ANDi
Health Innovation for Development

Strategic and business plan for the African Network for Drugs and Diagnostics Innovation (ANDI)

World Health Organization
TDR For research on diseases of poverty
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This document is presented by the ANDI task force as a mature draft for discussion at the ANDI meeting in Cape Town in October 2009. The information contained herein, including but not limited to the suggested secretariat and governance structure of ANDI, is subject to further consultations and change.

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Health Innovation for Development

Strategic and business plan for the African Network for Drugs and Diagnostics Innovation (ANDI)

"Creating a sustainable platform for R&D innovation in Africa"

TDR/ANDI/BP/09.1

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1. EXECUTIVE SUMMARY

Background

Effective health tools (drugs, vaccines and diagnostics) are fundamental to tackling the diseases that disproportionately affect the African continent. However, drugs, vaccines and diagnostics are lacking for many endemic conditions and, where available, are often ineffective or too expensive. It is of the utmost urgency to scale up research aimed at discovering and developing new and improved tools to address these diseases. Building research capability and leadership in developing countries is increasingly seen as essential to tackling these major health issues. The Global Strategy and Plan of Action (GSPA), outlined at the 61st World Health Assembly (WHA, 2008), provided the framework to drive health product innovation. A key element of this strategy is the formation of R&D networks in disease endemic countries to ensure that existing capabilities are leveraged, identified gaps are more effectively filled and local priorities drive the R&D agenda. As such, WHO/TDR, in conjunction with several African institutions and the African Diaspora, proposes the creation of the African Network for Drugs and Diagnostics Innovation (ANDI). ANDI's chief objective is to promote and support health product R&D led by African institutions for diseases of high prevalence in the Continent. The expected outcome is the discovery, development and delivery of affordable new health tools including those based on traditional medicine, as well as the development of capacity and establishment of centres of research excellence..

African R&D landscape – challenges and opportunities

In driving its chief objective, ANDI faces three major challenges. Firstly, there is a significant research gap; very few products are being researched or in clinical trials for the Continent's most prevalent diseases (e.g. malaria, schistosomiasis). Secondly, there is little collaboration between biomedical R&D centers across Africa. In fact, only 5% of peer-reviewed articles published from 2004-08 involved institutions in more than one African country and most collaborations are undertaken with the US and EU, often with the leadership, funding and ownership for such research outside Africa. This can result in misalignment between research efforts and African needs. Thirdly, there is insufficient investment in African R&D with overall yearly R&D spend of 0.3% of total African GDP, USD 14 billion below the world median. It is estimated that USD 1 to 2.4 billion per year alone would be needed to support health product discovery and development. However, there are promising trends that can be harnessed to address these challenges. One, African institutions already focus their health R&D efforts on local health priorities; a strong correlation exists between disease-focused peer-reviewed articles and disease burden as well as by increased budgeting for traditional medicine research. Two, there is capacity along the health product R&D value chain across the Continent as evidenced by published articles, patents granted, clinical trial competence and pharmaceutical manufacturing capacity. Three, there is commitment to increase investment, as illustrated by the African Union's target of allocating 2% of the Continent's healthcare expenditure for health research and countries such as South Africa or Egypt are progressively increasing their R&D spend to near 1% of total GDP. Given the challenges and trends, ANDI's role will cover

three key dimensions : i) foster the formation of health product R&D networks between African research centers; ii) fund networks for African-led and owned research aligned to local health needs; and iii) advocate for increased investment and priority-driven health product R&D agenda setting.

Proposed mission and business model for ANDI

As such, ANDI's mission is: *"To promote and sustain African-led health product innovation to address African public health needs through efficient use of local knowledge, assembly of research networks, and building of capacity to support economic development"*. To drive this mission, ANDI will establish and coordinate the formation of collaborative projects, of African health product R&D networks. These projects will aim to develop health products by progressing them from discovery, through clinical phases to manufacturing and by building capacity. To ensure the success of these network projects, ANDI's activities will cover the following: i) support for R&D activities through direct funding, project coordination and management, as well as intellectual property management; ii) support of network structure via investments in shared research equipment and facilities, as well as the provision of an IT platform for knowledge management; and iii) brokerage of relationships with key stakeholders and funders through advocacy, and fostering partnerships with various public and private players.

Operating model for ANDI

As an Africa initiative, ANDI's Secretariat will be based in Africa with a decentralized structure of hubs distributed in Africa's regions. A central office will help coordinate hub activities, manage network data infrastructure, and house ANDI's core functional teams in advocacy, IP/technology transfer and R&D management. ANDI's hubs and central office will be hosted by African institutions that have been selected through a transparent tender process along key criteria. A small Secretariat will be led by an Executive Director (ED), who is ultimately responsible for operational performance and strategy implementation. The African Innovation Fund (AIF) embeded within the financial structure of the ANDI host organization will collect, manage and account for ANDI finances i.e. funds applied for operations and network projects. The AIF will start as a collection fund then evolve into an endowment fund capable of guaranteeing ANDI's independence and sustainability. Potential sources of funding include traditional donor-based support and innovative health financing. Decisions relating to the management of funds in the AIF will be made by the ANDI Secretariat under the oversight of the ANDI Board. Overall, ANDI will be governed by the ANDI Board which is responsible for: i) setting scientific priorities, ii) defining and supporting implementation of the advocacy strategy, and iii) overseeing ANDI's financial performance. The Board will have strong African government and technical representation (~70% of members) as well as stakeholders such as relevant international or regional organizations, OECD, non-govrenment agencies including foundations and industry associations.

ANDI implementation plan and financials

Operationalizing the strategy will require WHO/TDR to take immediate steps starting during the 4th quarter of 2009. This will include laying the ground work for the formation of the Board, initiating the call for projects, facilitating a hosting arrangement with an appropriate hosting entity as well as the governance structure of ANDI including the process of identifiying the ED. This call for projects will be launched in 2010. Transition of ANDI to an Africa-based organization will be initiated in 2010 with the suggested establishment of agreements for legal hosting

of the Secretariat and AIF at the AfDB. The process for selection of sub-regional hubs will also be initiated in 2010 in consulation with the AfDB.. In 2011, ANDI will be established as a project with intergovernmental status at the AfDB and the AIF will be operational as a collection fund. Finally, in 2012, ANDI will have fully staffed hubs and a central office physically hosted at selected African institutions, and the AIF will be fully established as an endowment fund at the AfDB.

The envisaged 2010 budget of ANDI will be USD 2.1 million. This budget will be to support the preparatory activities leading up to the formation of ANDI and is expected to rise to USD 19 million in 2012 as ANDI becomes fully operational in Africa. In 2012, 2/3 of the budget will be directly dedicated to research support. The budget is predicted to steadily rise to USD 31 million by 2015 due to increased number of projects supported; running costs will remain stable and research investment reaches around 80% of total budget. By 2015, an endowment ~USD 620 million with an average 5% rate of return will be required to ensure ANDI's full sustainability and independence from donor support, government funding and economic downturns. Overall, ANDI aims to create a sustainable backbone of health product innovation in Africa through the support of R&D networks that leverage technology and human capital present on the Continent. This is a momentous initiative considering the urgent need for new and improved tools to tackle Africa's unique health needs and other challenges such as lack of collaboration, limited invetsment and infrastructure for R&D. ANDI is unique and adds significant value to the current health R&D landscape. In line with the GSPA, ANDI will foster *African leadership* by local researchers, support *African research priorities*, focus on *sustainability* of health product development and form an *African interface* for partners operating in Africa. Furthermore, ANDI will create an independent and sustainable financial model to which everyone, and especially all people of African descent, can contribute.

2. BACKGROUND

NEED FOR DRUGS, DIAGNOSTICS AND VACCINES

It is increasingly recognized that poor health hinders human and economic development[1,2]. Poverty creates favorable conditions for the spread of disease, while preventing access to care for whole populations. This is evident in the developing world in general and Africa in particular, where many diseases remain endemic and uncontrolled. In many instances, this stems from the fact that preventive and control measures, such as diagnostics and treatment (drugs, vaccines, etc.), are simply non-existent or are far too expensive[3]. Control of disease and sustained access to treatment are thus fundamental for poverty alleviation. This is, however, not a trivial enterprise and requires taking specific and immediate actions. Of key relevance, is the urgency to scale up research aimed at developing more effective tools and strategies to address the diseases that disproportionately impact the poor[4]. Building research capability and leadership in developing countries themselves, is increasingly seen as fundamental to this effort and a critical means to support human and economic development.

Recognizing this problem, African Ministers of Health, with support from the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF), developed the eight principles of the Bamako Initiative of 1987 calling for the implementation of strategies designed to increase the availability of essential drugs and other health services for Sub-Saharan Africa[5]. In recent years, global efforts and advocacy to improve public health in developing countries have been scaled up. For example, the Millennium Development Goals (MDGs) have set ambitious aspirations in addressing key health challenges through goals 4, 5 and 6[6]. In addition, new organizations and partnerships have been launched, such as The Global Fund and GAVI, and there has been significant increase in financial resources from private sources, such as the Bill and Melinda Gates Foundation and from innovative financing mechanisms such as UNITAID and the International Finance Facility for Immunization (IFFIm)[7]. Concurrently, this drive has allowed key traditional organizations to continue impacting global public heath. Of note is the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). This program has focused on fostering research and capacity building to develop new products and strategies against infectious diseases. Notably, since its inception in 1975, key focus diseases of TDR (e.g., leprosy) became targeted for global elimination. Meanwhile, TDR has also helped start-up important public-private partnerships (PPPs), which were spun-off as standalone organizations to drive product development. These include MMV (Medicines for Malaria Venture), FIND (Foundation for Innovative New Diagnostics) and DNDi (Drugs for

1. Marmot M. Lancet. Mar 19; 10991–11104 (2005)
2. Commission on intellectual property rights, innovation and public health report (2006)
3. Commission for Macroeconomics and Health – Tough choices: Investing in health for development (2006)
4. 61st World Health Assembly – Global strategy and plan of action on public health, innovation and intellectual property (2008)
5. UNICEF – The State of the World's Children (2008)
6. UN – The Millennium Development Goals Report (2009)
7. Estimated USD 3-4 billion extra funding from these organizations; institutional web pages & reports

Neglected Diseases initiative). The promise held by these organizations is to combine the public sector's financial resources, research centers and focus on health outcomes with the technical expertise and research and development (R&D) capabilities of pharmaceutical and medical product companies. Still, as efforts to improve health outcomes for low income countries have gathered pace, it is clear that tools necessary to achieve this – drugs, vaccines and diagnostics suitable for the specific diseases and patient populations in developing countries – are still insufficient. In addition, there is an increasing realization that the direct involvement and leadership of developing countries in generating new health tools has to increase.

LOCALLY-DRIVEN HEALTH R&D IN DEVELOPING COUNTRIES

There is a strong rationale to strengthen and enhance health R&D conducted in developing countries as a means to address the lack of tools needed to improve local health. Firstly, it will help to ensure that appropriate treatments are available. Historically, international pharmaceutical companies have focused on serving their core markets in the developed world, rather than on addressing diseases of the developing world due to low, or altogether inexistent, profit margins. Moreover, even when appropriate compounds exist, they are not always fully developed and commercialized in a form that benefits the poor. Local R&D efforts can help address these challenges by focusing on developing, or adapting, products to address health conditions prevalent in a country and/or region. Secondly, local R&D can tap into local knowledge and understanding of diseases, as well as encourage south-south collaboration. In particular, the local research community is best

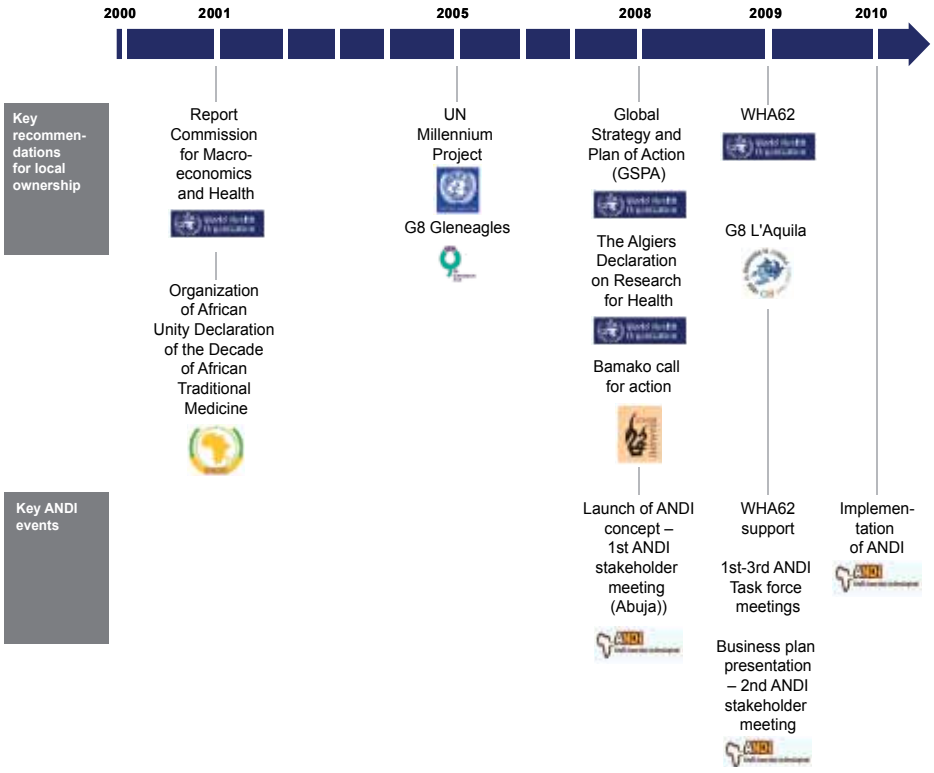


Exhibit 1 – Timeline of initiatives supporting local R&D ownership and leading up to ANDI

positioned to study and learn from traditional medicine approaches. This would enable traditional medicines to be systematically evaluated and developed, and for successful compounds to be produced and marketed at scale[8]. Thirdly, building local R&D capacity ensures that at least a portion of the growing health R&D resources are channeled to local researchers and institutions. This can help to drive economical development by creating skilled jobs and developing local ownership, while mitigating some of the "brain drain" among scientists in developing countries.

