At FIND, this imperative – to listen and learn – is at the heart of how we turn complex diagnostic challenges into simple, streamlined solutions.

FIND is a mobilizer, bridge builder and enabler. From initial development through final implementation, we use our expertise and create efficient partnerships to ease every step of diagnosing poverty-related diseases – and this all begins with dialogue.

We respect and leverage the knowledge of everyone involved in the development and use of diagnostic solutions – global and local. At each stage, we start not with answers, but with questions. The key is understanding local conditions from the perspective of the people living there, helping overcome technical, cultural or logistical barriers.

From the ground up, FIND designs and drives diagnostic solutions that are intuitive to use, easy to implement and readily embraced by the whole community. We accelerate progress leading from diagnosis – accurate treatment, diseases stopped before they advance, and lower costs across the entire health system.

With partnerships and opportunities growing, we are determined to keep our role simple: ask the right questions; team up for the right answers. That is after all, the root of diagnostic success.
Executive Summary

“Without diagnostics, medicine is blind.”

Dr. Alain Mérieux
President, Fondation Mérieux, and diagnostic pioneer
1. Driving diagnostic success in a changing landscape

FIND shares the goals of the global health community to fight diseases that impact the poorest populations in the world. We do this through a focus on diagnostic solutions. Knowing what is wrong with a patient is fundamental to all efforts to improve world health. We recognize that in order to capture the investments that the global community has made thus far to fight diseases of poverty, key diagnostic gaps must be filled. This strategic document aims to describe our thinking on how we can best fill these gaps over the coming five years and address post-Millennium Development Goal priorities.

FIND was founded in 2003 to bridge existing development gaps for essential diagnostics by initiating and coordinating research and development (R&D) projects in collaboration with the international research community, the public sector, and the in vitro diagnostics industry. Through our programmes in tuberculosis, sleeping sickness, and malaria, we have delivered 11 tests and have helped transform the diagnostics landscape for each of these disease areas. For example, tuberculosis patients can now get drug susceptibility testing in 90 minutes at a district hospital – this used to take up to 120 days and was only available at national reference laboratories. The development of a rapid diagnostic test for sleeping sickness has helped make eradication of the disease a reality. In malaria, joint FIND-WHO efforts to assure the quality of malaria rapid diagnostic tests have reduced the use of substandard products from 76% to 11%.

Today, many of the challenges that FIND was first created to address persist. New diagnostic solutions are sorely needed for almost all diseases of poverty: not many new tools are being developed and many diagnostics that are in development still encounter perpetual delays within fragmented regulatory and policy settings. Market penetration of existing tools is slow and expected impact is often stifled due to inefficiencies in the delivery system. The willingness to pay for diagnostics R&D remains low.

Since 2003, the landscape has also shifted significantly. There is more industry engagement in emerging markets. Small and medium enterprises, especially from middle-income countries, are playing a greater role in global health, and more donor and venture capital funding is directly available to manufacturers. In many countries, laboratories remain the weakest link of health systems, but governments are increasingly willing to invest in their improvement. Private healthcare service providers have an expanding role to play in addressing public health problems. While new challenges have emerged – for example, the threat of antibiotic resistance – we also see new opportunities: the information technology revolution may for the first time allow us to fully capture the value of diagnostics. Overall, since the landscape has become more complex, a more holistic, nuanced response is required.

Over the past years, FIND has begun to adapt to this changing landscape. In order to address the needs of countries, we have grown from a classic product development partnership into an international organization with a significant presence in low- and middle-income countries.

“Our goal is to fight diseases that impact the poorest populations through a focus on diagnostic solutions.”
2. Turning complex diagnostic challenges into simple solutions

In our new five-year strategy, our role as bridge builder and mobilizer becomes more important. We will continue to partner but we will partner differently; we will still bridge but we will bridge further. As we implement our strategy, we plan to shift our historical focus on developing new tests to one that is centred on “packaged solutions”. Our existing strength as a translator between the technical world of product development and the realities of end-users will expand, and we will no longer operate in a diagnostics vacuum but will make linkage to treatment and care paramount in everything that we do. In keeping with this, we will move from looking at problems through a single disease-specific lens to also consider syndrome-based approaches that better address clinical realities.

Our new vision and mission reflect this cultural and strategic shift: at FIND, we envision a world where diagnostics guide the way to health for all people. We aim to turn complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives.

To support our vision and mission, we will organize for action around four strategic goals:

1. Catalyse development: Identify needed diagnostic solutions and remove barriers to their development.
2. Guide use & policy: Lead products through the clinical trials pathway to global policy on use and market entry.
3. Accelerate access: Support uptake and appropriate use of diagnostics to achieve health impact.
4. Shape agenda: Improve understanding of the value of diagnostics and strengthen commitment to their funding and use.

In order to best achieve these goals, we will place a stronger emphasis on cross-cutting themes and build out new initiatives. One such example is our Support for Success programme, through which we will provide the support of industry experts to test developers – particularly to small and medium enterprises. Such mentorship is designed to help overcome product design, manufacturing and marketing hurdles faced by many of these developers. Themes that are relevant to more than one disease, such as eHealth or syndrome-based testing, will also be strategically targeted.

Our individual disease strategies aim to turn the theory of our strategic goals into action. Our priority disease areas for 2015 – 2020 are: Tuberculosis and Acute Febrile Respiratory Infections, Malaria and Acute Febrile Syndrome, Hepatitis C, and Neglected Tropical Diseases. We will also plan to have mini-portfolios in areas affecting reproductive and child health: HIV, sexually transmitted infections, and infections and nutritional deficiencies in children under five years old.

By the end of 2020, we envision having another 15 essential diagnostic solutions in use and contributing to improved health for all.
FIND’s Vision
A world where diagnosis guides the way to health for all people.

FIND’s Mission
Turning complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives.

To support our new vision and mission and promote this strategic shift, we will organize for action around four strategic goals:

1. Catalyse development
   • Lead dynamic needs definition
   • Support program for manufacturers
   • Scout technology
   • Match-make
   • Provide specimens

2. Guide use & policy
   • Lead clinical trials
   • Define evidence needs
   • Support WHO development of guidelines

3. Accelerate access
   • Facilitate national policy and development of rollout plans
   • Help MoHs identify gaps, coordinate solutions and deploy experts
   • Develop QA tools & strategies

4. Shape the agenda
   • Measure and communicate impact of Dx
   • Shape Dx ecosystem to foster willingness to invest/pay
   • Lead global discussion on emerging Dx topics

“Innovation begins with ideas. Ideas only have real value and are truly innovative when implemented as a solution.”
3. Translating strategy into action

**Tuberculosis and Acute Febrile Respiratory Illness**

Our Tuberculosis programme will enable access to fit-for-purpose diagnostics and linkages to treatment for all people afflicted with tuberculosis and to support the WHO in their goal of a world free of this disease. Priority objectives include:

1. Reducing transmission through early detection
2. Preventing antimicrobial resistance and decreasing mortality through improved drug susceptibility testing
3. Creating comprehensive solutions for countries to increase the impact of new and existing tools
4. Demonstrating the role of diagnostics in controlling the tuberculosis epidemic

**Malaria and Acute Febrile Syndrome**

Our work in Malaria will maintain our achievements on quality and disease control while also supporting the global elimination and eradication goals set forward by global stakeholders. Priority objectives include:

1. Enabling elimination of the disease and control of drug resistance through the development of new tools
2. Improving the management of fever patients with new tools and approaches
3. Maximizing the impact of existing rapid tests, especially for *P. vivax*
4. Increasing the prioritization of diagnostic solutions for malaria and fever management

**Hepatitis C**

Our new programme in Hepatitis C emerges at a critical juncture for management of the disease – new treatments are on the horizon that will make cure possible in low-resource settings. We will support the fight against the hepatitis C virus through the development, evaluation and delivery of appropriate and affordable diagnostic solutions. Priority objectives include:

1. Supporting development of affordable and fit-for-purpose diagnostic tests
2. Enabling access to care through simplified diagnostic pathways and linkage to treatment
3. Preventing further infections through improved blood screening
4. Demonstrating the need for and benefit of interventions, including exposing the true burden of disease

**Neglected Tropical Diseases**

Through our Neglected Tropical Diseases programme, we are committed to supporting both the «London Declaration on Neglected Tropical Diseases» and the WHO neglected tropical disease priorities. Our target is to address unmet diagnostic needs across this range of diseases, prioritizing sleeping sickness, Chagas disease, leishmaniasis, Buruli ulcer, dengue and soil-transmitted helminth infections in the near term. In human African trypanosomiasis, we aim to support global elimination efforts through improved screening with existing and new rapid tests, and to enable less burdensome disease confirmation. In Chagas disease, new point-of-care tools and diagnostic algorithms to reduce the burden of disease will be central to our efforts. For leishmaniasis, we will prioritize a sensitive point-of-care test that works in eastern Africa and allows for the detection of asymptomatic carriers, as well as a test of cure. And for Buruli ulcer, our aim is to prevent disease progression through improved approaches to early detection. We are still in the process of defining our specific priorities for dengue and soil-transmitted helminth infections.

Across all diseases in which we work, we will also dedicate resources and efforts to raising the prioritization of diagnostics by demonstrating their indispensable role in disease control.
“From dialogue to diagnosis, we advocate from the perspective of users in resource-poor countries.”
Today, diseases of poverty remain a major cause of mortality, illness and lack of economic progress. Each year these diseases cause an estimated 6.4 million deaths and the loss of 316.2 million years of healthy and productive life globally, according to G-Finder’s 2012 report. Their economic burden is immense. For example, loss of productivity due to malaria is thought to reduce national incomes across much of sub-Saharan Africa by 15-20%, while the World Bank estimates that in disease endemic countries the burden of tuberculosis may result in 4-7% losses of Gross National Product.

Over the past decades, the global community has increasingly recognized the need to combat these diseases and has expanded its financial and political commitment to ensure equitable access to healthcare and to improve disease control efforts. Unprecedented investments are being made to enable the development of desperately-needed medical tools (US$ 3.2 billion in 2012) and to finance their use (e.g. via multi-billion dollar funding mechanisms like the Global Fund to Fight AIDS, Tuberculosis and Malaria and the GAVI Alliance). For many diseases, global health objectives will only be reached with the benefit of new tools – drugs, vaccines and diagnostic tests. An increased focus on the development and use of diagnostics is critical to achieving global health priorities.

Historical examples and data clearly demonstrate that by leveraging the power of diagnostics, the world has a remarkable opportunity to simultaneously improve individual health outcomes, reduce the global burden of disease, and save costs:

- A very high rate of patients (70 – 90%) co-infected with HIV and drug-resistant tuberculosis die within weeks; earlier diagnosis of tuberculosis to allow intervention could save the vast majority of them.
- As the world nears polio eradication, ongoing surveillance and rapid investigation of suspected cases by the Global Polio Laboratory Network allow for the identification and prevention of potential outbreaks, consolidating years of progress.
- After the introduction of quality-assured rapid diagnostic tests for malaria in Senegal, approximately 50% of cases were found to have been previously misdiagnosed as malaria; the usage of malaria artemisinin-based combination therapies was cut in half, thus saving the Global Fund €1.2 million in that country alone.