In fact, the WHO's Commission on Macroeconomics and Health[9] has argued that investing in indigenous health research and R&D capabilities could play a critical role in improving health outcomes and therefore promoting economic and social development. Subsequent reports, such as the UN Millennium Project[10], the G8 Gleneagles report[11] have echoed these arguments (Exhibit 1). This clear rationale is the backdrop for recent international calls to increase the capacity of poorer countries to participate in and lead their own R&D programs, namely the May 2008 Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA, WHA 61.21). The GSPA provides a guiding framework to support needs-driven health R&D relevant to diseases that disproportionately affect developing countries. Globally, it calls for strengthening the innovative capacity of developing countries, to support local researchers in driving research efforts required to respond to the local public health needs. This is to be achieved by driving R&D prioritization and promotion, by building local capacities and regionally-driven R&D efforts, by supporting countries with technology transfer and IP management as well as by devising mechanisms to ensure the financial sustainability of local R&D efforts (Exhibit 2). These principles have recently been reaffirmed by African Ministries of Health

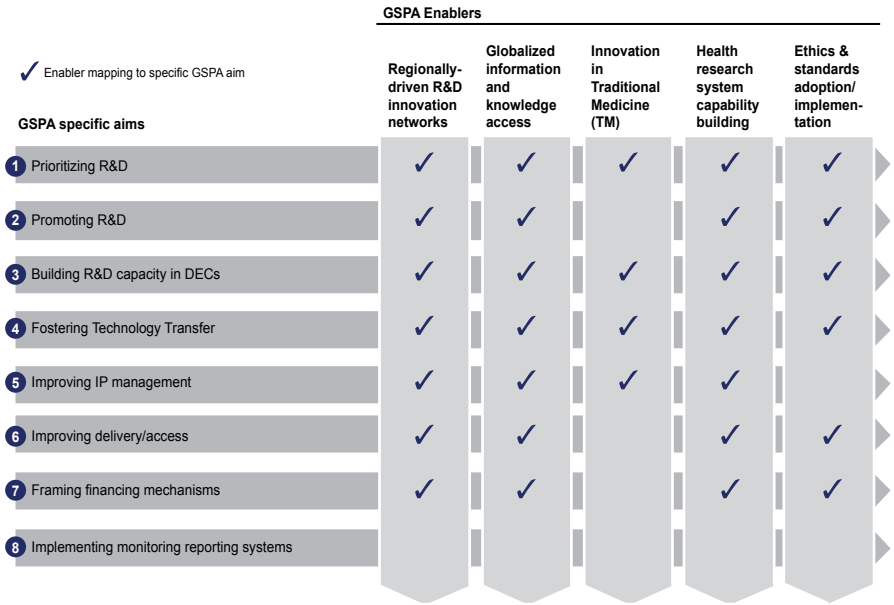


Exhibit 2 – The GSPA matrix

8. Organization of African Unity/African Union – Declaration of Lusaka on Traditional Medicine (2001)
9. Commission for Macroeconomics and Health – Investing in Health for Economic Development (2001)
10. UN millenium project – Investing in Development (2005)
11. The Gleaneagles Communiqué – Climate change, Energy and Sustainable development (2005)
12. Ministerial Conference on Research for Health in the African Region – "Narrowing the knowledge gap to improve Africa's Health" (2008)
13. The Bamako call to action: research for health. Lancet. Nov 29. 1855 (2008)
14. G8 Leaders Declaration – Responsible Leadership for a Sustainable Future (2009)

in the Algiers Declaration[12] and at the Global Ministerial Forum on Research for Health ("Bamako call to action")[13], and have also been at the recent G8 L'Aquila meeting[14].

ANDI, A KEY INITIATIVE TO SUPPORT HEALTH R&D IN AFRICA

In this context, the African Network for Drugs and Diagnostics Innovation (ANDI) was proposed by WHO/TDR, in conjunction with several African institutions as well as Africans in the Diaspora, as a strategic initiative to help drive the GSPA[15]. The central objective of this endeavor is to promote and sustain health product R&D led by African institutions and aimed at controlling and treating diseases of high prevalence in the Continent. The expected result is the discovery, development and delivery of affordable new health tools (drugs, vaccines and diagnostics), including those based on traditional medicine. The initiative was officially started after a meeting with African political and scientific stakeholders in Abuja, Nigeria, in the fall of 2008[16]. The significant momentum and support gathered during that meeting propelled the formal gathering of a Task Force[17] with representatives from African governments and research centers, from scientists of the African Diaspora, from the African Development Bank and from international organizations such as WHO, European Union (EU), the African Union (AU), World Intellectual Property Organization (WIPO). At its second meeting, in early May 2009 in Tunis, Tunisia, the Task Force initiated its effort to design a strategic and business plan for ANDI, with the objective of officially presenting and launching the plan at the 2nd ANDI stakeholders meeting in October 2009 in Cape Town, South Africa. As this effort was carried out (see Appendix Exhibit 1 for details), ANDI obtained ultimate recognition by the World Health Assembly (WHA 62.16, May 22th 2009) as a key initiative aimed at "… supporting and promoting African-led health product innovation for the discovery, development and delivery of drugs and diagnostics… ".

15. Mboya Okeyo T., Ridley R., Nwaka S. Lancet. May 2; 1507-1508 (2009)
16. African Network for Drugs and Diagnostics Innovation – Creating a sustainable platform for R & D innovation in Africa, Abuja meeting (2008)
17. Tom Mboya Okeyo – Chair (Permanent Mission of Kenya, Geneva), Tshinko Ilunga – Vice-Chair (African Development Bank, Tunisia), Alex Ochem – Secretary (International Centre for Genetic Engineering and Biotechnology, South Africa), Sanaa Botros (Theodor Bilharz Research Institute, Egypt), Uford Inyang (National Institute for Pharmaceutical Research & Development, Nigeria), Peter Atadja (Novartis, USA; representing African scientists in the Diaspora), Robert Ridley (WHO/TDR), Solomon Nwaka (WHO/TDR)

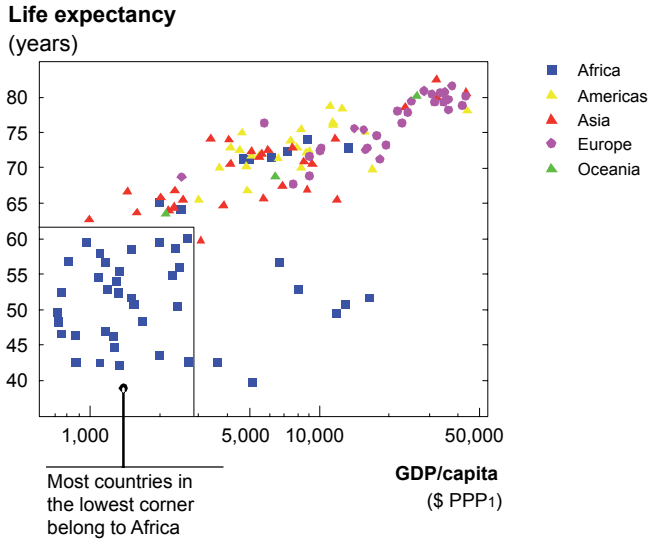
3. THE CONTEXT – AFRICAN R&D LANDSCAPE

AFRICAN UNMET HEALTH RESEARCH NEEDS

The health status of the African population remains, on average, far from that of populations in Europe and North America and also far from that of many other developing regions. Although lack of access to healthcare and serious health system deficiencies, such as low numbers of health workers and poor primary care, are the main reasons of this phenomenon, there are other elements that aggravate the situation. The lack of sufficient R&D aimed at addressing unmet health needs in Africa is one of these elements. It results in the lack of efficient therapies for many illnesses that affect almost exclusively the African continent and are, therefore, out of the scope of most research efforts conducted by the developed world. Consequently, lifting the health status of African populations implies not only addressing access and health system problems, but also driving Africa-focused health product development efforts.

A look at the correlation between GDP per capita and life expectancy illustrates the magnitude of this problem (Exhibit 3). Most African countries lie at the lower left quarter confirming the relationship between lower GDP per capita and lower life expectancy. Notably, the difference between African countries and others is more exacerbated now than it was 20 years ago, as the average African GDP has grown over 200% during that period while only 2 extra years of expected life were added (Appendix Exhibit 2). In addition, Asian countries with comparable GDP per capita tend to have average life expectancies of 5 to 10 years higher.

Furthermore, African countries that exceed the mean GDP per capita of their continent have lower than expected life span[18]. These "outliers" boast GDP per capita figures comparable to many countries in Eastern Europe, South America, and Asia but their life expectancies are 10 to 20 years lower. Undoubtedly, a major contributor to this trend is the HIV/AIDS epidemic. While recent data suggests stabilization of the number of new cases in some affected countries[19], the impact of this disease is very significant and affects Africa in particular (80% of global HIV/AIDS



1 Logarithmic scale; PPP-adjusted current international dollars

Exhibit 3 – Life expectancy versus GDP in different countries (source: UN)

18. Outliers include Botswana, Equatorial Guinea, Gabon, Lesotho, Namibia, South Africa, and Swaziland
19. South African National HIV Prevalence – Incidence, Behaviour and Communication Survey (2008)

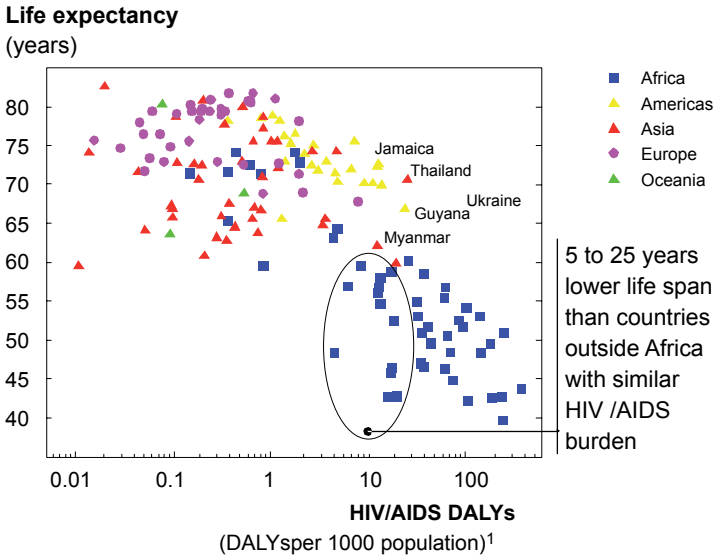


Exhibit 4 – Life expectancy versus HIV/AIDS DALYs in different countries (source: UN, WHO)

DALYs[20]). However, it must be noted that several countries, outside of Africa, bearing similar burden for HIV/AIDS per capita (Exhibit 4) still have 5 to 25 years longer life expectancies. Another element driving the poor health status of people in Africa, is the weakness of the local health systems. The correlation between number of health workers and life expectancy suggests this to be the case for African countries (Exhibit 5). All these facts suggest that solving the health problems in Africa requires to address a complex set of issues, including poverty, the HIV/AIDS epidemic, and access to care in general, without forgetting the lack of tools for specific diseases affecting the African continent.

Indeed, the lack of health products to address many of the most prevalent African diseases[21] is a key element driving the poor health status in the Continent. In some cases, available drugs are not fully effective and present high toxicity levels, as it is the case for Human African Trypanosomiasis (HAT), Lymphatic filariasis, Onchocerciasis and Leishmaniasis. Where drugs are available, they have progressively been rendered less effective due to acquired resistance, for example, for Malaria, Tuberculosis (TB), Schistosomiasis or bacterial desyntery[22,23]. To complicate the resistance problem further, there are few or no alternatives for those illnesses or, even when they exist, they might be significantly more expensive. Existing therapies are also often plagued by low levels of compliance due to the duration and complexity of treatment (e.g., for TB and Leishmaniasis). Similarly, the development of vaccines has been slow to deliver new products that are applicable to the African reality. For example, HIV/AIDS or malarial vaccines have remained elusive despite significant efforts[24]. In addition, where products are available they are not always applicable in the African context. Currently available vaccines against the human papilloma virus (HPV) illustrate this point. They target viral genotypes of low significance in Africa and are, therefore, ineffective against the HPV subtypes that most

20. Disability Adjusted Life Years; comparison based on latest available data from WHO (2004)
21. Commission for Macroeconomics and Health – Investing in Health for Economic Development (2001, 2003)
22. WHO-IFPMA Round Table – Priorities for Research and Development for New Drugs for Poor Country Diseases (2001)
23. Interviews – Theodor Bilharz Research Institute, Cairo, Egypt (2009)
24. IAVI – Spurring Innovation in AIDS Vaccine R&D: What will it take? (2009)

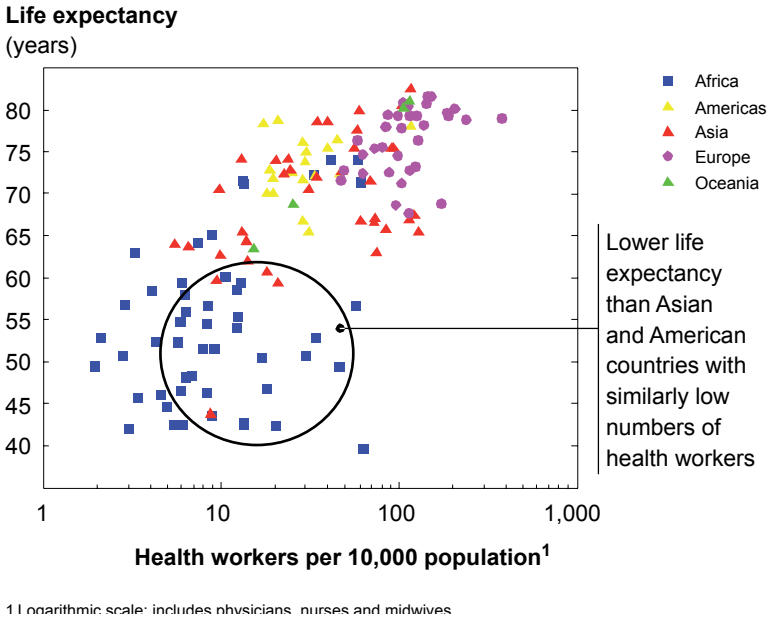


Exhibit 5 – Life expectancy versus health workers per capita (source:UN, WHO)

impact African populations[25]. In all these cases, while new drugs are sorely needed and feasibility is usually high, this is not the focus of the international R&D community[26]. There are, however, emerging efforts arising from partnerships between key organizations and pharmaceutical companies: DNDi and Sanofi-Aventis have made inroads into developing ASAQ (artesunate and amodiaquine) a product for Malaria; Wyeth is supporting late-stage development of a drug against Onchocerciasis (moxidectin) with TDR; J&J/Tibotec is working with the TB alliance to develop TMC207, a TB drug working faster than current therapies; and Novartis has developed Coartem whose dispersible version is developed and distributed with the support of MMV. However, these efforts are still few and far between and require a significant length of time to develop (e.g., Wyeth's effort with moxidectin has taken over 10 years so far with an investment of USD 20 million). In fact, only around 1% of new drugs developed from 1975 to 2004 are for diseases of the poor, which in turn are estimated to account for over one tenth of global disease burden during that period[27]. Additionally, the current efforts are, for the most part, directly dependent on organizations that are external to Africa such as TDR, MMV, MVI, TB Alliance, IAVI and DNDi. That is, they are not based on the principle of creating a truly sustainable discovery and development structure at the African level. In diagnostics, there is also a lack of appropriate tools for the Continent. For more "typical" diseases, diagnostics exist but can be difficult to handle, while requiring significant resources. For example, HAT requires splenic puncture, Leishmaniasis requires lumbar puncture and TB sputum smear microscopy requires multiple visits to a clinic[28]. As such, current designs and technological requirements make them cost prohibitive to test and monitor large groups of patients. In other cases, the tests are not expensive but show room for improvement in terms of specificity (e.g., Onchocerciasis, Lymphatic filariasis)[29]. In addition, there are other diseases increasing in prevalence for which better diagnostic strategies are required. For example, Hepatitis C is a major public health concern in Egypt, where it is responsible for 10%

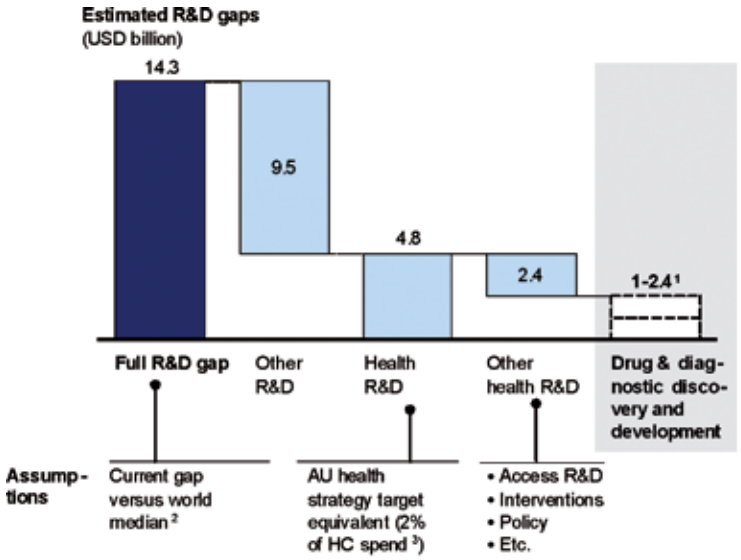
25. Interview – E. Rybicki, University of Cape Town (2009)
26. Commission for Macroeconomics and Health – Investing in Health for Economic Development (2001, 2003)
27. Chirac P., Torreele E. Lancet. May 12; 1560-1561 (2006)
28. TDR Annual Report – Accessible quality-assured diagnostics (2008)
29. WHO – Disease fact sheets

of total mortality[30]. One of the key challenges, is that current diagnosis can only be done in a clinic and is based on an invasive methodology (biopsy). A rapid and non-invasive test would be required to screen large portions of the Egyptian population, predict therapeutic outcomes and avert the spread of disease. As for drugs, the work on diagnostics developed by existing organizations, such as TDR or FIND, has been influential, but has not addressed the need to create a locally-driven platform development framework.