Despite these clear benefits, diagnostic tests constitute only 3 – 5% of healthcare spending and remain a lower priority than other health interventions. Only a miniscule proportion of R&D funding for neglected diseases is spent on diagnostics (~4% of the total in 2011) yet new tools are needed in most neglected disease areas.

“An increased focus on development and use of diagnostics is critical to achieving global health priorities.”
As the world embarks on increasingly ambitious global health agendas, access to data to monitor progress becomes more and more important. Especially in the context of elimination and eradication efforts, it is crucial that we know when and where disease transmission is occurring in order to stop it. Diagnostics are fundamental to this knowledge, providing information that allows us to understand the burden of disease, how it changes over time, where transmission is occurring, and how intervention programmes are succeeding or failing. In the future, all routine diagnostic results should feed into surveillance systems, an outcome that will become feasible through the development of eHealth solutions. Moreover, surveillance networks and centres of excellence need to be equipped with appropriate high-throughput diagnostics to enable continuous and targeted monitoring and outbreak management.

The role of diagnostics for surveillance

To promote individual and community health and as a first step towards universal access to healthcare.
Patients need access to diagnostics that can inform their treatment and halt the spread of disease in their communities.

To enable control, elimination and eradication of diseases.
The global community needs diagnostics to target interventions, identify outbreaks and monitor progress towards goals.

To stem the tide of increasing antimicrobial resistance and preserve the potency of existing treatments.
Patients and healthcare providers need diagnostics to detect the cause of infection and ensure correct treatment.

To improve the efficiency of healthcare spending.
Healthcare providers need access to diagnostics in order to prevent costly over-treatment or mistreatment.

To empower countries.
Policy makers need diagnostic data to guide health interventions.

To empower individuals and communities.
Patients and families have a right to know, and they can only understand their conditions if diagnosed.

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DIAGNOSTICS: ENABLING THE ADVANCEMENT OF GLOBAL HEALTH PRIORITIES

The role of diagnostics for surveillance

As the world embarks on increasingly ambitious global health agendas, access to data to monitor progress becomes more and more important. Especially in the context of elimination and eradication efforts, it is crucial that we know when and where disease transmission is occurring in order to stop it. Diagnostics are fundamental to this knowledge, providing information that allows us to understand the burden of disease, how it changes over time, where transmission is occurring, and how intervention programmes are succeeding or failing. In the future, all routine diagnostic results should feed into surveillance systems, an outcome that will become feasible through the development of eHealth solutions. Moreover, surveillance networks and centres of excellence need to be equipped with appropriate high-throughput diagnostics to enable continuous and targeted monitoring and outbreak management.
When FIND was officially launched at the World Health Assembly in May 2003, the importance of diagnostics in improving health outcomes and disease control was just beginning to be recognized. For over 100 years, the microscope was the primary tool for diagnosing tuberculosis in the public health sector in developing countries. R&D funding for more accurate and reliable tools for use in this sector was noticeably absent. Much progress has been made since 2003, with FIND playing a large and exciting part in this evolution. With funding from multiple donors, FIND has led the delivery of 11 new tests and enabled development of other diagnostics, working with partners to ensure their proper scale-up and use.

**TUBERCULOSIS PROGRAMME IN ACTION:**

*Market transformation for diagnostics*

We have introduced six new technologies that are revolutionizing the detection and treatment of tuberculosis and multidrug-resistant strains and have revitalized interest in the field. According to recent estimates, scale-up of these new tools in endemic countries is saving 300,000 lives per year. By building laboratory capacity, we are accelerating access to these new tools and enabling speedy diagnosis of tuberculosis and its multidrug-resistant form. In the past five years, FIND has trained close to 4,400 healthcare workers and worked with over 360 laboratories in 39 countries.

<table>
<thead>
<tr>
<th>The world in 2003</th>
<th>The world in 2014</th>
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<tbody>
<tr>
<td>1.7 million tuberculosis deaths per year</td>
<td>1.3 million tuberculosis deaths per year 24% reduction</td>
</tr>
<tr>
<td>Drug susceptibility testing takes</td>
<td>Drug susceptibility testing for key drug takes</td>
</tr>
<tr>
<td>120 days at reference laboratory level</td>
<td>90 minutes at district level hospital</td>
</tr>
<tr>
<td>5% of drug resistance cases detected</td>
<td>25% of drug resistance cases detected</td>
</tr>
<tr>
<td>Minimal public and private sector interest in fighting tuberculosis</td>
<td>Reinvigorated public and private sector interest in fighting tuberculosis</td>
</tr>
</tbody>
</table>

“By leveraging the power of diagnostics, the world has a remarkable opportunity to simultaneously improve individual health outcomes, reduce the global burden of disease and save costs.”
NEGLECTED TROPICAL DISEASES PROGRAMME IN ACTION:
Paradigm shift to rapid testing

For human African trypanosomiasis, also known as sleeping sickness, we are making major contributions toward reaching the 2020 disease elimination targets of the United Nations Millenium Development Goals by introducing three new critical tests: the first ever rapid test for screening, which is being rolled out in 10 endemic countries in sub-Saharan Africa; a fluorescence microscopy method for confirmation of the disease; and a next-generation molecular test for surveillance. We are now seeing a yearly drop in incidence; although this is largely attributable to existing tools, the availability of easier to use and more efficient diagnostics has made the feasibility of eliminating the disease a distinct reality.

The world in 2004

- 18,000 cases per year reported
- Reliance on the logistically burdensome card agglutination test for screening, followed by lengthy, insufficiently sensitive confirmation by microscopy before treatment
- Poor coverage of the population at risk due to lack of tools that could be deployed at primary health care level resulted in human reservoir of infection, reducing prospects for elimination of the disease

The world in 2014

- < 8,000 cases per year reported (> 50% reduction)
- Dramatically improved screening with first generation rapid test; a test and treat strategy has become an achievable goal with new treatments and a 2nd generation rapid test on the way
- Simple, easy to use screening and confirmation tests and the likely availability of a safe drug that can be administered at the primary health care setting provide an opportunity to improve coverage

FIND’s role in developing a rapid test for human African trypanosomiasis

<table>
<thead>
<tr>
<th>What FIND did</th>
<th>Impact</th>
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<tbody>
<tr>
<td>Coordinated biomarker validation and selection</td>
<td>Biomarkers and specimens made available so product development could begin</td>
</tr>
<tr>
<td>Managed prototype development, selection &amp; validation</td>
<td>Prototype selection &amp; validation completed</td>
</tr>
<tr>
<td>Created coalition for development (e.g., with endemic countries, ITM, SD, WHO, BMGF) &amp; managed project</td>
<td>Commercially launched in September 2013 at price of only US $ 0.50 / test</td>
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<tr>
<td>Provided clinical platform and coordinated evaluation &amp; demonstration</td>
<td>WHO support for RDT use in passive screening achieved; guidance on use for active screening expected soon</td>
</tr>
<tr>
<td>Worked with Ministries of Health in endemic countries to troubleshoot &amp; create plans for introduction</td>
<td>Introduction initiated in over 10 endemic countries in sub-Saharan Africa for passive screening (as of June 2014)</td>
</tr>
</tbody>
</table>

Together with new drug regimens, the rapid test will allow for a shift to a test-and-treat strategy that will support HAT elimination
MALARIA PROGRAMME IN ACTION:
Cost savings to health care programmes

A joint FIND-WHO undertaking has ensured the
use of high quality rapid diagnostic tests and has transformed malaria care, resulting in major cost savings for health programmes. The outputs of this collaborative quality assurance programme have formed the basis for United Nations malaria rapid diagnostic test procurement for the past four years and have made one of the strongest cases to date for use of a diagnostic test over symptom-based treatment. An improved blood transfer device that allows for safe collection and transfer of blood from a finger-prick reached over 100 million patients in 2013. Our R&D work has laid the foundation for a new generation of tests that are needed to achieve elimination.

Across diseases, FIND has also created an enabling environment that has spurred investment in diagnostics and facilitated the involvement of other stakeholders. By sharing reference materials and specimens from our widely-used collections, FIND has aided the discovery of new biomarkers for human African trypanosomiasis, leishmaniasis, and tuberculosis – a critical first step in the development of new tools. FIND’s work with WHO has helped forge a path to rapid policy review that speeds the introduction of new products. The market visibility created by Xpert® MTB/Rif (Xpert, a cartridge-based, fully automated molecular assay for detecting tuberculosis and rifampicin resistance in 90 minutes) has prompted the development of 14 “fast-follower” technologies in the field of tuberculosis. Lastly, through both its development and country-level work, FIND has also increased prioritization of diagnostics overall, working with country governments to include diagnostics in national plans and raising the profile of diagnostics through partnerships that support global priorities (e.g. sleeping sickness elimination).

<table>
<thead>
<tr>
<th>The world in 2008</th>
<th>The world in 2014</th>
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<tbody>
<tr>
<td>243 million cases and 866,000 deaths per year</td>
<td>207 million cases in 2012 (15% reduction) and 627,000 deaths (28% reduction)</td>
</tr>
<tr>
<td>All rapid diagnostic tests procured through United Nations agencies are of unconfirmed quality; an estimated 76% of rapid diagnostic tests in use are substandard</td>
<td>All rapid diagnostic tests procured through United Nations agencies are of confirmed quality; overall use of substandard rapid diagnostic test is ~ 11%</td>
</tr>
<tr>
<td>WHO recommends that presumptive treatment can be considered in children under 5 years of age</td>
<td>WHO recommends parasitological confirmation by microscopy or rapid diagnostic tests of ALL suspected malaria cases before treatment</td>
</tr>
<tr>
<td>29 countries using rapid diagnostic tests at community level; 24 million rapid diagnostic tests distributed worldwide; 22% suspected cases tested</td>
<td>48 countries using rapid diagnostic tests at community level; 205 million rapid diagnostic tests distributed worldwide; 64% suspected cases tested</td>
</tr>
<tr>
<td>Disease elimination not yet on the horizon</td>
<td>The world has committed to elimination; development of the tools needed to realize this goal is already underway</td>
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“Despite clear benefits, diagnostic tests remain a lower priority than other health interventions.”
Despite the successes previously described, a broad range of diagnostic needs and challenges still exist. To develop a strategy that addresses them, we conducted in-depth evaluations of today’s changing landscape to understand the causes, the shifting roles of other stakeholders and the evolution of FIND’s capabilities over time.

Current diagnostic gaps reveal four barriers to success

CHALLENGE 1: Few tests are in development
At the most basic level, many diagnostic needs remain completely unaddressed. Of the 28 disease areas that FIND has analysed as part of its strategy work, 21 have a significant need for new diagnostics tools. For at least five of these diseases, few if any stakeholders are working on new tools, and for many others the level of investment in development is far below what is needed to make significant gains. In some cases, this gap is due to limited knowledge of the basic science (e.g. on biomarkers) and technology. In other instances, manufacturers lack the understanding of end-user needs to develop fit-for-purpose products. Market dynamics still pose a problem - the financial incentives for manufacturers to develop products are simply too low, either because of price pressure (e.g. malaria and HIV) or the size of the markets (e.g. neglected tropical diseases).

CHALLENGE 2: Tests in development don’t make it to market
Far too many products that are in development are delayed or never make it to market entry. An analysis of UNITAID market reports across HIV and tuberculosis diagnostics shows that estimated launch dates for new products are continually pushed back, often by as much as four or five years. Of the ten companies developing new molecular tools for rapid decentralized tuberculosis and drug susceptibility testing (the so called “fast-followers” to Xpert), six stopped development despite having promising technologies that had the potential to meet patient needs. One of the most important reasons for these high attrition rates is the fact that the manufacturers working on promising technologies are often small or medium enterprises without access to the cash flow, know-how and/or capabilities needed to succeed.

UNITAID market reports show continuously pushed back launch dates

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
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<tbody>
<tr>
<td>HIV CD4</td>
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<tr>
<td>Product 1</td>
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<td>Product 2</td>
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<td>Product 3</td>
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<td>HIV Viral load</td>
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<td>Product 4</td>
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<td>Product 5</td>
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<td>TB</td>
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<td>Product 6</td>
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<td>Product 7</td>
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CHALLENGE 3: Slow market penetration for new tests

Manufacturers with tests that are ready for market entry often face further hurdles as they try to navigate the regulatory and policy pathways to uptake. Due to a confusing and fragmented regulatory landscape and the lack of harmonized processes for global and national policy guidance to inform product use, promising technologies have to be taken through long, confusing, and sometimes even redundant review processes. As manufacturers try to navigate their way through these processes, they face further difficulties as they try to determine the types of clinical trials that are required to secure global policy guidance and thus often expend effort collecting clinical data that are not useful. Because they are unable to conduct trials in a way that would allow rapid scale-up following policy guidance (e.g. in conjunction with local health authorities in endemic countries), they frequently end up having to repeat local studies in several countries. For example, following the advent of point-of-care CD4 technology for HIV, one particular manufacturer was required to do over 40 studies, conducted in over 20 countries, to support national policy decisions on use.

CHALLENGE 4: Inefficient delivery systems stifle impact

Once policy decisions are made, market penetration tends to be slow, and expected impact is often stifled, mostly due to inefficiencies in the delivery system. For example, in lower to middle income countries, ~50% of viral load and CD4 machines for HIV are not in use because of a lack of customized support or supply chain issues. Equally problematic are overly complex procurement systems: for example, in one country only ~30 machines for a specific diagnostic test are in use despite a policy and funding decision to buy 300 tests two years ago. Unaddressed user errors or test malfunctioning also lead to high false positive rates (10% to 40%), even for the simplest ones such as HIV rapid diagnostic tests. Most low- and middle-income countries also face the problem of linking diagnosis to care. An estimated 20% of tuberculosis patients with a positive Xpert test never make it to treatment because they are lost to follow-up. These problems are perpetuated by chronically weak health and laboratory systems and the fact that Ministries of Health often lack the capacity, technical knowledge and crosscutting tools (e.g. standard operating procedures, quality assurance programmes) to develop and ensure the effective implementation of country-specific plans for rollout of new diagnostic solutions.

“Most low- and middle-income countries face the problem of linking diagnosis to care.”
In response to the broad range of barriers previously detailed, various stakeholders are adopting new approaches and roles within the diagnostics ecosystem.

**Increased but fragmented participation in product development**

There is now greater and more diverse private sector engagement in diagnostic development, especially from less experienced small and medium enterprises. Increasingly, donors are also providing funding directly to manufacturers to spur product development, and there is more funding flowing towards technology for global health from venture capital (e.g. Global Health Investment Fund and Investment Fund for Health in Africa). Governments in emerging economies are increasing efforts to foster local industry directly, and academics and product development partners are also taking on new, albeit fragmented, work to guide product development.

**Early work to streamline regulatory and policy processes**

In the regulatory arena, multiple efforts are underway to strengthen and coordinate the regulatory system, including a revamping of the WHO prequalification process for diagnostics. Harmonization efforts across both stringent regulatory authorities and national regulatory authorities in endemic countries are in progress. Although they are somewhat disjointed, there have also been efforts to support generation of evidence to enable clearer guidance on use.

**Growing but still disparate efforts in implementation**

In the area of implementation, many groups are active in large-scale projects, providing technical assistance and working to build diagnostic capacity in lower and middle income countries. However, there is very little coordination of these efforts, and minimal attention is given to linking improved diagnostic use and laboratory strengthening with the broader health system. These efforts often target individual components of diagnostics implementation, whereas a comprehensive approach would ensure a more lasting impact through country-owned implementation.

“21 out of 28 analysed diseases of poverty have a significant need for new diagnostic tools.”
Building on our strengths

Over the last ten years, FIND has established itself as a dedicated player in the diagnostics field, specializing in poverty-related diseases. In the context of the challenges and shifting stakeholder landscape previously described, it has become clear that the success of diagnostics is predicated on the ability to bridge the world of technical diagnostics development and the realities of working in resource-limited settings.

Highly cognizant of this, FIND is building on a fundamental ability to incorporate input from both the scientific and end-user perspectives. Over the years, we have developed and refined our skill-set including:

- End-to-end product development experience that allows us to anticipate bottlenecks or missteps in development before they occur and to help product developers avoid them.
- Technical expertise covering the spectrum from early product development to implementation that allows us to act as translator between developers and end-users.
- Clinical trial experience and know-how that allow FIND to shape the entire clinical process (from specimen collection to coordinating clinical trials) and dramatically reduce the time for test development and validation.
- In-country knowledge and the ability to identify and act on the true needs, constraints and behaviours of end-users in endemic regions.
- Proven mechanisms to create feedback loops that enable communication between end-users, product developers and everyone in between.
- Strong relationships with country governments, laboratories and implementers that allow FIND to support rapid uptake of products and transmit lessons learned to product developers.

An increased focus on quality

The impact of any diagnostic, as well as its continued and trusted use, is dependent on the quality of the results it delivers. FIND is acutely aware of this and supports a trilogy of quality assurance cycles, the first the responsibility of manufacturers, the second of regulators and policy-makers, and the third of in-country laboratory systems. FIND’s “development” team works with IVD industry to ensure high product quality as well as industry buy-in for an expanded role in quality assurance of products once on the market, e.g. through provision of training, quality assurance panels for proficiency testing, remote monitoring tools etc. FIND’s “clinical and regulatory” team coordinates with WHO technical and prequalification groups, as well as regulatory authorities, to strengthen the timely availability of quality data for regulatory approval and post-market surveillance. Thirdly, FIND’s access team works with local laboratory systems to develop sustainable and locally appropriate quality assurance plans and helps with implementation, with a focus on routine data collection and monitoring of trends in performance indicators, as well as internal and external quality assurance with timely feedback of results and continued quality improvement. Strengthening basic analytic skills of laboratory workers and supervisors, implementing appropriate eHealth solutions and institutionalizing quality assurance as a fundamental laboratory network activity will be crucial.
“It has become clear that the success of diagnostics is predicated on the ability to bridge the world of technical diagnostics development and the realities of working in resource-limited settings.”
FIND’s Mission
Turning complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives.

FIND’s Vision
A world where diagnosis guides the way to health for all people.
3- A Strategy for the Future

We believe that our work can spark a real paradigm shift in the health care and well-being of lower and middle income countries and their populations.

FIND is an enabler and a mobilizer. We provide a resource platform for our partners and bring relevant stakeholders together to catalyse scientific and technical development. From dialogue to diagnosis, we advocate from the perspective of users in resource-poor countries. The ultimate purpose of our activities is to capture the value that flows from diagnosis, namely: access to accurate treatment, disease control, efficient healthcare spending and empowered individuals, communities and countries.

Innovation begins with ideas. Ideas only have real value and are truly innovative when implemented as a solution. FIND’s role in innovation is to turn complex diagnostic challenges into the simplest implementable solutions. For this to happen, ideas need to be nurtured, developed, engineered, tested, implemented and championed.

To execute our strategy, we will move from a focus on individual diagnostic technologies to supporting complete diagnostic solutions. It is not enough to develop innovative diagnostics. In order to transform a tool into a solution that has impact, more attention needs to be given to the accompanying “package”. A smart diagnostic solution comprises a diagnostic test that is just right for the need, together with a suite of ingredients that eases the way to improved access and use in a weak health system infrastructure. This package simplifies diagnosis for patients, users, clinicians and countries, and includes tools for implementers, among them those for training, advocacy, installation, quality assurance, support and maintenance, impact measurement and, importantly, an information technology solution that links results to patient care and surveillance programmes.

Elements of a complete diagnostic solution
What we can learn from Xpert: Successes, challenges and the need for complete diagnostic solutions

The launch and implementation of Xpert MTB/RIF provide a strong example of the lessons that the global community has learned with respect to the need for comprehensive solutions. While some elements of the package around Xpert were ready and available when the test was launched in 2010 (e.g., rapid policy guidance), many others were not. In fact, our direct experience with Xpert implementation brought home the overwhelming need for a solution-based approach and allowed us to define the package of tools that must accompany new tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert</td>
<td>Launch</td>
<td></td>
<td></td>
<td></td>
<td>Being used in 108 high burden countries</td>
</tr>
<tr>
<td>Policy &amp; regulatory guidance</td>
<td>Policy endorsement at unprecedented speed (2 years after design lock / trial start)</td>
<td></td>
<td></td>
<td></td>
<td>Expanded guidance for pediatric &amp; extrapulmonary TB</td>
</tr>
<tr>
<td>Quality assurance</td>
<td>Strong built-in controls</td>
<td>Calibration tool</td>
<td>Validation panels</td>
<td></td>
<td>Remote monitoring</td>
</tr>
<tr>
<td>Support and supply chain</td>
<td>Clear procurement system but long time to repair / replacement</td>
<td></td>
<td></td>
<td></td>
<td>Clear warranty conditions &amp; coverage</td>
</tr>
<tr>
<td>Impact</td>
<td>Strong trial data informed rapid policy (w/some impact data)</td>
<td>Early rollout not accompanied by data collection &amp; feedback on implementation</td>
<td></td>
<td></td>
<td>Scarce impact data available only from trials (not routine collection)</td>
</tr>
<tr>
<td>measurement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connectivity &amp; IT</td>
<td>Connectivity to lab management information systems</td>
<td>First independent IT tools to enable data transfer, mobile use</td>
<td></td>
<td></td>
<td>Chance to reach potential re: linkage to care &amp; connectivity by 2015</td>
</tr>
<tr>
<td>Training &amp; user manuals</td>
<td>1st implementation &amp; basic training guide</td>
<td>More complete job aids &amp; training package</td>
<td></td>
<td></td>
<td>Comprehensive online training</td>
</tr>
</tbody>
</table>

“FIND is an enabler and a mobilizer. We provide a resource platform for our partners and bring relevant stakeholders together to catalyse scientific and technical development.”
Furthermore, FIND will expand upon its current strengths as a translator between the technical world of product development and the realities of end-users. Achieving this requires a more thorough understanding of the diagnostics ecosystem and market segmentation, taking into account requirements at different levels of the health care system within the context of specific countries and settings (for example, the different roles of private and public sector markets). Such translation also requires more systematic approaches to information exchange across all the phases of development and access. By fostering an environment for multi-directional communication and knowledge sharing, we will be able to find the best solutions to meet end-user needs.

Significantly, FIND will no longer operate in a diagnostics “vacuum” – it is only through linkage to treatment and care that the transformative power of diagnostics can be fully realized. From the earliest phases of development to the final stages of treatment delivery, all diagnostic interventions will be informed by trends and needs regarding treatments and care, both current and future. For example, electronic health solutions are an integral part of any diagnostic intervention; the real time data-collection and prompt actions they allow will be important enablers of improved individual and community health.