A USD 1-2 BILLION GAP TO FILL

Developing new and/or better health products is thus a fundamental necessity in Africa and one for which the Continent is currently not financially equipped for (Exhibit 6). In fact, the Commission for Macroeconomics and Health[31] estimates that an extra USD 4 billion a year will be needed globally for health R&D on type II and type III diseases[32], with 50% of that to be dedicated to discovery and development of drugs, diagnostics and vaccines. If we consider that Africa has around one half of the world DALYs for these diseases, the extra financial yearly need in Africa is at least USD 1 billion.

On the other hand, the current gap between the African and the world median R&D spending per capita, adds up to a total of roughly USD 14 billion (Exhibit 6). Considering the aspiration, set by



1 Lower estimate (USD 1 billion based on extrapolations from the Commission on Macroeconomics and Health)
2 Total versus world median R&D spend per capita; Assuming as African average an R&D investment of 0.3% of total GDP with USD 11 R&D spend per capita
3 Estimated average for Africa at 5% of total GDP

Exhibit 6 – African drug discovery and development investment gap, PPP (source: Commission for Macroeconomics and Health, McKinsey & Co.)

30. Dr. W. Doss – National Hepatology Center – Ministry of Health of Egypt (2009)
31. Commission for Macroeconomics and Health – Investing in Health for Economic Development (2001)
32. Type I diseases – Incident in both rich and poor countries, includes communicable diseases (e.g., hepatitis B) and non communicable diseases (e.g., diabetes, cardiovascular diseases); Type II diseases – Incident in both rich and poor countries but with a substantial proportion of the cases in the poor countries (>= 90% of cases), includes HIV/AIDS, tuberculosis and also Malaria, know also as *neglected diseases*; Type III diseases – Overwhelmingly or exclusively incident in the developing countries, includes African sleeping sickness (trypanosomiasis), African river blindness (onchocerciasis), know also as *very neglected diseases*

the African Union's Health strategy[33], to spend the equivalent of 1/3 of total African R&D on health research, the added yearly investment should be about USD 5 billion by 2015. Out of this 5 billion, up to USD 2.4 billion would be required for health product discovery and development for Africa. In order to finance this increase in funding, a change in mindset is required from local governments. This change implies recognizing health R&D spending as an investment with very significant returns and a consequent reallocation of government spending to favor drugs and diagnostics discovery and development.

AFRICAN HEALTH R&D CHALLENGES

The need for more health R&D aimed at tackling diseases and conditions that disproportionally affect Africa, is also highlighted by the disease burden in Africa versus the research output of its countries. With only 15% of global population, African disease burden constitutes 25% of global burden measured in DALYs[34]. On the other hand, the most productive African countries in terms of biomedical research publications, such as South Africa, Egypt and Nigeria, generate 15 to 150 times less research articles than leading developed countries[35]. More alarmingly, they produce 1.2 to 8 times less than other developing countries like Argentina, Brazil, India, or Thailand[36]. These figures indicate that while research aimed at tackling diseases and conditions that disproportionally affect Africa is being conducted, there are still major challenges, as highlighted by different African stakeholders (Appendix Exhibit 3), which prevent research efforts to reach the scale and productivity they should. Below, three main African health R&D challenges are described:

- Significant knowledge gap for diseases disproportionally affecting Africa
- Low degree of collaboration among African researchers
- Insufficient investment and ownership of R&D in and for Africa

Significant knowledge gap for diseases disproportionally affecting Africa

Many diseases with high prevalence in Africa, are either almost exclusive to Africa (e.g., Onchocerciasis, Human African Trypanosomiasis, malaria) or disproportionally present in Africa (e.g., Tuberculosis, Lymphatic filariasis, lower respiratory infections; Exhibit 7). WHO estimates indicate that this group of diseases, account for over 50% of all African disease burden, representing 188 million DALYs.

Accurate quantification of the economic impact of disease burden is difficult, but rough estimations indicate that the diseases listed in Exhibit 7 carved as much as 20% out of African GDP[37]. This fraction translates, each year, into a significant USD 200 billion loss for the continent (100 times larger than the estimated funding gap for drug & diagnostic discovery and development). In spite of their decimating impact upon economic development and welfare of African

33. Africa Health Strategy 2007-2015 – Conference of Ministers of Health (2007)
34. Comparison based on latest available data from WHO (2004)
35. Comparison of 2004-2008 Pubmed records affiliated with Egypt, South Africa, France, Germany, U.S.A.
36. Comparison of 2004-2008 Pubmed records affiliated with Egypt, South Africa, Argentina, Brazil, India, and Thailand
37. Estimation based on DALYs per disease in Africa (WHO, 2004) and weighted average of GDP per capita (World Bank, 2005)

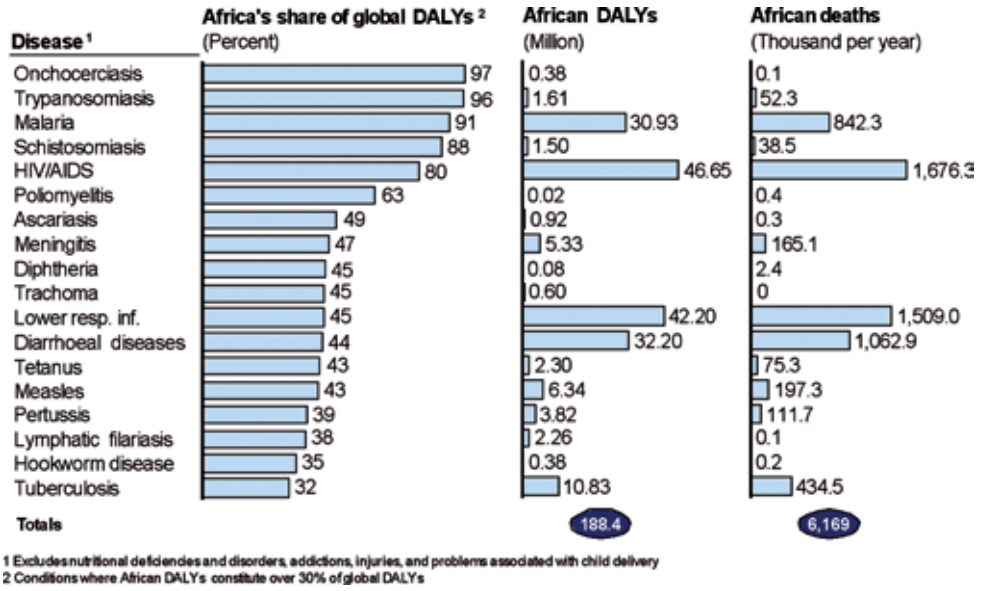


Exhibit 7 – Conditions disproportionately affecting Africa (source: WHO)

populations, there is serious lack of research on these diseases: with the exception of HIV and malaria, the pipeline of products aimed at treating them is virtually empty[38,39] (Exhibit 8). The almost exclusively African nature of these illnesses results in low interest from the international research community (Appendix Exhibit 4), emphasizing the need for Africa-owned drugs, vaccines and diagnostic R&D efforts.

Low degree of collaboration among African researchers

Productivity of R&D efforts, both public and private, is maximized by harnessing the synergies generated by networks of scientists with complementary skills and capabilities[40]. These collaborative networks also benefit from the transfer of expertise from one network member to another, resulting in capability building and increased capacity. In the academic environment, collaboration networks are driven by the availability of funds. This has led to a strong bias by African scientists to collaborate not with other African scientists, but with those in Europe and the United States, where research funding and technology are more readily accessible. In fact, for many public health research centers in Africa, 10% or less of their R&D funding is local, the rest being provided directly or via collaboration, mostly by the US and Europe[41].

The analysis of African research output in 17 selected disease and functional areas shows the low degree of collaboration within Africa, despite the substantial number of centers publishing in collaboration (Exhibit 9)[42]. For example, for Malaria a total of 1,844 research articles had at least one African author in the 5-year period 2004 to 2008. Out of these, over 40% had a lead author from Africa and most (over 90%) were published in collaboration. However, in spite of the importance Malaria has for many African countries, only 13% of these articles involved collaboration between authors in more than one African country. A more exhaustive analysis of all the African biomedical research output

38. Thompson Web of Science – Publication data for the 5-year period 2004-2008
39. Clinicaltrials.gov – Clinical trial data with participating trial centers in Africa (2009)
40. Nwaka S., Hudson A. Nat. Rev. Drug Discov. Nov 01; 941–55 (2006)
41. Interviews – Egypt, Kenya, Nigeria, South Africa, Burkina Faso (2009); ANDI – 3rd Task Force meeting (2009)
42. Thompson Web of Science – Publication data for the 5-year period 2004-2008

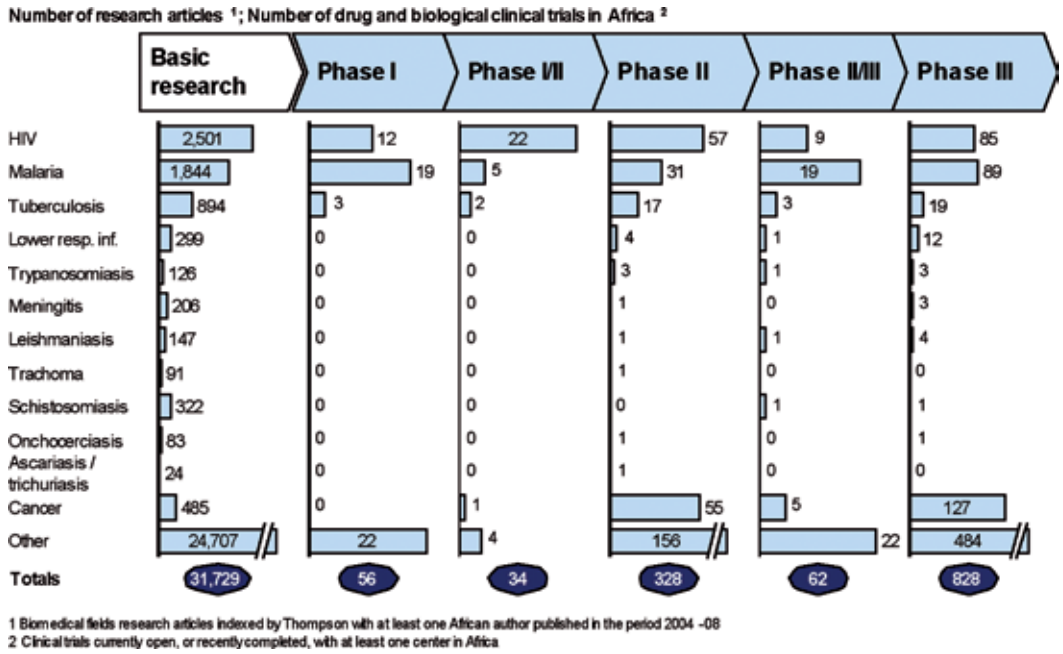


Exhibit 8 – Lack of research and empty product pipelines for most prevalent African diseases (source: McKinsey & Co.)

between 2004 and 2008[43] confirmed the trend. Over 92% of institutions collaborating with the 20 most productive and collaborative institutions in Africa are either from their own country or from outside Africa. In fact, while most publications result from collaboration, only 5% of them involve the collaboration of scientists in more than one African country. Notably, also only 5% of patents granted to African inventors result from collaborations between inventors in more than one African country.

Disease/Function	Main city[1]	Centers in Africa[1]	Research articles	Africa-led articles	Share of African collaboration[2]
AIDS	Johannesburg	1,461	2,501	1,062	7%
Malaria	Nairobi	1,011	1,844	785	13%
Chronic dis.	Cairo	879	1,705	1,060	3%
Tuberculosis	Cape Town[3]	610	894	489	7%
Helminthiasis	Cairo	397	522	228	10%
Lower. resp. inf.	Johannesburg	241	299	177	6%
Diarrheal	Cairo	253	293	137	6%
Bacterial	Cape Town[3]	286	287	158	8%
Kinetoplastids	Khartoum	258	271	132	15%
Other STDs	Johannesburg	138	125	49	10%
Epidemiology	Cape Town[3]	863	967	468	11%
Pharmacology	Cairo	241	299	178	6%
Clinical trials	Cape Town[3]	280	289	120	6%
Animal models	Cape Town[3]	153	235	82	9%
Traditional med.	Nairobi	205	241	169	6%
Proteomics	Cape Town[3]/Cairo	92	128	67	2%
Bioinformatics	Pretoria	81	89	40	9%

1 Main city indicates location of most connected institutions in the specific disease/function publication network; excludes centers publishing alone
2 Fraction of research articles in the disease/functional area affiliated with authors in more than one African country
3 Includes suburbs, e.g., Tygerberg, Rondebosch

Exhibit 9 – Overview of the health African research landscape, measured by peer-reviewed article publication in specific research areas (source: McKinsey & Co.)

43. 31,729 articles involving 20,714 institutions; Thompson Web of Science – Publication data for the 5-year period 2004-2008

The collaboration bias towards the US and Europe are illustrated in Exhibits 10 and 11. In these exhibits the most productive and collaborative institutions publishing in a disease area, HIV/AIDS (Exhibit 10), and a functional area, epidemiology (Exhibit 11), were placed in a world map. The links (based on co-authorship) between these institutions were then traced, and the circles marking the locations were sized according to the number of articles led by an author from that location.