To support our new vision and mission and promote this strategic shift, we will organize for action around four strategic goals:

1. **Catalyse development**: Identify needed diagnostic solutions and remove barriers to their development.
2. **Guide use & policy**: Lead products through the clinical trials pathway to global policy on use and market entry.
3. **Accelerate access**: Support uptake and appropriate use of diagnostics to achieve health impact.
4. **Shape agenda**: Improve understanding of the value of diagnostics and strengthen commitment to their funding and use.
Objectives
- Shape a robust, global product pipeline towards defined diagnostic needs
- Maximize chances of success for diagnostics most likely to meet defined needs

Indicators of success
- Availability of products: # of commercially available products to which FIND has contributed that meet priority needs

We believe that the best way to drive rapid development of diagnostics that are most needed is to build an open platform for manufacturer support that can be leveraged by all developers with promising new technologies.

This means that FIND will move away from large-scale direct funding to manufacturers. In the future, FIND will not champion individual products, but rather will use a virtual network of in vitro diagnostic industry and market entry experts to support the development of all products that have the potential to meet identified needs. While new biomarkers are urgently needed to enable the development of game-changing diagnostics, biomarker discovery is a lengthy, high-risk process in which FIND will not engage in directly. Rather, we will support scientists and academics by supplying well-characterised specimens that are essential for identification and validation of new markers. We will also play a coordinating role to ensure that discovery efforts are aligned with changing test needs.

Specifically, FIND will:
- **Lead dynamic needs definition** (target product profiles): work closely with end-users, WHO, other global policy groups, researchers, country partners and implementers to determine desired features and characteristics of needed tools.
- **Support manufacturers for success**: pair manufacturers who have promising technologies with R&D and market entry experts through our Support for Success programme.
- **Scout for technology**: identify technologies and manufacturers that have the potential to meet needs defined in target product profiles.
- **Match-make**: broker or form the best partnerships to initiate product development around target product profiles.
- **Provide specimen banks and platforms for feasibility studies**: leverage dynamic relationships with country research sites and existing know-how to provide high quality reference materials to manufacturers that can accelerate biomarker discovery and product development and enable rapid assessment of product feasibility.
New Support for Success programme eases the way to uptake for promising products

The problem  Market penetration for diagnostics relevant to Global Health markets takes 2x as long as product developers think:

The solution  Through IVD expert support, accelerate development and market entry:

<table>
<thead>
<tr>
<th>Technical expertise</th>
<th>Disease expertise</th>
<th>Market &amp; regulatory expertise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturing</td>
<td>Malaria/AFS</td>
<td>Logistics &amp; Distrib.</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>TB/AFRI</td>
<td>Quality</td>
</tr>
<tr>
<td>IT solutions</td>
<td>HIV</td>
<td>Market understanding</td>
</tr>
<tr>
<td></td>
<td>Hep C</td>
<td>Regulatory</td>
</tr>
<tr>
<td></td>
<td>NTDs</td>
<td>Commercialization</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

Given the poor profitability prospects for large manufacturers, investment in diagnostics for low- and middle-income countries is primarily made by small enterprises that struggle to move a product through development and commercialization quickly. One way to address these shortcomings is through direct funding to manufacturers, but success in terms of commercialized products has been low. FIND’s approach is to complement direct donor funding by providing support to manufacturers to help them navigate some of the more challenging aspects of product development and commercialization through a network of technical experts.

“We believe that the best way to drive rapid development of diagnostics that are most needed is to build an open platform for manufacturer support that can be leveraged by all developers with promising new technologies.”
Guide use & policy

Lead products through the clinical trials pathway to global policy on use and market entry

Objectives
- Reduce the time from development to market for diagnostic solutions meeting global health needs
- Create solid understanding of how, if and where to use diagnostic solutions in preparation for uptake

Indicators of success
- Availability of global policies: # of global policy recommendations that FIND has enabled
- Efficient and effective evidence generation: Average time from first registration to public sector introduction in a relevant country for FIND-supported solutions

To achieve this goal, FIND will expand upon its strength in the field of tuberculosis and support global processes for developing policy guidance and assuring quality across multiple diseases. We will operate an open clinical platform, working closely with WHO, industry, governments, and implementers to collect and synthesize the evidence that is needed to guide the use of new diagnostic solutions. Relevant groups, such as WHO and endemic country governments, will use this evidence to inform decision-making.

Specifically, FIND will:
- **Define evidence needs**: work closely with WHO and implementing country governments to establish the type of data that will be needed for decision-making on new technologies.
- **Lead clinical trials aligned with policy and regulatory needs**: as a WHO Collaborating Centre, leverage country partnerships to design and conduct clinical trials that meet the requirements of regulators and policy makers in the most efficient way possible.
- **Support development of WHO guidelines**: package evidence from clinical trials to facilitate policy decisions and support WHO in the creation of detailed guidelines, such as for quality assurance processes, and standard operating procedures to accompany new tools.

“FIND will operate an open clinical platform to support global processes for developing policy guidance and assuring quality across multiple diseases.”
The important role of economic and impact analysis

Simply assessing the accuracy and ease of use of a new diagnostic tool is not enough to evaluate its benefits. Cost-effectiveness analysis can also help global policy makers, countries and donors decide whether and how a new diagnostic should be scaled up, as well as which factors are critical for this process. During actual scale-up, impact will reveal whether the new tool is indeed beneficial for patients. A cornerstone of FIND’s work, will therefore be to collect the evidence that demonstrates the cost-effectiveness and impact of diagnostic solutions.

<table>
<thead>
<tr>
<th>Registration</th>
<th>Evaluation</th>
<th>Demonstration</th>
<th>Access</th>
<th>Scaling up &amp; continued adoption into national policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Test accuracy</td>
<td>- Comparative effectiveness (patient important outcomes, case detection)</td>
<td>- Test and resource utilization</td>
<td>- Test and resource utilization</td>
<td></td>
</tr>
<tr>
<td>- Ease of use</td>
<td>- Cost of diagnostic process and treatment, incl. for patients</td>
<td>- Patient impact</td>
<td>- Patient impact</td>
<td></td>
</tr>
<tr>
<td>- Surrogate patient important outcomes</td>
<td>- Operational requirements for implementation (infrastructure and human)</td>
<td>- Epidemiological impact</td>
<td>- Epidemiological impact</td>
<td></td>
</tr>
<tr>
<td>- Basic cost-comparisons</td>
<td></td>
<td>- Economic impact</td>
<td>- Economic impact</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Health system impact</td>
<td>- Health system impact</td>
<td></td>
</tr>
</tbody>
</table>

Is scale-up worth it? Economic analysis

Introducing new diagnostic technologies does not come cheap, and in resource-constrained settings, high costs are often perceived as an obstacle to infrastructure upgrade and sustainable technology use. Global and local policy makers can use decision analysis modelling to assess the cost-effectiveness of diagnostic interventions. The incremental cost-effectiveness ratio describes the difference in cost, divided by the difference in effectiveness, between two or more diagnostic scenarios and is an important information piece for selection and prioritization. Establishing the full cost per test goes far beyond simple consumable or equipment cost comparisons and includes, for example cost for staff, space, specimen transport and quality assurance. Effectiveness assessment requires measuring the diagnostic tool’s effect on patient-important outcomes when applied at large enough scale and thus relies on demonstration studies. Already over the last few years, FIND has placed a strong emphasis on comparative cost-effectiveness data. In the coming years, we will grow our in-house capacity further and standardize assessment tools.

Is scale-up successful? Impact analysis

Determining the impact of diagnostic interventions during programmatic roll-out (rather than during clinical trials) is challenging and requires analysis at multiple levels: patient impact, including shortened time to diagnosis and treatment, reduction in morbidity or mortality; epidemiological impact, or short-term increase in case notifications and longer-term decrease in incidence; economic impact, the money saved through avoidance of mistreatment; and health system impact, such as resulting availability of a strong disease surveillance system. Often, diagnostic impact is indirect and depends on multiple health system factors. For example, impact is only possible if correct treatment follows correct diagnosis. With partners, we will strive for more systematic and pragmatic impact measurement and help define standards on what to measure and how. Transmission modelling will be combined with measurement of real-life data. To allow for impact measurement at programmatic scale, we will keep indicators relatively simple and in some instances rely on surrogate markers.
Support uptake and appropriate use of diagnostics to achieve health impact

Objectives

- Support rapid translation of global policy into relevant and actionable country plans
- Enable quality-assured scale-up and use of proven diagnostic solutions
- Support creation of long-lasting, broad diagnostic capacity as a center-piece of disease control

Indicators of success

- Speed of country adoption: # of countries with FIND-supported Ministries of Health that introduce diagnostic products within two years of global guidance
- Coverage: % of target population tested with appropriate diagnostics for diseases in countries within FIND’s focus
- Quality assurance: % of FIND-supported rollouts accompanied by a quality assurance plan

Reaching WHO targets for disease control and elimination, across diseases, will require not only new, easy-to-use and rapid tools, but ensured and universal access to early and accurate diagnosis.

In addition to strong political commitment and managerial ability to translate plans into action, a robust laboratory and health system is essential to fully capture the benefit of new diagnostics. From the diagnostics’ perspective, we need to focus on meeting three key objectives over the coming five years in order to achieve integrated, patient-centred care: i) an expanded and strong network of high-quality diagnostic facilities, equipped with the right tools; ii) engagement of all care providers in diagnostic service delivery; and iii) the provision of effective information and support programmes to prompt and enable patients to seek diagnosis and care.

Taking into account these key needs, FIND will work with governments, national disease programmes and implementing partners to ensure that diagnostic solutions are holistic and tailored to country needs; to help countries prepare for their adoption; and to strengthen the underlying infrastructure and capacity to enable effective uptake and impact measurement. We will do this through a three-pronged approach that builds off our established in-country presence and laboratory expert network and takes advantage of the unique linkage that we have established between our upstream activities that focus on test development and our in-country access teams.

First, we will make sure that the right tools are available, and by this we mean packaged solutions that are tailored to local needs. From an access perspective, it is particularly important to deliver a packaged solution to facilitate impactful uptake. We will make sure that the package includes ready-to-use tools and/or strategies for implementers and is available at the same time that the test is WHO approved. Our access teams will focus on getting these tools, such as the eHealth, M&E and quality assurance packages, effectively applied. Second, we will help countries develop and execute implementation plans to use these solutions in their local contexts. Third, we will help ensure that countries have the underlying capabilities...
needed to implement solutions. Through long-term in-country presence and our expanding cadre of technical experts, we will work with endemic country governments to secure evidence-based political commitment for implementation, supporting the strengthening of health and laboratory systems (with an emphasis on diagnostics), and enabling impact measurement. We will also ensure that mechanisms are in place to communicate progress and lessons learned during implementation to industry and the broader global health community.

Key activities for FIND will be to:

• Facilitate national policy decisions: share and, if needed, generate evidence to support country policy making on the use of new diagnostic solutions rapidly and without redundant evaluation.

• Support the development and execution of rollout plans: work with national disease programmes and implementing partners to develop detailed country plans for the rollout of new diagnostic solutions (the elements of such a plan may include an updated diagnostic flow, plan for laboratory strengthening, and a clearly articulated approach to training, supply chain and logistics, quality assurance, impact measurement, data information management, and linkage to care).

• Support Ministries of Health to identify gaps and deploy solutions: work hand-in-hand with governments and implementers to troubleshoot implementation, coordinate country specific solutions, and deploy external experts where needed.

A three-pronged approach to ensuring impact in countries

1 Ensure that holistic solutions tailored to specific country needs are in place

2 Support development and execution of country implementation plans

3 Strengthen country capabilities to implement and capture benefit of solutions

“FIND will work with endemic country governments to secure political commitment for implementation, supporting the strengthening of health and laboratory systems and enabling impact measurement.”
Improve understanding of the value of diagnostics and strengthen commitment to their funding and use

Objectives
- Champion the role of diagnostics as an essential ingredient to good healthcare
- Shape the diagnostics ecosystem to foster industry investment and country willingness to support

Indicators of success
- FIND thought leadership: # of diagnostics-related articles published by FIND and collaborators that reach a relevant and wide audience
- Funding: % of total funds and % of total health resources contributed to diagnostics for diseases in FIND’s portfolio

Recognition of the importance of diagnostics and their potential impact on patient outcomes is essential to encourage investment in test development and rollout. As a thought leader in the field of diagnostics, FIND is one of the few players to have produced data showing the cost-effectiveness of correct diagnosis and to have highlighted the importance of diagnostics in disease elimination strategies. However, greater and more concentrated efforts are needed to bring about a fundamental shift in the way diagnostics are viewed. To achieve this, FIND will significantly expand its efforts to increase prioritization of diagnostics through dedicated, evidence-based advocacy. FIND will actively engage country governments and global procurers to support improved market dynamics and increase funding for diagnostics. The extreme pressure on product pricing that disincentivizes manufacturers and leads to poor product quality and market failures will also be addressed. We are committed to working with partners to make diagnostics affordable but will advocate against narrow and unyielding approaches that drive prices so low that the quality or sustainability of tests are compromised.

Specifically, FIND will:
• Measure and communicate the impact of diagnostics by building on our modelling and impact measurement capabilities and disseminating the outcomes, put diagnostics on global health agendas.
• Lead global discussion on emerging diagnostics topics by convening stakeholders and sparking debate about the latest issues, advance discussions on the role of diagnostics in health systems.
• Create market opportunities by working with global health funders to design strategies to turn market failures into opportunities and successes.
“The recognition of the importance of diagnostics and their potential impact on patient outcomes is essential to encourage investment in test development and roll-out.”
Principles to guide our work

- Serve as an open platform
- Maintain transparency and communicate openly
- Foster interaction across development and delivery
- Work within output-oriented partnerships
- Aim for sustainability and local ownership
- Remain flexible, responsive and adaptable
Acting on FIND’s new vision means that we not only need to change what we do, but how we work. We need to ensure that a new mind-set and new behaviours are communicated and embedded within our organization. To do this, we will restructure to optimize staffing strengths, implement key tactical changes, measure and communicate our results and progress and regularly review our core and disease strategies to ensure that we remain responsive to the needs of an ever-evolving field.

Our organizational culture for the future will revolve around the values of empathy, openness and progress. We want to act as enablers, match-makers, bridge builders and translators. We need to listen to all stakeholders, be reactive, agile and adaptable. We also need to be inventive and strengthen our scientific, technical and organizational expertise even further. And lastly, we need to match resources to needs in the most flexible and efficient manner by leveraging partnerships to the maximum and minimizing fixed costs.

A new structuring for the future

Our new organizational structure is designed to emphasize the importance of our strategic goals and cross-cutting themes. As our efforts shift from simply developing innovative tools to the more comprehensive “solution” approach, a move away from working in disease siloes to using a matrix approach becomes necessary. In pursuit of this, senior positions that are aligned with each of the strategic goals will work closely with the disease programme heads to ensure coherence between cross-cutting functions and diseases.

FIND will continue to operate as a lean, expert organization based in Geneva and will deepen its fund of knowledge by building out its already broad network of external consultants. In the area of development, we will call on \textit{in vitro} diagnostics industry and market entry experts to provide tailored support to manufacturers with promising technologies. To develop and maintain an adequate understanding of regional and local contexts and to provide continuity, FIND will have a small, ongoing presence in the countries where we work. We will complement this presence with a comprehensive network of technical consultants who can cover topics such as national laboratory strategic plan development and diagnostic quality assurance, among others. Throughout all our work, this structure will allow for the flexibility and rapid scalability that are needed to address country and manufacturer needs on demand.

“We will have an ongoing presence in the countries where we work, complemented by a comprehensive network of technical consultants.”
FIND’s global footprint

Geneva headquarters
- Overall organizational oversight and management
- Home to leadership, programme and support staff
- Hub for all FIND activity

Country offices /nodes
- Currently in India, South Africa, Uganda and the Dominican Republic with likely expansion pending
- Responsible for FIND implementation activities in a country/region, trial support & coordination with local partners

Global expert network
- Network of experts provides expertise to enable development & access work
- IVD industry experts provide developers mentorship, support
- Access experts across multiple countries support implementation

Note: locations of expert network and country offices / nodes are examples only

A new way of partnering

To be successful, FIND must also employ new approaches to partnerships. This requires clearly defining what we do and do not do, which is influenced by factors such as whether an activity is already addressed by partners or is not one of our strengths. We have traditionally operated through bilateral partnerships, primarily with industry. In the future we will adopt a coalition- and initiative-based approach to achieve broader reach and stronger outcomes. For example, in order to meaningfully improve the quality of diagnostics used in countries, we will form a coalition with WHO, the U.S. Centers for Disease Control (CDC), and African Society for Laboratory Medicine to enhance in-country success and sustainability. Financial support to test developers will be sought through strong relationships with funders in the global health arena. To enable this, we will need to strengthen our existing relationships with donors and build new partnerships with venture capital firms investing in technologies for global health.

FIND will also build more output-oriented partnerships, for example with other product development partnerships, where alignment of disease-level strategies is pursued and development of complementary, rather than duplicative or conflicting, initiatives is encouraged. Such collaborations would also facilitate joint funding and implementation opportunities. Our partnerships with Drugs for Neglected Diseases initiative, Clinton Health Access Initiative (CHAI) and the TB Alliance, for example, have the potential to achieve more and have greater impact.
Innovative partnerships with emerging economies

Today, emerging economies (including “BRICS countries” – Brazil, Russia, India, China, South Africa) are leading the charge to replace traditional models of “North-South Aid” with new forms of global partnerships and cooperation. As part of our new strategy, we will embrace this shift and strive to develop new approaches to collaboration. We will pursue closer alignment with the priorities of our country partners and develop new tactical partnerships that bring together resources from all sides – whether that means partnering with national research labs in Russia to support test development or with the government of Brazil to implement a new solution for Chagas disease.

Emphasizing communication and transparency

Increased clarity and transparency in decision-making will be part of the strategy implementation. Having detailed and transparent processes for reviewing, assessing and ranking potential candidates or choosing which activities to pursue will be of utmost importance, especially where there are limited resources for conducting a given activity. FIND will rely on its Scientific Advisory Committee (SAC) to make direct, public recommendations that guide our work. For example, if there are multiple manufacturers with products that could meet a defined need, the SAC will assess available evidence and render a decision about which products we should support (e.g. through Support for Success or its clinical platforms). The SAC will also provide oversight for day-to-day activities, such as controlling access to FIND specimen banks.

Strong monitoring and evaluation as a tool to measure progress

To measure successes, FIND will build a lean monitoring and evaluation system, targeting only the most essential and relevant information to assess progress. This will include improved reporting mechanisms and expanded internal modelling and impact measurement capabilities. A framework that is designed around the new strategy will allow us to quantify and express organizational progress, value for money and achievement in implementing the strategy. Fiscal discipline and control of programmatic and administrative expenses remain a high priority for FIND. It is likely that as our new approach becomes our primary way of working, the way our activities are funded will also change – for example, some of our activities are more likely to be undertaken using a fee-for-service model. We will need to adapt our fundraising and financial management practices to accommodate these changes. To measure progress towards achieving our desired operating model, FIND will include organizational indicators in its monitoring and evaluation framework.

“FIND will employ new approaches to partnerships, form coalitions and promote initiatives to achieve broader reach and stronger outcomes.”
“Across diseases, FIND will expand upon its current strengths as a translator between the technical world of product development and the realities of end-users.”
As part of its recent strategic review process, FIND has refined its focus with respect to diseases and syndromes. As mentioned earlier, 28 disease areas were analysed as part of this strategy exercise, and of those 21 were found to have significant needs for new diagnostic tools. A more detailed disease landscaping exercise followed, which took into account unmet diagnostic needs, strategic alignment with FIND’s mission and vision, as well as our existing organizational capabilities. The outcome was that we would prioritize four disease areas from 2015 to 2020:

- Tuberculosis and Acute Febrile Respiratory Infections
- Malaria and Acute Febrile Syndrome
- Hepatitis C
- Neglected Tropical Diseases

We also plan to have mini-portfolios in areas affecting reproductive and child health: HIV, sexually transmitted infections, and infections and nutritional deficiencies in children under five years old. Although we will not have any immediate activities with respect to diarrhoeal diseases, cervical cancer or certain childhood cluster diseases, we will continue to monitor these areas.

Non-communicable diseases were considered as potential areas for strategic attention. Despite the high burden of these diseases and growing global efforts around them, they were deprioritized for the near term to ensure sufficient organizational attention would be given to our priority diseases and to avoid diluting the effects of our efforts. Specific reasons for not including them were:

- Simple diagnostic solutions are already available in many of these areas, e.g. for diabetes and cardiovascular disease.
- The current focus of global strategies for non-communicable diseases and family health is rather on prevention and broad health system strengthening.
- There is already strong industry interest in developing solutions for these diseases, especially for emerging economies and middle income countries.

- There is limited overlap with current FIND capabilities in communicable diseases.

Given the dynamic nature of the diagnostics arena, mainly attributable to changes in available treatments, we will re-evaluate our disease focus regularly so that we can respond to changing landscapes in a timely manner.

As part of this effort we also assessed FIND’s role in responding to emergencies and outbreaks. A less common but vitally important application for diagnostics is disease outbreak confirmation and surveillance. FIND will support the international public health community in the management of emergency outbreaks, by providing assistance from our extensive network of disease, technology and laboratory specialists to whatever extent possible, when and if needed, e.g. Ebola virus outbreak.
During the development of our disease strategies, we identified several themes that were relevant to more than one disease. We believe that strategic emphasis on these themes is likely to have a large impact, and we intend to pursue interventions that will realize synergies across disease areas and geographies.

**Core themes identified in the development and evaluation of diagnostics:**

- **Syndrome-based approaches to diagnosis** to best address patient and clinician needs, e.g. focusing on cough or fever. The ability to distinguish between viral and bacterial infection or determine the severity of disease would be a transformational step in patient management.

- **Infection detection in asymptomatic patients** to enable disease elimination and eradication (this requires more accurate tests).

- **Antimicrobial resistance** and the importance of diagnostic strategies to avoid incorrect and over-treatment.