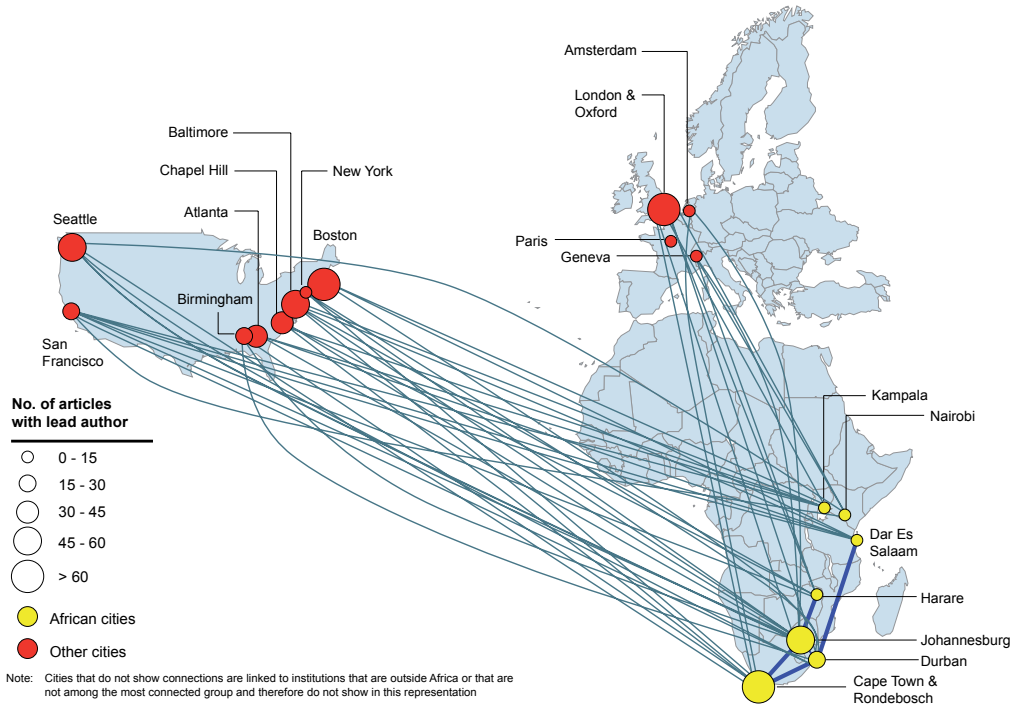


Exhibit 10 – Example of HIV/AIDS collaborative research networks involving African research centers (source: McKinsey & Co.)

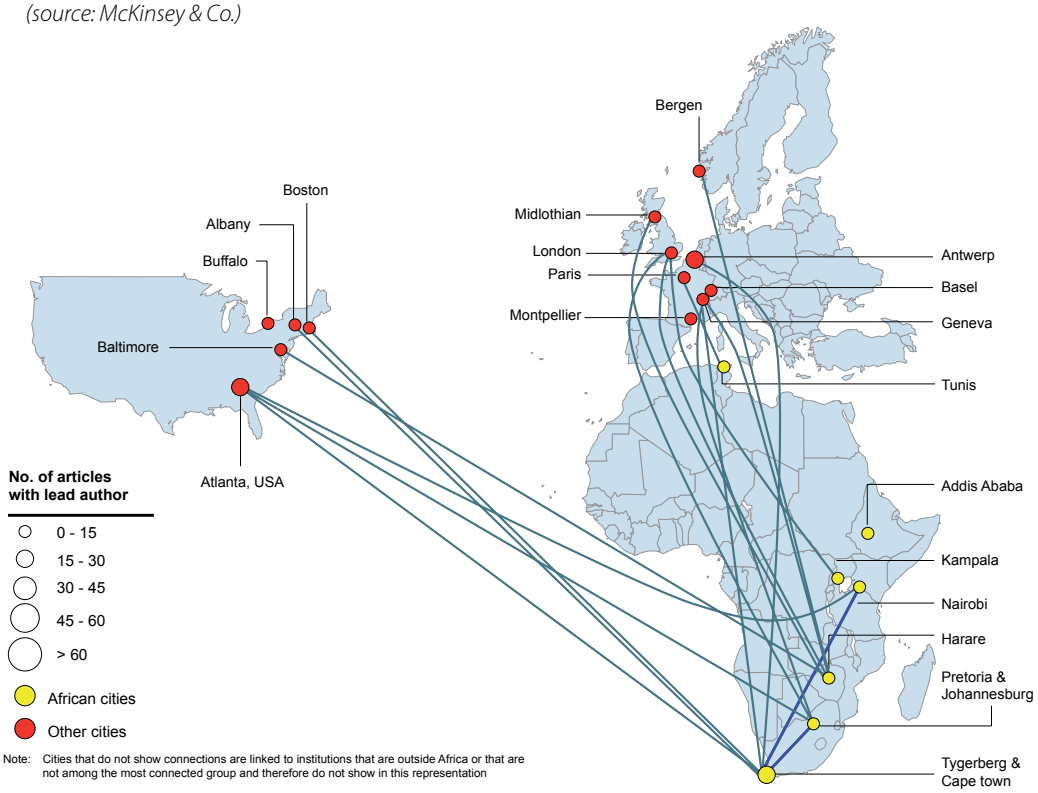


Exhibit 11 – Example of epidemiology collaborative research networks involving African research centers (source: McKinsey & Co.)

While there are some links between African institutions, suggesting a certain degree of local collaborative networks, these depictions show that collaboration is clearly oriented towards the US and Europe. Although HIV/AIDS and epidemiology are areas of great interest also for developed countries, a disease that mostly affects Africa, such as Malaria, shows the same pattern (Appendix Exhibit 5). Such a bias represents a major challenge because this type of scientific collaborations foster the misalignment of research efforts with African health priorities. Overcoming this challenge would not only allow benefiting from the synergies of Africa-based research networks, but it would also take advantage of local R&D leadership and ownership to align research agenda with African health priorities.

Insufficient investment and ownership of R&D in and for Africa

Lifting the health status of whole populations involves the concerted effort of governments and other local stakeholders including the private sector, the research community, and influential individuals. As long as the bulk of R&D investment comes primarily from foreign sources, true alignment between local R&D efforts and local priorities will remain difficult to achieve. The previous two challenges, "significant knowledge gap for diseases disproportionally affecting Africa" and "low degree of collaboration among African researchers", show to what extent there is a misalignment between R&D efforts and African needs. Despite the urgent attention that this situation demands, African governments are still lagging behind in terms of R&D spending[44] (Exhibit 12). In order to close the gap with the world median, R&D spending per capita in Africa requires a USD 14 yearly increase (resulting in a total extra yearly funding of USD 14 billion, see Exhibit 6). Africa, as a whole, lags behind other developing regions of the world, like South America and South East Asia, in terms of R&D spending per capita. However, a look into the different African sub-regions shows the great disparity within the Continent (Exhibit 12; Appendix Exhibit 6). While the Southern region invests, on average, above the world median, Western and Central Africa present a grim picture when compared to other regions of the developing world and to the rest of Africa. This intra-Africa inequity magnifies the funding gap challenge. Currently, four out of the five regions of Africa need to lift their spending on R&D if they want to reach world median. For the neglected Central and Western

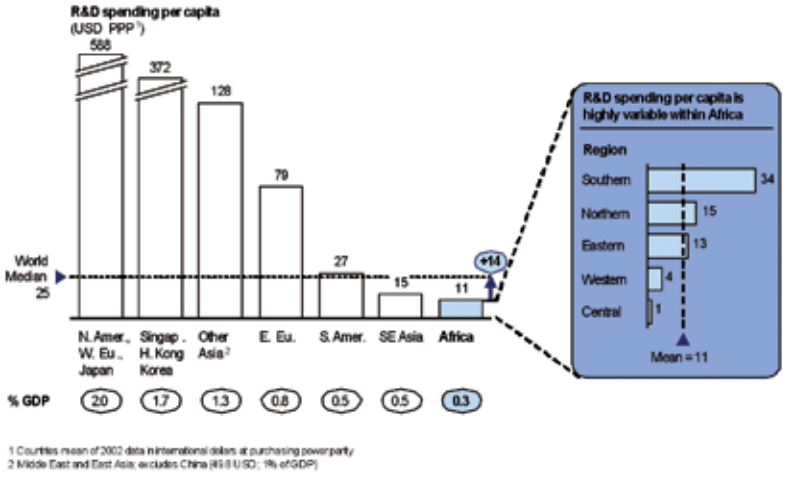


Exhibit 12 – African R&D invesment gap and regional inequalities (source: McKinsey & Co.)

44. Lastest comparable data available for R&D spend (UNDP, 2002) and GDP per capita (World Bank, 2002)

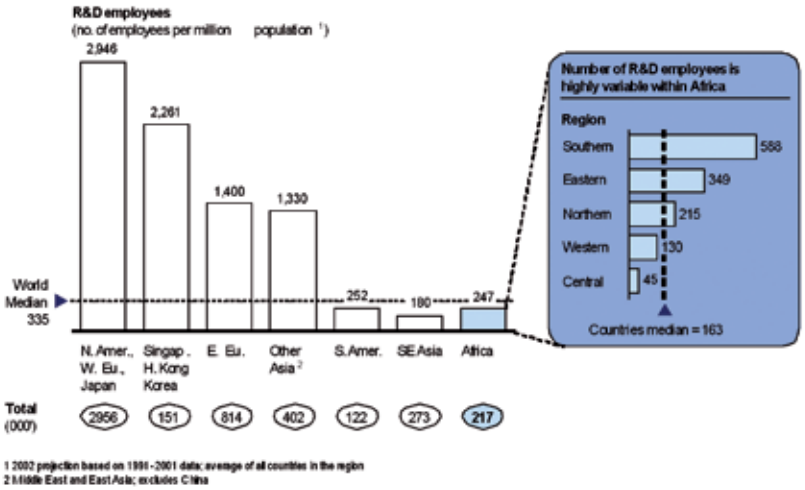


Exhibit 13 – African R&D human capital gap and regional disparities (source: McKinsey & Co.)

regions, this aspiration represents a 5 to 25-fold increase in total R&D spending. The disparities are also confirmed by other R&D indicators such as number of R&D employees[45], although Africa is, in this case, at par or better than other southern regions (Exhibit 13). The concerted effort to increase R&D investment in alignment with research agenda involves, therefore, not only raising average spending but, more importantly, working to eliminate inequities within Africa. Investment does not only mean funding. In fact, lack of investment also manifests itself in the form of regulatory and legal barriers that make access to technology and collaboration difficult. Examples of such barriers are taxes on imported scientific equipment destined for research, differences in regulatory frameworks for intellectual property or immigration restrictions for scientists. Lifting these barriers would positively impact the efficiency of research efforts and contribute to the more effective use of resources.

The ownership challenge is also illustrated by the low representation of Africans in organizations dedicated to tackling the health problems of the developing world. International organizations focused on HIV/AIDS, tuberculosis, and malaria for example, average a meager 9 to 14% of Africans in their Boards[46]. Although these organizations have been achieving great successes, the agenda they carry forward is not in African hands. This may not present a problem within the scope of those organizations. However, local African ownership of the research agenda is necessary to establish a sustainable mechanism to address the local health needs. For example, consecutive declarations have been outlined, between 1996 and 2000, with ambitious actions to be taken against Malaria[47]. However, these have in general failed to be implemented by local stakeholders due to lack of funding, lack of true multilateral agreement and lack of a fully aligned and prioritized agenda, shared by all stakeholders[48].

45. UNDP – The human development report (2004)
46. Tucker T., Makgoba M. Science. May 23; 1016-1017 (2008)
47. Addis Ababa Declaration – "African Plan Of Action Concerning The Situation Of Women In Africa In The Context of Family Health (1996); Harare Declaration – "Malaria Prevention and Control" (1997); Abuja Declaration – "Roll Nack Malaria in Africa (2000)
48. ANDI – 3rd Task Force meeting (2009)

PROMISING TRENDS TO HELP OVERCOME R&D CHALLENGES

Within the challenging environment faced by African R&D efforts, there are some promising trends. These trends, if properly harnessed, could contribute to overcoming the challenges discussed in the previous section.

Alignment of African research and traditional knowledge with local health priorities

Although the vast majority of African biomedical research output is not directly dedicated to tackling diseases that affect Africa[49], there is a promising emerging trend. Analysis of research articles, which directly focus on disease conditions, shows that the relative article output correlates with the burden of disease in Africa for those conditions[50] (Exhibit 14). Furthermore, 80% of Africans resort to traditional medicine to address their health needs[51]. The power of these locally-tailored, long-standing, traditional remedies has been progressively recognized over the last few years. For example, support at the local level is increasing, with over a third of African countries having traditional medicine research centers and 8 of them dedicating national budget funds to indigenous knowledge[52]. Besides the well known use of *Artemisia annua* to treat malaria, several other traditional medicine-based therapies have undergone placebo-controlled clinical trials with 34% of those showing promising effects[53]. This is important since traditional

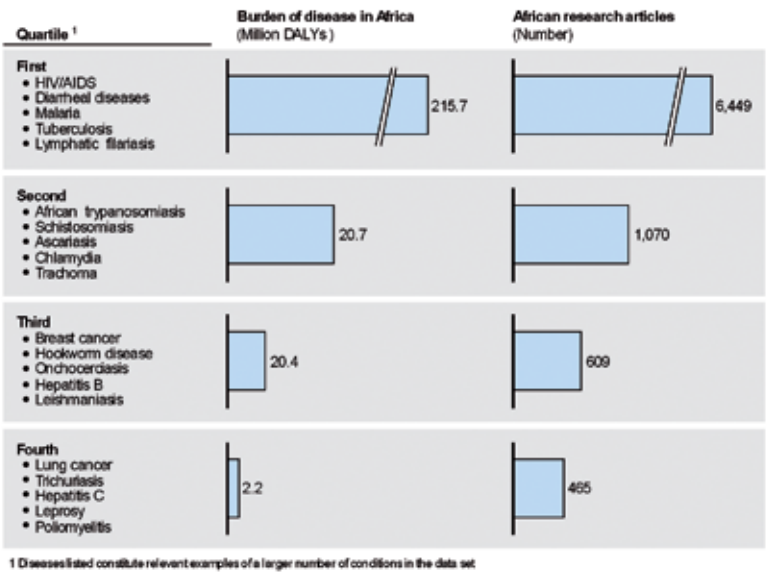


Exhibit 14 – Alignment between African burden of disease and research output (source: McKinsey & Co.)

49. Thompson Web of Science – Publication data for the 5-year period 2004-2008; At most, only 30% of all articles mention one of the diseases in Exhibit 5
50. Thompson Web of Science – Publication data for the 5-year period 2004-2008; Analysis based on keyword searches of all biomedical research on 78 diseases and conditions affecting the African Continent
51. WHO – Global Traditional Medicine strategy 2002-2005 (2002)
52. Nigeria, Ghana, Mali, Senegal, Rwanda, Ethiopia, Eritrea and Ivory Coast
53. WHO – Global Traditional Medicine strategy 2002-2005; Based on a sample of 50 randomized clinical trials with 10 herbal medicines for 18 therapeutic indications

medicine has the potential to further focus and support Africa-owned drugs and diagnostics R&D on conditions that disproportionally affect African regions. Harnessing such a potential will require building up African research capacity and ensuring the highest scientific quality is reached in product discovery and development.

Local capacity in research, clinical trials, and manufacturing willing to collaborate

In spite of the comparatively low research output of Africa (Exhibit 15), several countries in the Continent show a pool of human capital and a number of research centers that could collectively form strong R&D networks (Exhibit 16), as already shown by the mapping of the product R&D landscape in Africa presented during ANDI's founding meeting in Abuja, Nigeria[54]. In addition, a few of the established African research centers have a wide range of expertise. The analysis of 17 publication networks for different disease and functional areas resulted in the identification of centers that reach prominence in several areas[55]. These centers are essential elements of well developed international research networks and of emerging African networks (Exhibit 17). They participate in research efforts that, although linked to the North, result in good numbers of research articles. Furthermore, they are true originators of research and central elements of the collaborative efforts involving African countries. The existence of high-quality, productive and connected centers in Africa highlights the plausibility of active R&D networks in Africa, and substantiates the need to support the scale up of ongoing efforts.

It is also worth noting that some initiatives have been started to make better use of technological platforms at the country level and to improve efficiency of the R&D process through collaboration and partnership. South Africa, for example, started a national effort to share technology platforms, the Center for Proteomic and Genomic Research (CPGR). In Nigeria, the Sheda Science and

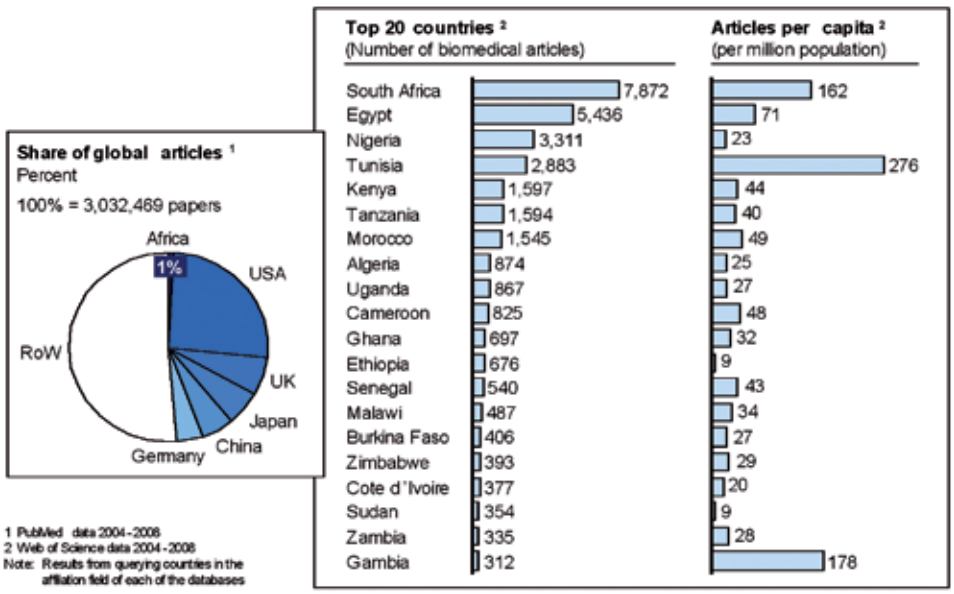


Exhibit 15 – Overview of global and African research output (source: McKinsey & Co.)

54. African Network for Drugs and Diagnostics Innovation – Creating a sustainable platform for R & D innovation in Africa, Abuja meeting (2008)
55. Thompson Web of Science – Publication data for the 5-year period 2004-2008

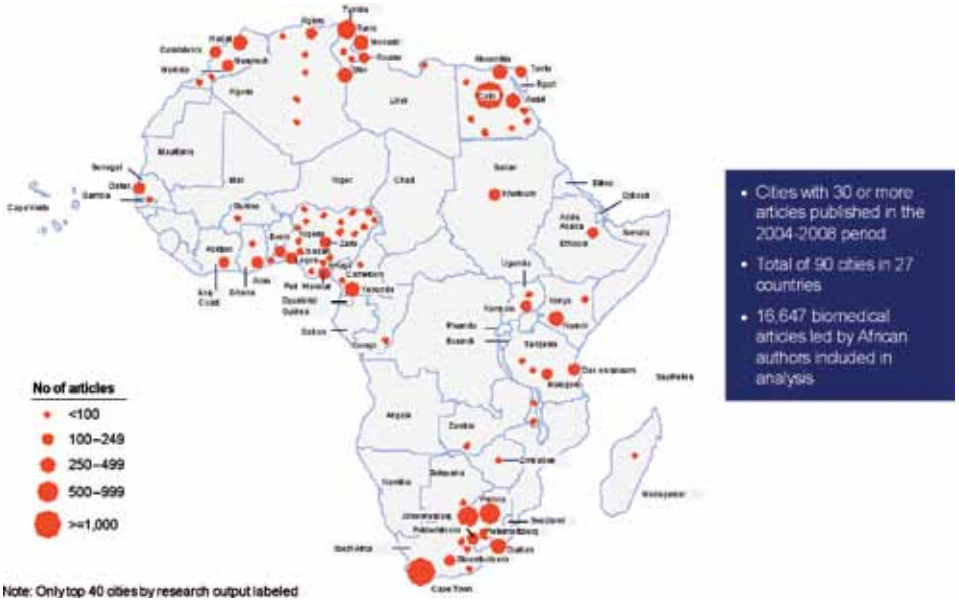


Exhibit 16 – Mapping of top 40 African cities by research output (source: McKinsey & Co.)

Technology Complex (SheSTCo) provides shared access to equipment, facilities and expertise while also hosting ventures to foster collaboration between researchers from the public and private sectors. In Egypt, the Mubarak City for Scientific Research & Technology Applications (MuCSAT) nurtures the formation of centers of excellence across the country, namely via support on development and transfer of technology.

Capacity in the clinical research arena also exists in many African centers. Ongoing and recently completed clinical trials that involve sites in Africa show that the spread of existing capacity reaches 37 countries[56] (Exhibit 18; Appendix Exhibit 7). The capacity also spans from phase I to

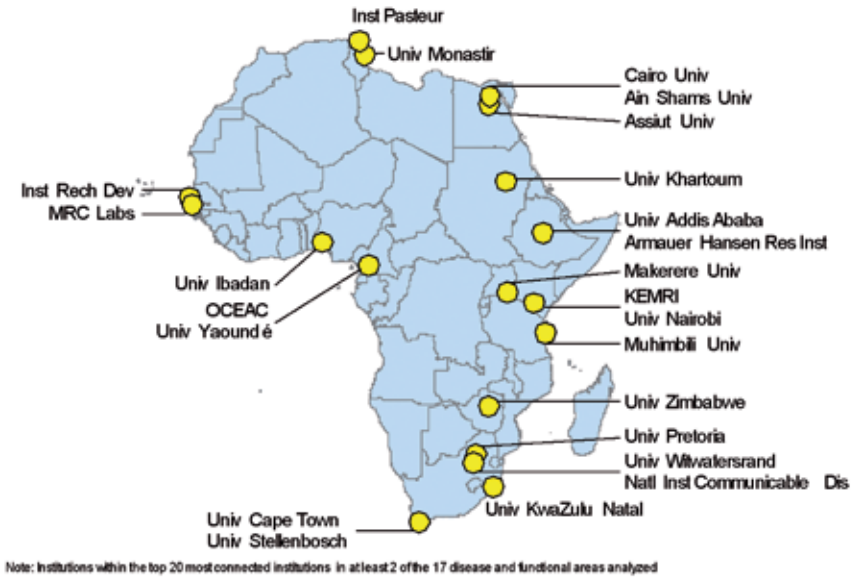


Exhibit 17 – Most globally networked research centers in Africa (source: McKinsey & Co.)

56. Clinicaltrials.gov – Clinicals trial data with participating trial centers in Africa (2009)

Exhibit 18 – Mapping of clinical trial capabilities in Africa (source: McKinsey & Co.)

phase III and IV (Appendix Exhibit 8). Additionally, an initiative focused on increasing clinical trial efficiency through collaboration, the European and Developing Countries Clinical Trials Partnership (EDCTP), has successfully assembled networks to conduct trials for Malaria, Tuberculosis and HIV/AIDS across Africa.

Moving further down in the R&D value chain, it is important to note that many African countries also harbor pharmaceutical manufacturing capacity[57] (Exhibit 19). Although the industry is still at its early stages of development and lacks some of the capabilities present in other developing countries such as India, China and Brazil (e.g., API bulk production), there is the potential for collaboration between African academic researchers and African manufacturers with the goal of producing locally originated medicines. It will be necessary to overcome important barriers in order to bring these local private companies into the research process, as they are geared for the low cost, price-pressured, generics-based African pharmaceutical markets[58,59]. However, there are examples of public pharmaceutical players that already have a strong focus on research for drugs and vaccines and which can serve as case examples for increased collaboration between research and manufacturing in Africa[60]. In addition, some African countries are investing in incubators to nurture the establishment of new pharmaceutical/biotech endeavors focused on research-driven product innovation (e.g., iThemba in South Africa, or LaGray Chemical in Ghana). This should provide a platform to translate discovery research into product development.

The combination of analyzing research output, clinical trial capabilities, and manufacturing capacity, indicates the emergence of countries leading the African R&D landscape. African leading institutions should thus be essential vehicles to lift the global R&D status in Africa via collaborative links with other neighbor countries. These links will ultimately result in more efficient tackling of regional health problems and better access to necessary therapies.

57. Onesource Global Business Information
58. Espicom – World Pharmaceuticals Market Fact Book (2009)
59. Interviews – South African and Egyptian Pharmaceutical companies (2009)
60. Example – Vacsera, www.vacsera.com

Exhibit 19 - Mapping of pharmaceutical manufacturing capacity in Africa (source: McKinsey & Co.)

The current African R&D value chain overview described above also highlights a challenge described in the previous section: the disparities within Africa. The central region shows little capacity for basic and clinical research, and for pharmaceutical manufacturing. The consistency and extent of these inequities call even more strongly for the need to network centers in Africa, not only within but also across regions. Increasing collaboration would harness the power of existing competence centers to lift the level and augment capabilities in institutions with lower ouput.

Increasing consensus around the need to boost R&D spending by governments

At an average of 0.3% of GDP, African R&D spending remains low by global standards[61]. Only a minimal portion of this is likely to be dedicated to health-related R&D. In Nigeria, for example, health R&D spending is in the order of 0.001%[62] of GDP, whereas in South Africa it is higher at around 0.07%. In spite of the low figures, the necessity to increase R&D spending for health is well recognized. The African Union has set the target of dedicating the equivalent to 2% of total healthcare spending to health research by 2015. This target converts into 0.1% of GDP or 33% of total R&D, assuming the current average healthcare and R&D spending. Kenya spending 0.15% of GDP on health research illustrates that 0.1% is a plausible target[63]. In addition, some countries are aggressively increasing total R&D spending. South Africa, for example, is about to reach 1% of GDP spent on total R&D. Egypt is reaching 0.6% at end of 2010 and attempting to match the 1% aspiration by 2017[64]. Matching the African Union target, together with more countries pushing for higher R&D spend, could result in a major boost in research aimed at African ailments. The increasing consensus around the need to step up investments

61. UNDP – The human development report (2004)
62. Interview – Federal Ministry of Science and Technology of Nigeria, Department of Physical and Life Sciences (2009)
63. Kenya 2001/2 National Health Accounts study indicates that 3.3% of healthcare spending went into health research; total healthcare spending in 2000 (closest available data point) was 4.5% of GDP (WHO data)
64. Interviews – South African and Egyptian Ministries of Science and Technology (2009)

Current challenges	Current trends	Potential solutions
• Significant research and knowledge gap for unique African diseases	• Many African institutions already focused on R&D to address local health needs Initial efforts to harness wealth of indigenous knowledge	• Funding research focused on identified health needs Supporting African ownership of product development
• Low degree of scientific collaboration within Africa	• Existing R&D and manufacturing capability scattered in centers across Africa • Emerging research networks and collaboration with the private sector	• Fostering African R&D network development by linking existing research centers
• Gaps in R&D investment and research ownership	• Increasing R&D spend in some African countries (e.g. South Africa) • Pan-African efforts promoting increases in health research spend (e.g. AU Health Strategy 2007 -2015)	• Advocating for increased investment and agenda setting capability, especially with local stakeholders

Exhibit 20 – Summary of African R&D challenges, promising trends and potential solutions

in health R&D, together with the GDP growth experienced by some African countries, makes this a propitious time to redouble advocacy efforts aimed at engaging governments and local stakeholders to increase their ownership of the product development process by increasing national funding for R&D.

HARNESSING CURRENT TRENDS TO SOLVE THE AFRICAN R&D CHALLENGES

In the previous sections, three major challenges faced by African R&D efforts were introduced. These challenges, appear to prevent ongoing research from reaching the adequate scale and productivity required to address Africa's unmet health needs. However, the overall picture is not as grim. Ongoing trends offer possibilities to overcome the challenges, and doing so will set in motion a mechanism to achieve the goals articulated by the GSPA. In that context, fundamental and new solutions must be put to practice (Exhibit 20). The successful implementation of the proposed solutions requires a concerted African-led and Africa-based effort . One new mechanism to help address these problems has already received strong support from African stakeholders and endorsement by the World Health Assembly. The organization is called ANDI, the African Network for Drugs and Diagnostics Innovation.

ANDI is a pan-African not-for-profit organization that aims to promote sustainable product R&D and access through collaborative networks and partnerships. In the words of a Ministry official: "ANDI is needed because through ANDI Africa can achieve much more than what one country could achieve".

4. ANDI'S MISSION DEFINES ITS BUSINESS MODEL

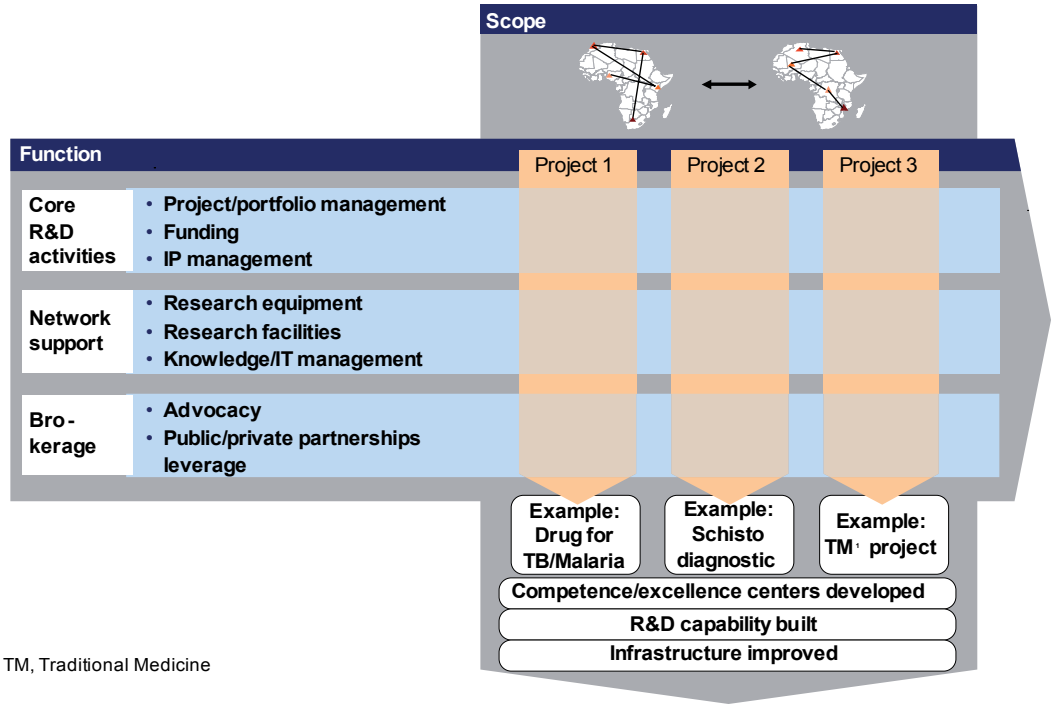
ANDI'S MISSION

The mission defines the core of an organization by stating its purpose and articulating its business model. As such, the mission statement of ANDI is:

> *"To promote and sustain African-led health product innovation to address African public health needs through efficient use of local knowledge, assembly of research networks, and building of capacity to support economic development"*

THE BUSINESS MODEL FOR ANDI

The business model for ANDI defines what the organization does and, therefore, it is the tangible manifestation of ANDI's mission. In accordance with this principle, the business model consists of two major dimensions (Exhibit 21): Scope and Function.