**Core themes identified in the delivery of diagnostic solutions:**

- **Electronic health (eHealth) and improved information management.**

- **Post market surveillance and quality control** to ensure better tests and correct use.

- **Intervention design around specific market characteristics** and healthcare system landscapes to maximize patient access, e.g. public/ private sector.

**FIND’s vision for connected diagnostics**

FIND believes in the transformative power of IT health care to overcome barriers that prevent diagnostic impact such as loss to follow-up and stock-outs. All diagnostics, digital or non-digital, should have the ability to communicate through a standardized digital interface and so make use of the omnipresent mobile technology in low- and middle-income countries.

FIND and partners are working to develop a globally implementable aggregator that supports the secure exchange of patient and system data is based on standard protocols and is designed to integrate with multiple third party eHealth applications to maximize the value of diagnostic results.
Comprehensive strategies for each of FIND’s focus disease areas will be available as separate documents. In the following pages, we provide a brief overview of our emerging disease strategies, including our understanding of the gaps and needs and our priority objectives in each area:

- Tuberculosis and Acute Febrile Respiratory Infections
- Malaria and Acute Febrile Syndrome
- Hepatitis C
- Neglected Tropical Diseases
  - Human African Trypanosomiasis
  - Chagas disease
  - Buruli ulcer
  - Leishmaniasis

“We believe that strategic emphasis on cross-cutting themes will realize synergies across disease areas and regions.”
Tuberculosis is the second most common cause of death from an infectious disease in adults in low-income countries. In 2012, there were an estimated 8.6 million tuberculosis cases and 1.3 million deaths, the majority of which were likely preventable with existing treatments, according to the 2013 WHO Global TB report. Although progress has been made towards tuberculosis control, major gaps remain.

After almost 100 years without new tuberculosis diagnostics, the development of innovative molecular diagnostic tests for tuberculosis in the past decade, with FIND’s dedicated involvement, has revolutionized tuberculosis care. Despite this, we still fail to reach an estimated three million people, in part due to lack of access to adequate diagnostics. Existing tests lack the operational characteristics that would allow for implementation in lower levels of the health systems. They are also not sensitive enough, particularly for certain sub-populations of tuberculosis patients (HIV+, children, etc.) and for patients in early disease stages with low bacterial load and few or no symptoms. To reach more patients we need novel tests that are more rugged, easier to use and that can penetrate deeper into the health care system than current tools. Better diagnosis of the disease could also be achieved through improved integration of tuberculosis care into the broader public health system. A syndrome-based approach to the diagnosis of tuberculosis and lower respiratory tract infections could facilitate this.

Beyond this, the threat of drug resistance continues to grow and, if left unaddressed, could not only undermine the progress we have made, but could also spread the burden of tuberculosis to countries where it does not currently have a significant impact. Novel tests are needed to enable rapid resistance testing and to track markers for treatment monitoring that can be used to detect inadequate treatment early. This is critical to prevent the development and spread of resistance and to protect new treatment regimens entering the market.

Large scale implementation of new diagnostic tools has highlighted some major shortcomings in the health systems, specifically here in low- and middle-income countries, which limit the impact of improved tests and demonstrate the need for more comprehensive diagnostic solutions. Supply chain management, quality assurance of laboratories, particularly at peripheral sites, training of healthcare workers and referral of specimens for further testing (e.g. second line drug susceptibility testing) have to be improved to increase the impact of diagnostic tools. Attention must also be focused on strengthening the rapid linkage of diagnosis to treatment and further care.

To diagnose more patients with tuberculosis and start the correct treatment, we need novel tests that are more sensitive, enable the detection of drug resistance, are more rugged, easier to use and can penetrate deeper into the health care system than current tools. The FIND tuberculosis programme aims to achieve this by focusing development primarily on point-of-care tools for case detection (active, passive and triage), rapid drug-susceptibility testing and by facilitating integrated diagnostic solutions, e.g. through a syndromic approach and eHealth solutions.
The FIND tuberculosis programme envisions access to fit-for-purpose diagnostics and linkage to treatment for all people afflicted by tuberculosis and aims to support the WHO in their goal of a world free of tuberculosis. The FIND tuberculosis five-year strategy supports the 2020 Global targets of reducing tuberculosis incidence by 20% and mortality by 35%.

FIND’s tuberculosis strategy will be based upon four core objectives:

1. Cut transmission through early detection
2. Prevent antimicrobial resistance and decrease morbidity and mortality by enabling appropriate treatment through early drug susceptibility testing (DST)
3. Enable impact by translating needs of countries into comprehensive solutions for tuberculosis
4. Demonstrate the role of diagnostics in controlling the tuberculosis epidemic and support guidance for use

Because so many of the tests that are needed for tuberculosis today depend on biomarker discovery work, we plan to take a two-tiered approach to prioritizing development and policy work for new tools. In the near term, we will concentrate on supporting tools that do not require new biomarkers and have the potential to bridge gaps. To support mid- and longer-term gains, FIND will stay involved in (but not conduct) biomarker discovery for potentially transformational tools. If and when biomarkers are discovered, our support for the development of new, transformational tools would become a top priority.

In the near term, our top priority is an improved test for passive case detection that would replace smear-microscopy (and potentially reach even lower levels of the healthcare system) and have increased sensitivity to support the diagnosis of patients with paucibacillary disease (e.g. HIV patients, children). Given the state of current technologies, we believe that molecular solutions offer the best chance to have an impact in the near term and will pursue them most aggressively.

Our second highest priority for the near term will be a rule-out (or triage) test with low specificity but high sensitivity. This test could be used together with a more expensive test with high accuracy to decrease cost and possibly increase the number of patients tested.

We also believe that better molecular solutions for centralized and decentralized drug susceptibility testing are feasible in the relatively near term and will pursue these (likely in combination with a test for passive case detection for decentralized solutions).

To enable longer-term gains, we plan to play a coordinating role to support biomarker discovery for new tools for: a syndromic approach to diagnosis, active case detection at lower levels of the healthcare system through a sputum-free rapid test, treatment monitoring and predicting progression from latent to active disease. If and when suitable biomarkers are discovered for any of these needs, development of an appropriate test would become a top priority.

Beyond the priorities for new tools listed above, FIND will also support its objectives for tuberculosis through a set of enabling activities that are not tied to the development of any specific product. Our publicly available specimen and strain bank will continue to expand and be improved upon to best support the development of new tools.

In addition to supporting clinical trials and policy development for the new tools described above, FIND will support evidence generation and policy development to optimize the use of existing tools.
To do this, FIND will work with WHO to jointly define key research questions. We will conduct operational research and demonstrations and help analyse and compile evidence.

For implementation activities, we will continue our work in support of countries to maximize the impact of current tools and to promote integration with other tests. Key activities are listed on the following page.

Across all of our activities in tuberculosis, FIND will maintain and strengthen relationships with longstanding partners and establish new affiliations. WHO remains an important partner for us across all of our activities, particularly through our position as a WHO Collaborating Centre. Similarly, maintaining our existing relationships with industry, national tuberculosis programmes, national laboratories, academics and in-country researchers will be paramount.

FIND will also build new partnerships. Since we intend to further promote integration with co-morbid diseases, linkage to care and syndromic approaches, we shall expand our country partnerships and seek to identify partners with scope beyond tuberculosis (e.g., partnerships with HIV implementers and/or disease agnostic organizations like ASLM and MSF). Stronger ties to the private sector will also be established. To improve efficiency and reduce redundancy, we will aim to partner more closely with other PDPs (e.g., TB Alliance, Aeras) to leverage the same trial infrastructure, specimen collections, approaches to impact measurement, etc. We will also seek to develop new coalitions for clinical trials, e.g. with the Clinical Diagnostics Research Consortium, members of the European & Developing Countries Clinical Trials Partnership, and others.

To generate evidence that makes the case for prioritization of tuberculosis diagnosis, we will expand our work with academics, in-country researchers and modellers and build partnerships with advocacy organizations (e.g., TAG) to ensure our messages reach a wider audience.

“Every year, an estimated three million people suffering from tuberculosis fail to obtain quality care, in part due to lack of access to adequate diagnostics.”
# FIND 2015 – 2020 Tuberculosis Priorities and Interventions

## Development / Policy priorities:

1. Passive detection  
   (likely molecular)  
2. Rule-out test  
3. Drug susceptibility testing  
4. Syndromic approach  
5. Active case finding with sputum-free rapid test  
6. Treatment monitoring  
7. Latent to active progression

## Enabling interventions:

- Expand on the publicly available specimen and strain bank  
- Evaluate implementation of highly sensitive tests for screening  
- Conduct operational research to optimize the use of existing tools  
- Support country development/execution of national guidelines and integration of novel tests into country disease control programmes in accordance with global policy recommendations and guidance on use  
- Develop/implement comprehensive package of tools for: QA, training, M&E, eHealth, maintenance, etc.  
- Strengthen impact assessment, modelling, and cost-effectiveness measurement and communicate impact  
- Facilitate integration of tuberculosis care with co-morbid diseases  
- Provide structured mentoring for quality management systems and laboratory strengthening  

*Note: for items in italics FIND will coordinate biomarker discovery and take on a more active role if and when suitable biomarkers are discovered*
Effective diagnostic solutions are needed to accelerate malaria elimination and to guide management of non-malaria febrile patients. To achieve this, people at risk must have access to basic diagnosis that can distinguish malaria from other acute fevers. FIND’s malaria programme is working on the development of simple, accurate diagnostic tools to: support global elimination of malaria and control of antimalarial drug resistance; improve management of people with acute fevers; and maximize the impact of existing good quality rapid tests.

Malaria is still one of the four most burdensome infectious diseases and the fifth highest cause of child mortality in the world. In 2012, approximately 207 million people were infected with malaria and 627,000 died of the disease – more than three quarters of these deaths were among children. In spite of these figures, remarkable progress has been made in malaria control. 52 out of 103 endemic countries are on track to meet the World Health Assembly target of reducing incidence by 75% by 2015, and in 2013, 19 countries were already in pre-elimination and elimination phases, as stated in the WHO’s 2013 World Malaria report. While efforts to control the disease in high endemic areas should be continued, new cost-effective strategies to accelerate malaria elimination in low endemic countries and to prevent its reintroduction in eliminating countries should be implemented.

Population screening for the detection and treatment of symptomatic and asymptomatic infections is needed to accelerate malaria elimination in areas of low, unstable transmission. Tools at different levels of the health system should be considered – a rapid diagnostic test to detect submicroscopic parasite densities in blood is essential in remote areas, as are surveillance methods at a centralized level. The decrease in the incidence of malaria due to Plasmodium falciparum has highlighted the importance of detecting and treating malaria due to other Plasmodium species. Accordingly, tools to detect and treat reservoirs of P. vivax parasites are urgently needed to eliminate this second most severe type of malaria. To enable radical cure of P. vivax, a point-of-care test is needed for G6PD deficiency that could guide use of drugs able to eliminate hypnozoites, the dormant form of P. vivax parasites. Successes in malaria elimination also greatly depend on the efficacy of antimalarial drugs. Adequate surveillance tools to detect and rapidly contain the recent emergence of artesinin resistance and any new resistance to other antimalarial drugs are also needed.