1 TM, Traditional Medicine

Exhibit 21 – The ANDI business model

ANDI will focus on addressing Africa's unmet disease needs by harnessing the untapped power of collaboration among African researchers. It will do this by driving and supporting the formation of research networks composed of research centers located in Africa, engaged in a specific research project. In turn, each of these projects drives the development of multiple potential health products (compounds, leads, platforms, etc.) by moving them from discovery into clinical trials and manufacturing for access. Hence, a fundamental concept is that ANDI brings together centers that complement each other technically and functionally into a cohesive unit (the network). The fact that all efforts are organized around projects allows ANDI to seek for highly focused impact, with the objective of developing new tools to address specific African diseases. Since networks are composed of investigators doing research in Africa, who come to work together to address specific local research questions, this approach guarantees full alignment with the African research agenda, and promotes local ownership. In addition, by supporting these networks and their products, it is expected that ANDI's deliverables will go beyond new and/or improved products. The investment will also permit the development of structural and human capital by building capabilities in the context of network projects and by contributing to further developing the existing African health R&D infrastructure. These elements of the model were shaped by the opinion of African stakeholders and represent a new approach to capability and infrastructure building.

To ensure the delivery of its proposed outcomes, ANDI will center its functions along 3 main dimensions. One, it will directly support the R&D activities of the networks. This will be achieved by providing close project coordination to each network and also across the portfolio of complementary projects, by ensuring significant funding to push products through development, and by helping researchers and stakeholders understand and manage intellectual property in a way that responds to both, the needs of local inventors and of the African public in general. Two, ANDI will support networks to enhance their research equipment and facility standards, while providing the IT and database backbone and services (including training) to guarantee that projects are competitive and fully implemented. Three, ANDI will broker relationships with key stakeholders in Africa and beyond (e.g., through South-South, North-South collaborations, global technology transfer agreements etc.) to warrant that health products move into production for access. This will be achieved via substantial financial and management support for a select group of high-quality projects, and via advocacy efforts aimed at encouraging local involvement, funding and ownership. The objectives are to generate and manage partnerships with public and private players, and to leverage contributions to ANDI made by other organizations to ensure product success and the future access to those products by African people.

ANDI adds significant value to the current global health R&D landscape through four elements that distinguish it from ongoing initiatives. Firstly, it focuses on bringing African researchers together into African research networks to harness and leverage the capacity and capability that exists in the Continent. Secondly, it involves the local stakeholders ensuring that the initiative aligns its activities with African health priorities. Thirdly, it aims to develop a sustainable stream of projects leading to new health tools. The emphasis is not on specific products or specific diseases but rather on creating the backbone and developing the mind-set for continuous health

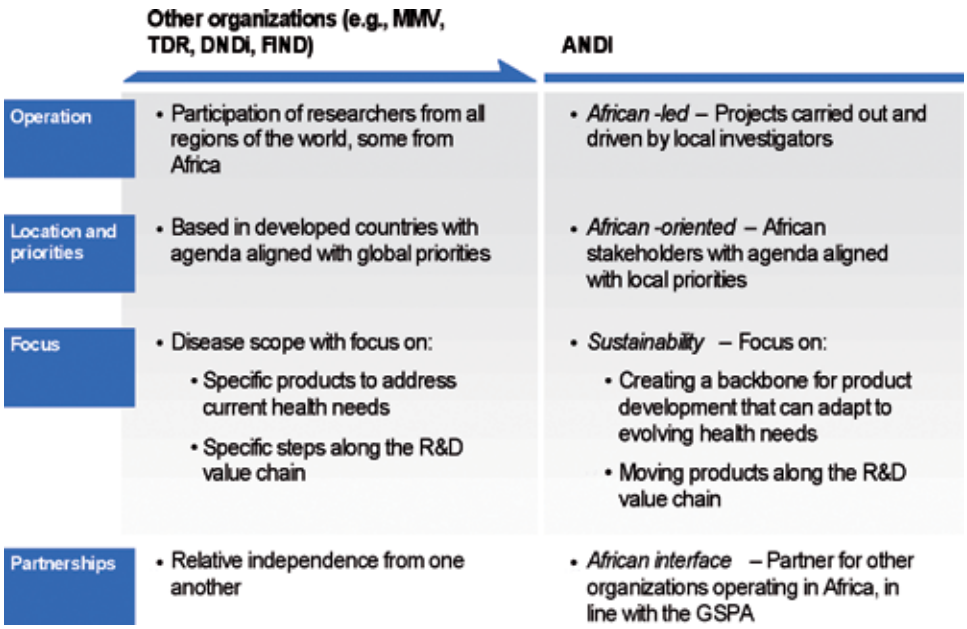


Exhibit 22 – ANDI value-adding role in the African health R&D landscape

product development. As a direct consequence, ANDI aims to expand research capacity and build the capabilities necessary to create a self-sustained health product R&D system. Finally, the fact that it is framed in the context of the GSPA, allows ANDI to position itself as a key interface in Africa with which other organizations can more effectively partner (Exhibit 22). Currently, no other organization places its strategic emphasis so strongly on African leadership and ownership. Important efforts foster the development of tools to address African diseases with the participation of some African researchers. These include, for example, TDR and EDCTP, working through their intergovernmental support and focusing on capability building, or MMV, DNDi and FIND, non-governmental organizations developing specific products for specific conditions. Notably, none of these institutions focuses on having a sustainable R&D process fully driven in Africa and by Africans themselves. However, while being clearly distinctive, ANDI does not aim to compete with existing players, but rather to partner to avoid duplication of efforts and to make product development and access more efficient and sustainable. In that sense, it will be important to capture the interfacing opportunities created by newer efforts that are significantly increasing the level of funding for research in Africa. Examples of these efforts include the Bill and Melinda Gates Foundation's anti-malarial resistance network funded with approximately USD 20 million and the Rockefeller Foundation support of health systems research with approximately USD 100 million. While not fully dedicated to Africa, a significant portion of these budgets is expected to be spent in the Continent. In addition, the EU has launched the call for health research in Africa (HEALTH) with approximately USD 55 million and the Wellcome Trust has started to fund consortia formed by research centers from one third of African countries, with a total budget of USD 49 million. The scope of funding of this consortia network spans broad areas such as environmental health or vocational excellence in health. Nonetheless, it is expected that a fraction of this investment might support some of the research leading to new health products for Africa.

SCOPE

Defining the scope is essential to ensure ANDI functions according to the principles laid out by its mission. As such, the selected scope for the initiative is composed of two key dimensions: disease and R&D function along the value chain (Exhibit 23).

The disease scope should be specific enough to focus ANDI's resources onto areas with potential to achieve high impact on the health status of African populations, yet flexible enough to accommodate the dynamic nature of priority diseases. This implies that disease areas fitting into ANDI's scope will need to be monitored to evaluate impact on Africa in terms of reducing mortality, morbidity and infection rates. For those reasons, ANDI's disease scope is defined generally, to focus on impact rather than on particular diseases that represent current unmet needs. The scope of ANDI's support is also defined by the position along the R&D value chain, and the specific associated R&D functions. The different functions in the value chain go from basic research (e.g., molecular mechanisms of disease aimed at target identification) to phase III clinical trials, and even manufacturing and access. Although ANDI's direct role is not manufacturing, its goal of translating research into products that address African needs will require involvement in the later stages of the R&D value chain so as to promote access. For this dimension, the evolution of risk along the R&D value chain, and the potential availability of partners (public or private) to undertake responsibilities were taken into account. For example, early in the R&D value chain, the risk is high and the likelihood of finding partners that would share that risk is low. In such a high risk scenario, ANDI will concentrate only on urgent African unmet health needs, where other form of support is limited. As a product advances along the R&D value chain, the risk goes down and ANDI can allow a broader scope to support product development for any disease affecting the African continent. To facilitate efficient project advancement along the R&D value chain, ANDI will be more involved at the riskier early stages, and progressively broker and leverage partnerships with other organizations to support the project as it approaches the commercial stage. It should be noted that ANDI will need to be flexible on its roles on the downstream sections of the R&D value chain. While it will look to partner with other players

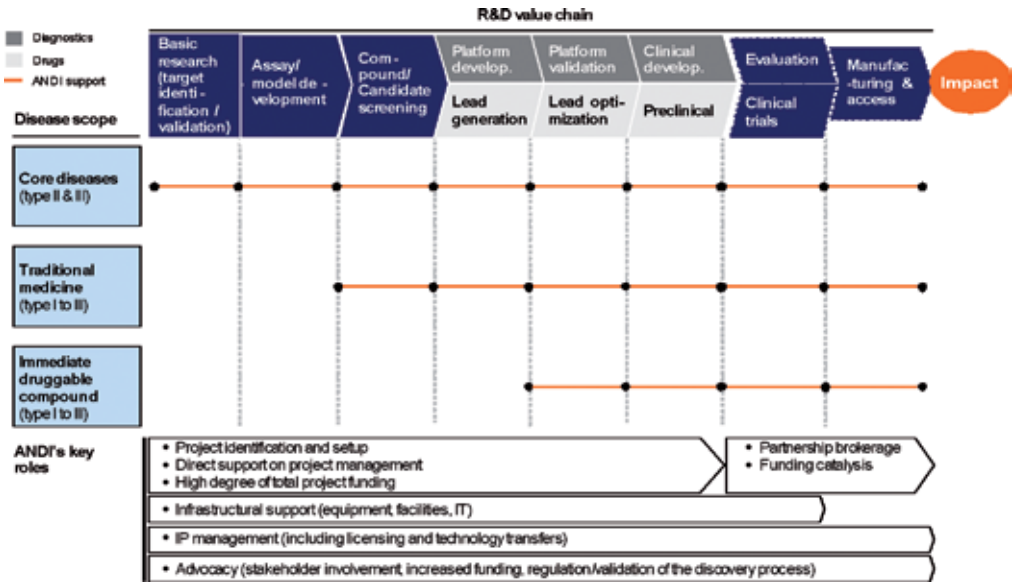


Exhibit 23 – The scope of ANDI

operating in these sections as possible (e.g., EDCTP for clinical trials) it must ensure that products do not get stalled should high potential be demonstrated. A logical consequence is that ANDI will need to monitor projects very closely to constantly assess risk and define its strategy accordingly.

Considering the logic for the two scope dimensions, ANDI identifies three target categories for support – core diseases, traditional medicine, and immediate druggable compounds. Research projects that fit in one or more of these categories are candidates for ANDI's support along the R&D value chain. The overriding logic is that ANDI will guarantee focus by covering large parts of the R&D value chain for specific diseases, and by covering specific steps of the chain (namely downstream) for a larger set of diseases.

Core Diseases

This category relates to conditions that constitute an unmet need, are endemic to Africa, are underinvested, and present great impact potential. Currently, conditions in this category include type III diseases, and areas of type II diseases that are neglected by international or global research efforts. Lymphatic filariasis, Onchocerciasis, Human African trypanosomiasis (HAT) are examples of type III diseases with relevance for Africa today. While in relative terms these neglected diseases (Type III) generally have lower DALYs and actual mortality compared to other diseases types, they have strong social and economical impact in absolute terms. For example, HAT affects 500,000 people and Lymphatic Filariasis affects 40 million people[65]. In addition, Type II diseases such as HIV and tuberculosis still contain neglected aspects with special relevance for Africa, e.g., therapies for pediatric HIV/AIDS, effective management of multi-drug resistant tuberculosis and shorter treatments to resolve compliance problems. By focusing on this category ANDI truly drives the GSPA agenda of addressing diseases that disproportionately affect developing countries. The Core Diseases category is supported from early basic research to clinical trials for both therapeutic and diagnostic products (Exhibit 23). For clinical trials, however, ANDI will look to leverage partnerships with public, private, international and non-governmental organizations, for example EDCTP or TDR. The partnership model would help mitigate the financial impact of late clinical trials. ANDI should financially support trials for those conditions where the lack of market incentives or development partners prevents the advancement of the project.

Traditional medicine

The disease scope is more flexible for this category (types I-III), as long as clear impact in Africa can be shown. As such, focus is not necessarily on neglected or underinvested conditions, and efforts aiming at substantially lowering the cost or increasing the efficiency of delivery of existing therapies will also be considered. Some examples of diseases in this category are lower respiratory infections and diarrheal diseases that, despite being easily managed in other regions of the world, still account for a large portion of African DALYs. Cheap and easy-to-deliver treatments with long shelf life in harsh environmental conditions could have clear African impact in these cases.

Projects that fit in the Traditional Medicine category should present successful progression through early research phases dealing with compound identification and extract fractionation, for products

65. CDC – Parasitic disease information (2006)

with known clinical use. ANDI support is expected to focus on the subsequent development phases (Exhibit 23). The impact of these projects relies on the competitive advantage that indigenous knowledge offers in addressing regionally prevalent ailments.

Immediate Druggable Compounds

This category also has a wide disease scope (Types I-III). Examples range from lymphatic filariasis and HIV to diabetes and cancers. Efforts in this category can be originated from traditional or conventional knowledge, but should demonstrate potential impact on the health status of African populations.

The less restrictive requirements in terms of disease focus are tied to a much more restrictive R&D value chain scope (Exhibit 23). To ensure proper use of ANDI's resources, projects in this category should be extremely advanced, close to the clinical phases, and they should show solid evidence for short-term commercial product and licensing potential. It should be noted that local pharmaceutical manufactures foresee their direct involvement with this type of project, either by collaboration with researchers in other centers to more rapidly move new products into clinical or by linking with experts to optimize existing products for other applications[66]. Consequently, projects fitting in this category will quickly contribute to product development ownership and engage the local pharmaceutical industry to collaborate in Africa-led research efforts. As with the other areas, projects in this category might present an opportunity for North-South collaboration, especially leading to technology transfer and licensing agreements.

ANDI's roles are defined along the R&D value chain

Specifically for the early elements of the R&D value chain, ANDI aims to provide support for proposal writing and project design, help with the identification of collaborating partners if needed, facilitate projects management, and provide substantial and continuous funding. Once projects advance into clinical phases, ANDI brokers partnerships with organizations that specialize in those

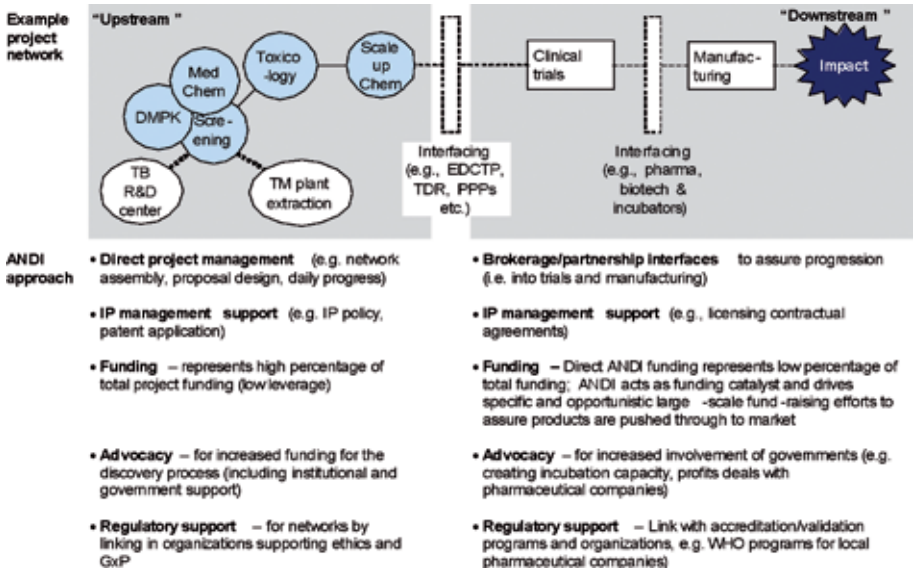


Exhibit 24 – Example project network and key ANDI roles

66. Interviews – Pharmaceutical companies Vacsera and Deltapharma (Egypt, 2009)

portions of the R&D value chain. Depending on the availability of partners as well as their expertise and capacity, ANDI will seek to collaborate with them, transfer project support to them, or proceed with full project support if partner availability is limited or non existent. For example, for products that fulfill a clear unmet need but have little market potential, ANDI will continue full project support up to very late stages. However, working in coordination with its advocacy function, ANDI will try to engage other organizations, governments, and the private sector to ensure that project discoveries advance. As an example, Exhibit 24 illustrates how ANDI would directly support a project and how it would interface with other organizations to form partnerships aimed at advancing product development as efficiently as possible. In this case, tuberculosis research centers and laboratories specialized in traditional medicine research come together to identify promising compounds. ANDI fully supports the project at this early stage. Once the candidates have been identified, ANDI interfaces with clinical research organizations to ensure optimized leads are clinically validated. Upon successful clinical results, ANDI links to private or private-public organizations with capacity to manufacture and distribute the product. During the whole process, ANDI also engages governments to maximize local ownership through funding, but also to overcome regulatory challenges with the goal of facilitating access once the product is ready for the market. Overall, this differential involvement model benefits from the available expertise in other organizations, public or private, to participate in relevant parts of the R&D value chain.

GUIDING PRINCIPLES

To address its scope, ANDI is guided by four fundamental principles (Exhibit 25).

With the aim of ensuring the practical execution of these principles, ANDI will engage in 3 distinct sets of functions to support its project portfolio, at the individual as well as at the collective level: Core R&D activities, Network support and Brokerage.

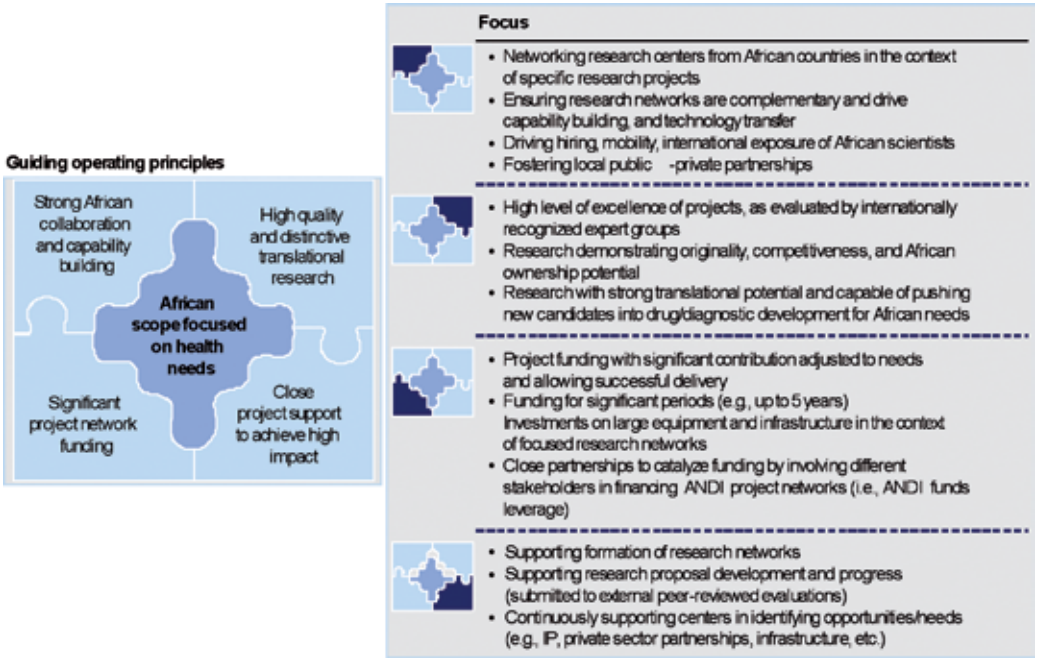


Exhibit 25 – The guiding operating principles of ANDI

ANDI FUNCTIONS – CORE R&D ACTIVITIES

Project and portfolio management

This activity aims to prioritize and select existing R&D efforts to turn them into peer-reviewed projects that are assembled as research networks. In addition, it also aims to coordinate the ANDI project portfolio to ensure delivery (in terms of health products, capability building, etc.) and manage project network support (e.g., link to IP management, databases, collaboration with the private sector).

Building networks

An essential element of ANDI's mission is the assembly of collaborative research efforts. An ANDI network is a group of collaborating research centers, and the links among those centers. ANDI will strive to create project networks that bring together strong disease and technical focus and expertise around specific goal (Exhibit 26). These project networks only expand as needed, for example when a product moves beyond the initial scope of the specific network. As such, these networks benefit from the fact that expertise can be flexibly pooled, while keeping project ownership to a single network. Over time, centers will collaborate with others, and share skills and expertise in different project contexts. ANDI project success is then a vehicle to attract research grants from sources other than ANDI and successful participants would be able to use ANDI's projects as an opportunity to expand their sources of funds. This maximizes overall capacity and capability building. A possible shortcoming would be the lack of sustainable funding for centers that are not part of ANDI projects. However, the flexible composition of these networks allows ANDI to maximize the impact of its resources so as to reach a larger number of research institutions across the African continent.

Call for project proposal

To ensure alignment between funded projects and ANDI's mission, project management starts from the very beginning, with the call for proposals. The call establishes the rules of engagement between ANDI and the project network. It is prescriptive enough to make sure projects fall within ANDI's scope, while allowing enough flexibility so as to "cast a broad net" to tap into any innovative ideas arising in Africa. The guidelines for the call for project proposals derive directly from the operating principles of ANDI (Exhibit 27 and see Exhibit 25).

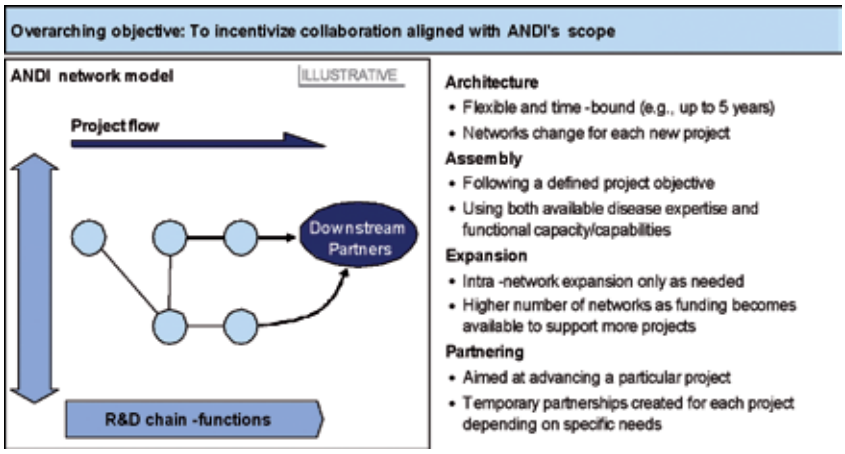


Exhibit 26 – Logic for ANDI combined focus (disease and R&D function) network assembly

Operating principle	Guidelines
Strong African collaboration and ccapability building	• Emphasis is on collaborative efforts, networking up to 3-5 African research centers, ideally from different countries; Public-private partnerships are also favored • Networks to show detailed plans for complementation of work, capability building, and technology transfer (especially between existing competence centers and undeveloped laboratories) • Proposals with plans to hire scientists (PhDs, postdocs), drive mobility efforts and international exposure are favored
High quality and distinctive translational research	• Emphasis is on scientific excellence, with proposal evaluation being conducted by internationally recognized expert groups, (STAC) • STACrecommendations to consider originality, competitiveness, and African ownership potential • Project shortlist to be created by ANDI, prioritizing research with strong translational potential and · capable of pushing new candidates into drug/diagnostic development for African needs
Significant project network funding	• Projects funded for up to 5 years, with up to around USD 1 million per project per year, for which a detailed financial plan is to be presented; Other funding (travel, large equipment, infra-structure) available separately • Yearly funding renewal with progress analyzed for full network • · Close evaluation to identify non-viable/non-functional projects to allow for rapid termination or adjustment
Close project support to achieve high impact	• ANDI coordinating and supporting: proposal development, set-up of network following Board approval, monthly interactions andprogress report preparation • Progress reports submitted to STAC yearly, for analysis and recommendations going forward; Networks will report progress to the STAC in presence ("face-to-face") • · ANDI coordinators continuously supporting centers in identifyingopportunities/needs (e.g., IP, infrastructural needs, private sector partnerships)

Exhibit 27 – Guidelines of calls for project proposals

Importantly, the proposals will include a clear scientific plan that articulates its competitiveness, potential for African impact, and that sets milestones aimed at tracking progress. It also requires a plan to build capacity and share capabilities among the participating centers (Appendix Exhibit 9, 10 and 11). In exchange, the call for proposals will explain the level of financial, technological and human support that ANDI will provide to participating research centers. This sustained support is aimed at maximizing progress and increasing success rate, with a focused, manageable number of projects. Then, paramount to ANDI as an R&D initiative, is the direct "everyday" support to the network. This consists initially of helping the participating researchers to craft a proposal that follows ANDI's requirements and in successfully taking it through evaluation and selection to ultimately launch a project. In addition, it entails support for project management, including progress monitoring against set milestones from the inception of the project until its end. Concurrent with supporting networks to design project proposals, ANDI's R&D coordination functions also include the call process itself and the underlying overall portfolio management. In order to achieve this, proposals go through a 5-step process leading from design to inception (Exhibit 28). The fundamental logic of this process is that ANDI helps in identifying and tailoring proposals to befit the scope (step 1) and then submits these to fine scientific scrutiny through an internationally recognized scientific and technical advisory committee (STAC, step 2). The STAC will initially analyze letters of interest (LOIs) and then analyze a smaller number of full proposals, which are designed, with the support of ANDI. The first two steps then guarantee that focused high quality proposals can be selected and short-listed. The next stage (step 3) is to short-list the key proposals so as to align them with the mission, in general, and with the existing efforts and needs, in particular. This step is important in increasing the probability of success of the projects, and of ANDI as a whole. The short-list is then recommended to the governance of ANDI for final approval and alignment with the overall budget of the initiative (step 4). Finally, financial support is disbursed (see Chapter 5) and ANDI starts its project management support of the networks, with the help of external advisors such as the STAC (step 5). The overall process is scheduled to take only a few months, including network identification and proposal design (see Chapter 7 for further details).

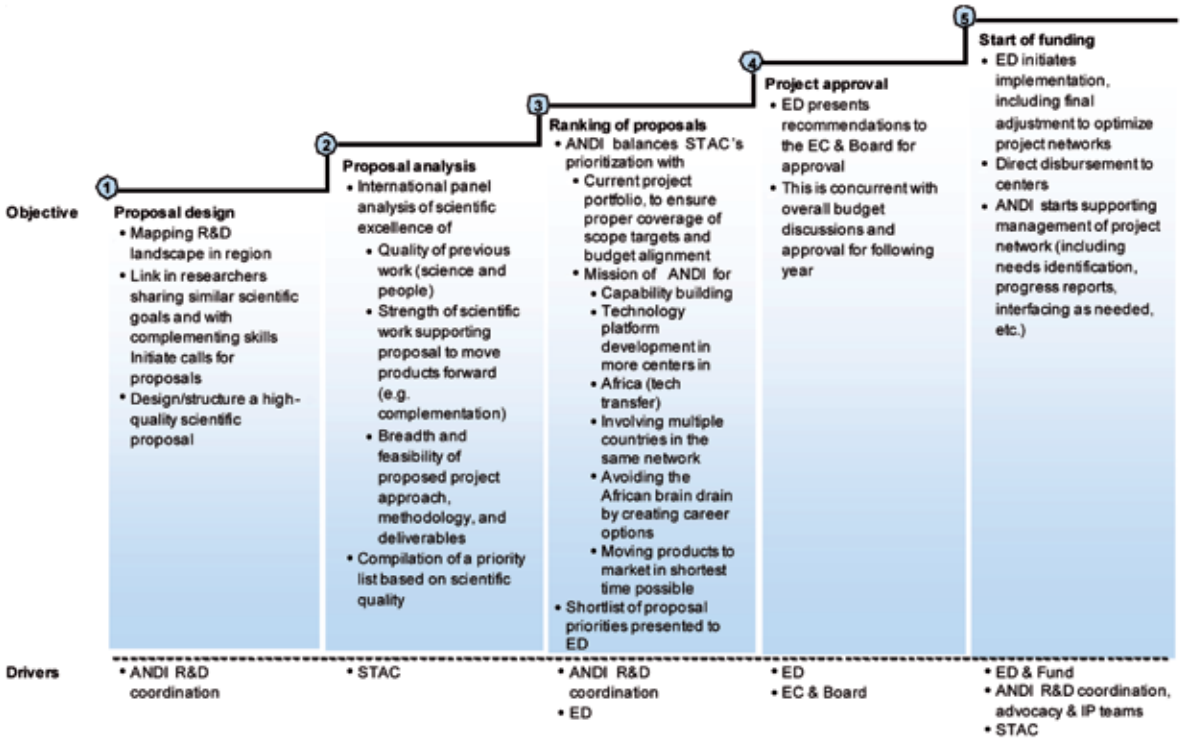


Exhibit 28 – 5-step strategy to select ANDI projects

Funding

Funding is a core area that does not operate in isolation but in close cooperation with R&D project and portfolio management, as well as with other areas and functions of ANDI. There are two major objectives: to drive project funding for the African research networks (both funder and broker roles) including support infrastructure. An ANDI project is defined as having 3 pillars. The scientific workstreams pillar concentrates on funding for the actual lines of research in which multiple compounds, candidates, leads, platforms, etc. are being developed. In this case, support focuses on researchers themselves (e.g., salaries, mobility), as well as consumables and other non-exceptional costs. Secondly, the technology platform pillar focuses on supporting the acquisition of critical technologies needed by the centers in the context of their projects. Finally, the infrastructure pillar funding focuses on targeted support for infrastructural improvement, especially when such structures already exist and can be the focus of upgrades/expansions. Also in this case, support is awarded in the context of a project. The concept of project is thus fundamental. It is the mechanism through which ANDI is able to focus its support into key research initiatives that ultimately drive the broad disease and functional scope. Upstream, ANDI's funding is expected to be the main driver for the scientific workstreams pillar. In addition, ANDI will bear a majority investment for selected critical equipment and infrastructure. ANDI will help generate momentum and support for very fundamental research on high priority African needs but with unclear product potential. Moreover, ANDI might also work with partners to thrust investments on new research centers and on the assembly of large multinational efforts (e.g., genome projects) that will impact the drug discovery and development process in Africa.