In addition to the development of new tests, efforts to maximize the impact of existing tools are also needed. While huge improvements (which can largely be attributed to the WHO-FIND malaria RDT evaluation programme) have been made to the quality of rapid tests detecting P. falciparum in the public sector, improvements to rapid tests detecting other species (i.e. P. vivax) and quality assurance in the private sector are still needed. In some cases, even when rapid tests work correctly, inability to identify other causes of fever can lead health workers to administer antimalarials after a negative malaria result. Quality control tools (e.g., positive control wells) that could be used by health workers in remote areas would increase the confidence in negative results and help prevent mistreatment. To enable better management of country control programmes and capture the wealth of data being produced by malaria tests, Ministries of Health also need support to develop better country surveillance programmes and leverage eHealth technologies.
As malaria incidence declines, alternative causes of acute fever also need to be addressed. Differential diagnoses of malaria include pneumonia (1.4 million deaths per year in under 5 years of age), typhoid fever (21.6 million cases per year), dengue (100 million infections per year), and bacterial meningitis (170,000 deaths per year). While causes of acute fever are multiple and vary widely with geography, living conditions and occupational exposure, tools to guide use of antibiotics, supportive treatment, and referral decisions should be incorporated into improved algorithms for fever management. A test that triages patients with fever and assesses severity to guide referral decisions would have tremendous impact. Similarly, a test that identifies the pathogen or type of pathogen (e.g., differentiates between a virus, bacterium, and parasite) causing a fever could help guide treatment decisions and minimize the development of anti-microbial resistance. Although there are some tests on the market for these purposes, their quality and effectiveness are unknown and must be assessed.

Through our malaria and acute febrile syndrome programme, FIND supports the long-term goal of the Global Malaria Action Plan (GMAP) and WHO to eradicate malaria by reducing the global incidence of malaria to zero. The vision of our programme is a world where everyone with acute fever has access to simple, accurate tests to enable appropriate care. Our five-year goal is to support global malaria elimination and fever management efforts by demonstrating the usefulness and impact of new diagnostic solutions in areas of need.

FIND’s malaria and acute febrile syndrome strategy will be based upon four core objectives:

1. Enable global malaria elimination and control of antimalarial drug resistance through development of new tools
2. Improve management of acute febrile patients
3. Maximize impact of existing good quality rapid tests (especially for P. vivax)
4. Guide global prioritization of diagnostic solutions for malaria elimination and fever management

Our top priorities for the development of new tools for malaria are highly sensitive rapid diagnostic tests for elimination, serology tests for vivax malaria to enable surveillance and detection of reservoirs and molecular tests for surveillance of antimalarial drug resistance. We will also support policy development to guide use of recently developed tools, including molecular diagnostic tools for surveillance and positive control wells for country quality assurance of rapid tests. These developments and policy priorities are all relatively low risk and will allow us to support a set of quick wins that will be critical to supporting elimination and sustaining quality of diagnostics in countries. For all our top priorities, emphasis is equally given to falciparum malaria and vivax malaria.

For longer-term impact, FIND will play a supporting and coordinating role to facilitate the development of point-of-care tests for fever triage and determining the cause of fever. If these tests were developed, they would be hugely beneficial, but because they require biomarker discovery, FIND will not yet be able to take on a full role in their development. If and when suitable biomarkers are discovered, these tests would become a top priority for us.

Although tests for G6PD deficiency are needed for radical cure of vivax malaria, we will not prioritize these tests because we believe PATH is already adequately addressing this need. However, we will support P. vivax malaria diagnosis through other projects. In addition to the above priorities, we will promote enabling activities to support our objectives for malaria and acute febrile syndrome as listed on the following page.
Across all of these activities, collaborating with partners will be indispensable. We will strive to maintain and strengthen the longstanding relationships we have established with partners in development and quality assurance. Across all the work that we do – from development through to implementation – the WHO Global Malaria Programme has been and will remain one of our most important partners. We will continue to work closely with our historical partners, for example, the US CDC and the Hospital for Tropical Diseases in London on quality assurance, and the Swiss Tropical and Public Health Institute for our work on fever. We will foster new types of collaborations to support other elements of our work. For example, to develop a highly sensitive rapid test for malaria, we will work in close partnership with PATH, the Bill and Melinda Gates Foundation, and a range of manufacturers. Given the inherently multi-disease nature of work on fever, our efforts in this domain will require new cross-disease partnerships, which will involve FIND’s other disease teams.

To support implementation activities and rollout of new tools and the handover of quality assurance to countries, good relations with national malaria control programmes will be critical. We will also strengthen our affiliations with implementing agencies in countries doing work on malaria diagnostics, for example, PSI, Malaria Consortium, and CHAI. Lastly, as we continue to encourage prioritization of diagnostics for malaria and investment in quality assured products, we will continue to maintain strong partnerships with global procurement agencies (e.g., the Global Fund) and country policy makers.

FIND 2015 – 2020 Malaria and AFS Priorities and Interventions

<table>
<thead>
<tr>
<th>Development / Policy priorities:</th>
<th>Enabling interventions:</th>
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<tr>
<td>1. Highly sensitive rapid tests</td>
<td>• Establish publicly available specimen and strain banks to support development of new tests</td>
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<tr>
<td>2. <em>Vivax</em> serology tests</td>
<td>• Conduct operational research, demonstrations and evaluations to determine if and how the use of existing tools can be improved and support accompanying policy guidance through work with the Malaria Policy Advisory Committee</td>
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<tr>
<td>3. Surveillance of antimalarial resistance</td>
<td>• Support country development and execution of national guidelines and plans for implementation of new and existing tools based on global policy</td>
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<tr>
<td>4. Point-of-care tests for fever</td>
<td>• Support improved global and local quality assurance of rapid tests (e.g., for <em>P. vivax</em> and through transition of existing lot testing to country programmes)</td>
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<tr>
<td>5. Positive control wells</td>
<td>• Measure and communicate the impact of improved diagnostics based on randomized control and cost-effectiveness studies</td>
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<tr>
<td>6. Molecular surveillance tools</td>
<td>• Work with procurement agencies and other stakeholders to guide decision-making and shape markets for malaria diagnostics</td>
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*Note: tests in italics have completed development; focus will be on policy development*
Over 420 million people globally are chronically infected with hepatitis B and C, according to the WHO. Given the availability of a vaccine and effective oral therapy for hepatitis B, the major emphasis on improving diagnostics and treatment has been on hepatitis C, although there are synergies between diagnostic needs for both diseases. Hepatitis C is transmitted through unsafe injection practices, transfusions and more rarely sexual intercourse, disproportionately affecting vulnerable populations (often those co-infected with HIV or tuberculosis). If left untreated it can progress to liver cirrhosis and cancer, causing significant morbidity and mortality. Today, an estimated 350,000 people die of hepatitis C per year, although actual mortality numbers are likely much higher.

The changing treatment landscape for the hepatitis C virus offers a unique opportunity to tackle the epidemic in poorer countries that have thus far not prioritized the fight against this disease. Diagnosis is the critical gap that needs to be addressed to maximize the impact. By optimizing existing diagnostic tools and developing improved tests that are adapted for use in low-resource settings, FIND aims to close this gap.

In order to capitalize on the promise offered by new treatments, the diagnostic landscape for hepatitis C has to be dramatically improved. Molecular tests adapted for use in low-resource settings are needed to confirm active infection. A core-antigen test at low-cost could conceivably be used as a one-step solution for diagnosis (combining detection and confirmation). As we wait for development of these novel tests at appropriate price-points, improvements to serological tests to increase quality and specificity in sub-Saharan Africa are also needed, as are better tools for staging of fibrosis that can inform treatment decisions in programmatic settings.

Beyond novel tests, there is an acute need to improve the approaches and programmes through which hepatitis C services are delivered. Here, taking advantage of the delivery structures already in place for co-morbid diseases like HIV and tuberculosis will be hugely beneficial. Moreover, increasing prevention and advocacy efforts would limit the spread of infection and increase prioritization of hepatitis C care.
As already observed in high income countries, viral hepatitis is likely to overtake HIV as a leading cause of death. With new drug regimens that could make the cure of hepatitis C in resource-limited settings possible, the world finds itself at an important juncture in the management of this disease. FIND aims to help the fight against hepatitis C by supporting development, evaluation and delivery of appropriate and affordable diagnostic solutions for resource-limited settings in order to cut transmission, decrease morbidity and mortality and reduce the socio-economic impact of viral hepatitis.

FIND's hepatitis C strategy will be based upon 4 core objectives:

1. Enable affordable and fit-for-purpose diagnosis
2. Enable access to diagnosis
3. Support the prevention of infection
4. Demonstrate the need and benefit of interventions to support scale-up

In the areas of development and policy, our top two priorities are the development of a core antigen test and a molecular test, both for use in decentralized settings.

FIND will support development and creation of policy guidance for improved serology tests, which we believe will help bridge the gap until we have better decentralized tests and improved staging tests. In addition to the above priorities, support for hepatitis C management will include enabling activities on the next page.

In view of FIND’s new hepatitis C programme, we will need to forge new partnerships with a broad range of stakeholders. As noted, our strategy is predicated on the promise of access to better treatments. To ensure the availability of these treatments at affordable prices, we will rely on close collaboration with organizations focused on shaping market dynamics (e.g., Coalition Internationale Sida and CHAI) and with pharmaceutical companies developing new treatments. These partners can also play a critical role in helping to negotiate lower prices for diagnostics.

Today, hepatitis C is relatively low on the priority list of global health funders; given this fact, partnering to support advocacy efforts that raise the profile and prioritization of the disease will be especially important. We will work together with other organizations that have begun to pioneer conversations about hepatitis C within the global health community, including MSF, CHAI, TAG and more recently, through discussions on their own funding priorities, UNITAID. Across all of the work that we do, the Global Hepatitis Programme at WHO will be a crucial partner, leading policy development, advocacy and surveillance efforts.
## Development / Policy priorities:

1. Decentralized antigen test
2. Decentralized molecular test
3. *Improved serological test*
4. *Improved staging tests*

## Enabling interventions:

- Establish a publicly available specimen bank to support development of new tests
- Conduct demonstration trials to determine optimal diagnostic and care algorithms and support guidance on use (including on blood screening for prevention of infection)
- Support country implementation of new tools in public and private sector
- Advocate for increased prioritization of hepatitis C diagnosis and blood screening using impact and cost-effectiveness data & modelling

*Note: for items in italics we will only play a supporting and coordinating role*

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“Over 420 million people globally are chronically infected with hepatitis B and C. An estimated 350,000 people die of hepatitis C per year, although actual mortality numbers are likely much higher.”
Neglected tropical diseases (NTDs) comprise a wide array of infections caused by diverse pathogens and distributed all over the globe. What they have in common is that over the years, they have been systematically neglected by public health interventions as well as drugs/diagnostics developers, and cause unacceptable human suffering and death in the regions where they are endemic.

Recognizing that nearly all NTDs have various unfilled diagnostic needs, FIND will support both the WHO roadmap and the London Declaration on Neglected Tropical Diseases of 2012. Our main focus will be on a number of core diseases with the greatest unmet needs and on which there is limited attention by other stakeholders, while at the same time providing strategic support for the other non-core NTDs. FIND would also seek to work with current manufacturing partners to expand disease menus on existing platforms so that groups of related NTDs can be dealt with simultaneously.

Core diseases: objectives and activities

Based on a detailed analysis, human African trypanosomiasis, Chagas disease, Buruli ulcer, leishmaniasis, soil-transmitted helminths and dengue have been identified as core NTDs. Setting of objectives and activities for soil-transmitted helminths and dengue is ongoing. Priorities for the first four diseases listed are described in the following section.

Human African Trypanosomiasis

Human African trypanosomiasis is caused by parasites of the genus *Trypanosoma*. This tsetse-transmitted disease has been targeted for elimination by 2020 in the WHO roadmap on NTDs. In 2012, there were only 7,216 reported cases. While a FIND-developed rapid diagnostic test has transformed screening for human African trypanosomiasis, there are still remaining diagnostic needs.
Over the coming five years, FIND will continue its work in support of the WHO roadmap on the elimination of human African trypanosomiasis, with a focus on implementation research on emerging tools and development of a next generation test. Together with safer, easier to administer drugs, this work will allow the move to a paradigm-shifting “test and treat” approach that will accelerate and sustain elimination.

FIND’s strategy for human African trypanosomiasis will focus on two objectives:

1. Increase detection of human African trypanosomiasis through improved case finding
2. Facilitate faster, less-burdensome confirmation of human African trypanosomiasis through improved tools

To support these objectives we will prioritize development and policy work for three new technologies:

- A second-generation rapid test based on recombinant antigens that can be manufactured in large volumes (manufacture of the 1st generation rapid test is limited because antigens are produced from human infective parasites obtained from infected animals).
- A combined test for both malaria and human African trypanosomiasis to be used in endemic areas with the aim of ensuring continued surveillance and case finding as the disease nears elimination, and to sustain elimination.
- A low-cost tool for reliable confirmation of disease at lower levels of the healthcare system.

In addition, we will support a set of enabling interventions, some of which are mentioned in the overview on p. 56.

Chagas disease

Chagas disease, caused by the protozoan parasite Trypanosoma cruzi, affects more than seven million people worldwide, as reported by WHO. The disease can lead to a range of pathologies, including cardiac damage and death if not promptly treated. Diagnosis of Chagas disease in newborns is mainly based on parasitology, which is insensitive. Serological diagnosis is unreliable until after ten months of life, yet many of the tests in development are variations on the serology tests. In remote endemic regions, there is limited access to information on congenital Chagas disease, diagnostics and treatment. As a result, many women of childbearing age living in these regions, and children born there, are rarely tested for Chagas disease. While treatment of chronic Chagas disease is quite aggressive, confirmation of cure in treated patients is difficult.

FIND’s strategy will be to contribute to improved diagnosis of congenital Chagas disease, reduction of incidence of Chagas disease in women of childbearing age, and improved assessment of the efficacy of treatment.

We will focus on two objectives and a number of related activities:

1. Reduce burden of congenital Chagas disease through improved diagnostic solutions
2. Improve diagnosis of Chagas disease and monitoring of treatment efficacy for chronic patients
To support these objectives we will concentrate on two main priorities in development. To realize short-term gains in the field and bridge gaps, we will work on a molecular test for congenital Chagas disease. A longer-term, higher-risk priority will be on developing a field applicable point-of-care test for Chagas disease and/or congenital Chagas disease that could also be used as a test of cure. This will start with coordinating efforts to validate biomarkers. We shall also support a number of enabling interventions for Chagas disease, including those mentioned in the overview on p. 56.

Buruli ulcer

Buruli ulcer is a debilitating and stigmatizing disease caused by *Mycobacterium ulcerans*. 5,000 to 6,000 cases are reported annually in 15 of the 33 endemic countries, according to WHO. It is among the most neglected of all diseases on WHO’s list of 17 NTDs. Current diagnostic tools are labour-intensive and insufficiently sensitive. Disease confirmation is often delayed because it requires referral of patients or specimens to tertiary level laboratories, resulting in potentially avoidable progression of the disease to a more advanced, stigmatizing and debilitating stage. Although its overall burden is comparatively low, we have prioritized the disease because of the potentially transformational impact that improved diagnostics could have.

**FIND’s strategy on diagnostics for Buruli ulcer will be to contribute to accelerated control of the disease through early and near-patient detection of cases.**

**Our strategy will center on two objectives and a number of related activities:**

1. **Support the use of improved case finding strategies**
2. **Establish diagnostic solutions for early detection of Buruli ulcer close to where people live and faster, less-burdensome confirmation of disease through improved tools**

We shall take a two-tiered approach to support diagnostics development for Buruli ulcer. To realize gains in the short term and bridge immediate gaps, we will support trialing of a thin layer chromatography test for detecting mycolactones and development of a molecular test based on LAMP. To support the longer-term goal of having a test for screening symptomatic patients with ulcer at the primary or community level, we will play a coordinating role as partners to pursue validation of biomarkers. If and when suitable biomarkers are found, development and assessment of a screening test will become our top priority. We will also support a number of enabling interventions for Buruli ulcer, among which those listed in the overview provided on p. 56.

**Leishmaniasis**

Leishmaniasis comprises a group of infections with widespread clinical and epidemiological diversity across Africa, Asia, Europe, and the Americas. The global burden of these infections combined, including cutaneous and visceral leishmaniasis, is estimated to be in the order of millions of disability-adjusted life years. There are approximately 0.2 to 0.4 million visceral leishmaniasis cases and 0.7 to 1.2 million cutaneous leishmaniasis cases each year, as reported by WHO Leishmaniasis Control Team. Yet, both visceral and cutaneous leishmaniasis present distinctly different clinical manifestations and are managed differently. Confirmatory diagnosis of visceral leishmaniasis is important, as treatment is lengthy, toxic and difficult to
implement in resource-limited settings. A proportion of treated visceral leishmaniasis patients develop post-kala-azar dermal leishmaniasis, which has important implications on control of the disease. Diagnosis of visceral leishmaniasis in HIV co-infected patients is challenging, as it could compromise performance of serological tests. As therapy is often lengthy and relapses occur, a test to monitor the efficacy of treatment is crucially important. The proportion of asymptomatic infections in visceral leishmaniasis endemic regions is relatively high and their contribution to epidemiology of the disease not well understood. For cutaneous leishmaniasis, a point-of-care diagnostic that can differentiate between species is important.

Our strategy on leishmaniasis will be to contribute to the elimination of visceral leishmaniasis by developing diagnostic solutions for accurate detection of cases, monitoring therapy and sustaining elimination.

To achieve this, we have defined the following objectives:

1. Reduce burden of leishmaniasis through improved diagnostic solutions
2. Improve detection and understanding of asymptomatic infections and post-kala-azar dermal leishmaniasis cases in regions targeted for elimination

To support these objectives, FIND will focus on two main priorities for development and assessment of novel tools: a test to monitor the efficacy of treatment in visceral leishmaniasis patients and a sensitive point-of-care test for visceral leishmaniasis in eastern Africa. At a later stage, we will also explore the possibility of developing a species-specific test for cutaneous leishmaniasis. In addition, we will support research and implementation strategies if/when novel diagnostic tools become available. More information is provided in the overview on p. 56.

The role of partnerships in NTDs

Across all of the priorities and diseases defined above, it will be very important that we work closely with partners. We will aim to establish and strengthen collaborations on specific diseases and with the NTD community at large. As the landscape of stakeholders for NTDs is mainly disease-specific, we will tailor our approach to partnership for each disease where we work. We will collaborate closely with the Neglected Tropical Diseases teams at WHO and DNDi to ensure that our priorities are aligned. In order to avoid duplication and maximize synergies across our efforts, we will also coordinate with other organizations working on diagnostics development for NTDs (e.g., PATH).

Due to the neglect around NTDs, communities working in this field tend to be small, making alignment with partners even more critical. For the same reason, funding and a lack of financial incentives are bigger barriers to diagnostic development for NTDs than most other diseases. Close partnerships with potential funders (traditional donors, endemic country governments and venture capital firms) will therefore be critical so that we can help guide funding flows to the most promising products.

To support implementation and advocacy, we will tailor our approach with partners based on the landscape of a given disease. For example, for diseases with strong existing advocacy and implementation organizations (e.g., Chagas disease) we will rely heavily on partners. In areas with less established stakeholders, we will take a more leading role in advocacy or implementation efforts.
FIND 2015 – 2020 Neglected Tropical Disease Priorities and Interventions

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<th>Enabling interventions:</th>
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</thead>
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<td>1. Second generation rapid test</td>
<td>• Provide specimens for product development</td>
</tr>
<tr>
<td>2. A combined rapid test with malaria</td>
<td>• Conduct operational research to support roll-out of 1st generation rapid test and other diagnostics</td>
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<tr>
<td>3. A low-cost tool for confirmation</td>
<td>• Support countries in designing implementation strategies to scale-up new / existing tools</td>
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<tr>
<td></td>
<td>• Demonstrate feasibility and impact of 2nd generation rapid test in a “test and treat” approach, once suitable drugs are available</td>
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<table>
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<tr>
<th>Chagas disease</th>
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<tbody>
<tr>
<td>1. Molecular test for congenital Chagas disease</td>
<td>• Generate evidence to support new testing strategies (e.g. for screening of pregnant women)</td>
</tr>
<tr>
<td>2. Point-of-care test</td>
<td>• Support countries in designing and implementing plans to scale-up new tools and strategies to improve diagnosis and treatment</td>
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<td>• Partner with advocacy organizations to raise awareness on congenital Chagas disease, including demonstrating the role of diagnostics in combatting the disease</td>
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<table>
<thead>
<tr>
<th>Buruli ulcer</th>
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<tbody>
<tr>
<td>1. Thin layer chromotography and LAMP for confirmation</td>
<td>• Support joint priority setting in Buruli research and control community for appropriate tests for detection and management of cases</td>
</tr>
<tr>
<td>2. Point-of-care test for confirmation</td>
<td>• Support countries in designing and implementing strategies to scale-up new tools if/when they are available</td>
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<tr>
<th>Leishmanisiasis</th>
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<tbody>
<tr>
<td>1. Treatment monitoring for visceral leishmaniasis</td>
<td>• Research to identify needs for additional new tests or testing strategies (starting with asymptomatic infections and post-kala-azar dermal leishmaniasis)</td>
</tr>
<tr>
<td>2. Point-of-care test for eastern Africa</td>
<td>• Support countries in designing plans for implementation and scale-up new tools and strategies if/when they are available</td>
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<tr>
<td>3. Test for cutaneous leishmaniasis</td>
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</tbody>
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Priorities for dengue and soil-transmitted helminths still to be determined

Note: for items in italics, we will only play a supporting and coordinating role
“Bridging local understanding, global expertise and international partnerships to advance smart diagnostic solutions, and overcome diseases of poverty.”
Simple, rapid, robust and affordable diagnostic solutions are the first step on a journey to removing, alleviating and treating endemic diseases, thus enabling entire populations to be freed from the shackles of illness and countries to begin reducing their healthcare cost burden. With improved health comes greater hope: individuals become endowed with the strength to support their families, revive businesses, and thrive in school, thus contributing more profoundly to their communities and their countries. Conversely, while diseases lie undetected, are improperly treated or stigmatized, they will continue to erode attempts at advancement within these regions. FIND tackles these issues at the source, with expertise, insight and empathy. In tandem with the efforts from our partners and target countries, FIND will strive to be a real agent for change in a broader tapestry of hope and opportunity.