Downstream, direct funding will focus on selected activities, mainly to ensure that projects do keep progressing. This includes validation and proof-of-concept studies to support entry into a specific phase of trials and to increase the potential to find downstream partners. It also includes taking a lead role in bringing in other potential partner organizations. These organizations could include groups such as EDCTP for clinical trials and WHO for accreditation/validation support. As with upstream support, ANDI will do targeted investment in IP management. ANDI will again leverage its catalytic potential with selected partners to help move products along the downstream steps. This might include support for build-up of manufacturing capacity (e.g., production lines), construction/building of clinical trial centers, planning/launch of new biotech startups and accreditation/validation of private companies (e.g., local pharma). However, ANDI will neither fund nor push fund-raising for activities such as clinical trials performed in Africa without participation or leadership of local centers or with low impact for the region/continent itself (Africa as a simple "test tube"). Also, the build-up of capacity and capability for OECD private companies will not be supported by ANDI itself.

Beyond, upstream and downstream funding, ANDI will also explore the option to establish other incentives, such as award schemes. These have been contemplated in the GSPA as a key measure to build R&D capacity in disease endemic countries and ANDI leverage them to reward exceptional projects and thus promote health-related innovation.

IP management

The focus of this area of activity is to facilitate the access to and the sharing of intellectual property (IP) related to health product discovery and development, so as to promote, recognize, enhance and protect local ownership of health products. To achieve this, ANDI has clear objectives along 3 broad categories of support:

- **Network IP support**
  - *Project setup* – To support projects through the provsion of advice and assistance relating to IP involving health products.
  - *Project management* – To continuously support networks with management of IP related issues.

- **Global IP support**
  - *IP policy* – To design overall IP policy to support the R&D process in the project networks, in collaboration with WIPO/local patent offices *Business-oriented training* – To provide learning/developmental opportunities for researchers and stakeholders in Africa on IP management, R&D marketing and R&D product commercialization, in collaboration with existing training programs, e.g., those offered by WIPO and local organizations (e.g., Egyptian Academy of Sciences)
  - *IP landscape analysis* – To generate regular analysis of IP productivity (e.g., filing, approval) and leverage (e.g., licensing, tech transfer) to instruct ANDI's R&D coordination and Advocacy teams, in coordination with global institutions such as WIPO but also EPO, USPTO, JPO, WTO and WHO/PHI[67]

67. EPO – European Patent Office; USPTO – United States Patent and Trademark Office; JPO – Japan Patent Office; WTO – World Trade Organization; PHI – Secretariat on Public Health, Innovation and Intellectual Property

- **IP technical support**
  - To assist African inventors operating in project networks with preparing/filing patents and trademarks at African and international patent offices (including maintenance) and/or in licensing from and to third parties; in addition, this area of support will also help networks in contributing to and/or leveraging drug patent pooling.

The IP management activities will concentrate in linking ANDI's scientists and research centers with the right partners to support them with contractual negotiations, confidentiality and material transfer agreements, etc. It should be noted that such an approach has been successfully tested, albeit in a smaller scale, in Colombia[68]. In this case, WIPO devised and established an IP hub through extensive consultation and with significant support from 12 Colombian organizations (universities, institutes, foundations). The hub was responsible for training, supporting patent drafting, licensing and maintenance, IP policy design and landscaping as well as IP advocacy work. Importantly, 8 new patents were filed and 1 was granted after the first year of operation. Through a similar but larger scale approach it is envisaged that ANDI will tap specialized organizations and that these, together with ANDI, can be brought together to form a pan-African IP network (Exhibit 29). On one hand, international institutions, such as WIPO, are looking for organizations that can work as interface between their activities and different African players. While focused on drug discovery and development, ANDI would befit this role at least for this research area. On the other hand, it was observed that some countries in Africa are already organizing their IP efforts at the national/regional level. ANDI will make every effort to link these into the broader Pan-african network in the context its projects. For example, the Egyptian Academy of Science is responsible for the operation of the Egyptian patent office (EYPO) and it networks the different research centers and their technology transfer offices across the country. In addition, it is also spearheading an initiative to centralize the patent office activities of different countries in the North African region. Another example of IP organization is the self-assembly networking of academic IP offices in South Africa (SAPO), which is allowing for practice sharing, cross-examination support, etc. Beyond these more local efforts, there are other broader IP platforms that ANDI will tap to include in its IP network. These include the African Regional Intellectual Property Organization (ARIPO), an IP cooperation-focused body bringing together 16 English-speaking countries (mostly in the Southern region) and the Organisation Africaine de la Propriété Intellectuelle (OAPI), also focusing on IP cooperation but bringing together 16 French-speaking countries (mostly in the Western and Central regions). In due time, ANDI should also position itself as a key partner of the Pan-African Intellectual Property Organization (PAIPO) should that joint African Union/African Ministerial Council on Science and Technology (AMCOST) effort come to fruition.

Exhibit 29 – Potential ANDI-driven Pan-African IP network

68. SECOPI (Servicio Compartido de Propiedad Intelectual) Agreement (2007)

NETWORK SUPPORT

Infrastructural network support facilitates collaboration and performance management. It covers all areas of ANDI's projects, from the initial assembly of the project network to the management of the results and intellectual property generated by projects.

Equipment and facilities support

This category of support was inspired by multiple African researchers (Appendix Exhibit 12). It finances the acquisition of critical equipment and facility upgrades or construction to reinforce or establish fundamental technology platforms along any position in the R&D value chain. The key requirements are clear regional impact, functional gap bridging, and the potential for durable and sustainable activities beyond the project for which the support is originally granted. In addition, the institution hosting the equipment or facility should commit to its maintenance and to make it accessible to scientists in the region that do not belong to ANDI's project networks.

The case for critical equipment should be clearly linked to the progress of an ANDI project. Its location needs to be justified with its projected use and/or the ability to establish needed local capabilities or fill a technological gap. In addition, ANDI will request a clear plan for expertise building tied to equipment purchase. In other words, the researchers requesting that particular piece of equipment should be able to demonstrate that its use will not only advance ANDI project, but also create local technical expertise that can be sustained and developed over time.

These are some examples of equipment support that ANDI would be able to provide, considering an estimated average cost per single critical equipment of around USD 300 thousand[69]:

- Nuclear magnetic resonance (NMR) machine, with dedicated service contract, to be placed in an existing center with space, with adequate maintenance, and with researchers that can operate the equipment and teach others
- Liquid chromatography-mass spectrometry (LC-MS) apparatus for a laboratory involved in the identification of traditional plant extract components Pilot production or scale up laboratories (e.g., small volume bioreactors, protein purification devices) necessary to drive preclinical and early clinical work on an ANDI project, but also to share in the context of other African projects

For facilities construction or upgrade, a business plan should be put together with the help of ANDI. Such a plan needs to include a forecast of demand for the facility at the regional level to ensure its proper future utilization. Furthermore, the plan should detail a financing model to show the sustainability of the facility over time. Potential models include sustained institutional commitment for the maintenance and operating costs of the facility, or its use as a contract research organization that serves both public and private institutions in the region. It is worth noting that facilities support should also be linked to an ongoing ANDI project despite its wider reaching regional impact and its longer lasting horizon.

69. Interviews, country visits – South Africa, Egypt, Kenya and Nigeria (2009); Vendor quotes

Some examples of facility support ANDI envisages, considering an estimated average cost per each facility upgrade/construction of around USD 200 thousand[70], are:

- Support to certify/pre-qualify a pilot plant to produce drugs or diagnostics for clinical trials
- Upgrade of animal facility to increase capacity of separately handling animals infected with different pathogens
- Building/upgrading regional analytical chemistry shared service center in collaboration with research institutions and private sector partners

Information management and sharing support

Information management and sharing depends on a sound and efficient IT platform. ANDI's support to its networks, its governance structures, and the wider African research community is built into the design of such an IT platform.

The platform is divided in two components. A first one aimed at providing open access information to the African research community and other stakeholders. And a second component, for internal use, to facilitate project management, internal project data sharing and monitoring, and the analysis of results generated by ANDI's project networks (Exhibit 30).

The open access search engine component is based on a networking and knowledge management space. This space constitutes the visual interface to the data held by the open access search engine component, and some of the data held in the IT platform component destined for internal use. The publicly accessible data modules are:

- A repository of African scientific capacity and capabilities for scientists to identify potential collaborators and sources of technical help
- A database of African traditional medicine and plants with medicinal potential
- Technical resources with standard operating procedures, protocols, open access tools and links to other relevant databases (e.g., patents, patent pools, etc.)
- Information about ANDI activities, including calls for proposals, success stories, etc.
- Information about other grants, fellowships and opportunities for scientists to access funds and collaboration opportunities
- Fundraising and Diaspora liaison information
- ANDI policies regarding intelectual property, terms of collaboration, materials transfer, ethical guidelines, etc.

The networking and knowledge management base of this component also provides communication services to ANDI's staff and network members. These services include e-mail and remote data storage for ANDI staff, voice over IP with toll-free numbers for staff and network scientists to participate in teleconferences, and virtual lab meeting space for network scientists in different locations to share presentations and visualize data during teleconferences. In addition, the sharing

70. Interviews, country visits – South Africa, Egypt, Kenya and Nigeria (2009); HLW International LLP, ACCU-COST (2008)

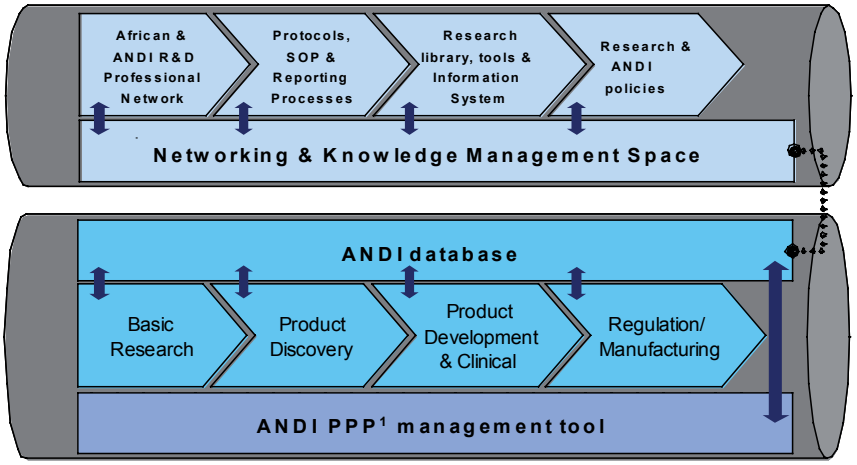


Exhibit 30 – Schematic of ANDI's IT platform ([1] portfolio/pipeline/products)

of information will also extend to the dissemination of the health R&D priorities set by different regions and fora (e.g., those supported by TDR). This is expected to help clarify the most important areas where health researchers in Africa should focus and create transparency across the ANDI networks. In turn, the internal use component is a secure backbone built around ANDI's database and portfolio/pipeline/products management tool. It holds all proprietary data of ANDI and of the scientists that are part on ANDI's networks. It also contains internally accessible data from ANDI's partners for use on specific projects or in the frame of defined collaboration areas. This secure component includes licensed software for use by ANDI network scientists and R&D Directors to analyze and visualize data, to manage project progress, to securely communicate, and to produce the appropriate reports for ANDI's governing bodies and scientific advisors.

To operationalize the described IT platform, ANDI will use existing capacity within TDR as a temporary solution. In the meantime, ANDI's IT team will work towards the end goal of building a platform that suits ANDI's unique needs, preserves the ownership of the data and tools within ANDI and its networks, and at the same time is as cost efficient as possible. To that end, the IT team will make efficient use of available commercial and open access software tools while internally developing the necessary interfaces to combine those tools. Finally, to ensure maximal and efficient utilization of ANDI's IT infrastructure, support in this area will also include training of scientists and ANDI staff.

BROKERAGE

Brokerage is a cross cutting element of all the activities that ANDI performs to engage partners with the goal of developing drugs and diagnostics that ultimately reach afflicted populations. As such, one of the essential activities of ANDI is advocacy. The aim of ANDI's advocacy activities is to promote the sustainability of African-led and Africa-based research efforts through the involvement of governments, local stakeholders, individuals and organizations driving the African health research agenda. Such involvement is not limited to financing, but extends to collaborating in fact gathering, research efforts and capability building, for example, by engaging African scientists in the Diaspora. This results in the creation of important advocacy tools such as fact-based reports, white papers, and workshop and meeting materials. While not normative in nature, these tools are designed to foster key discussions in Africa and to support the ANDI representatives that will drive

such discussions. The advocacy role is structured along three elements: R&D financing, product regulation, and research promotion. Advocacy on R&D financing seeks to increase funds and align investments with local priorities. This element concentrates in engaging local governments, businesses and individuals to fund health research. While it is clear that there are difficulties in ensuring local funding in Africa, the recent drive for improved investment has raised expectations (see Chapter 1 and 2). In addition, it is apparent that initiatives with a fundamental local focus, such as ANDI, will require strong local support if significant funding is also to be secured from non-African sources, i.e., the "first dollar" must come from Africa. As called for by the GSPA, this ensures local ownership and clear south-south collaboration, without excluding north-south partnerships (Exhibit 31). The targets for R&D financing advocacy activities are, depending on the country, the various ministries including Health, Higher Education and Science and Technology, but also multilateral organizations such as AMCOST or the AU. In addition, local pharmaceutical manufacturers and multinational drug companies with stakes in Africa, as well as private foundations and wealthy African individuals living in Africa or abroad, are also targeted. Advocacy on regulation of medicines seeks to contribute to the unification of frameworks across African countries and establishment of international standards. An important regulatory barrier is the need to separately register medicines in each country. Nascent regional initiatives, however, are working to unify regulation and cross-country recognition of product registration, manufacturing facility inspections, and quality control tests (e.g., the initiative to unify GMP inspections across different member countries of the Common Market for Eastern and Southern Africa, COMESA). ANDI will target these regional initiatives, the regional economic and trade blocks, as well as ministries of Economy/Finance and customs. This task is essential to ensure products resulting from ANDI's projects quickly reach the intended target populations.

Exhibit 31 – Global collaborations supporting African R&D centers

With that objective in mind, ANDI also seeks to facilitate research by promoting the unification of procedures for material transfers across borders, import of scientific equipment, and the exchange of human capital aimed at building capacity and fostering capabilities. This implies engaging research institutions but also all sectors of government. Additionally, it also seeks to promote the establishment of international standards for research across African countries. As such, assuring fundamental support by organizations leading the way in establishing standards as well as ethical guidelines, such as the WHO[71], will be imperative. This will ensure recognition and inclusion of locally developed products in the purchasing lists of governments and international organizations, and the possibility to export African-owned discoveries to other regions of the world.

Leveraging partnerships to take part both in funding and in the latest stages of drug development is an important approach that ANDI must use to achieve its goals of health impact. As such, ANDI will focus on implementing shared investment models, including seeding funding to catalyze increased project financing from other partners (Exhibit 32). In leveraging downstream partnerships, especially

71. Examples – WHO/US/American Society for Clinical Pathology/Clinton HIV/AIDS initiative for a Pan-African lab accreditation system; WHO/TDR Empowerment initiatives

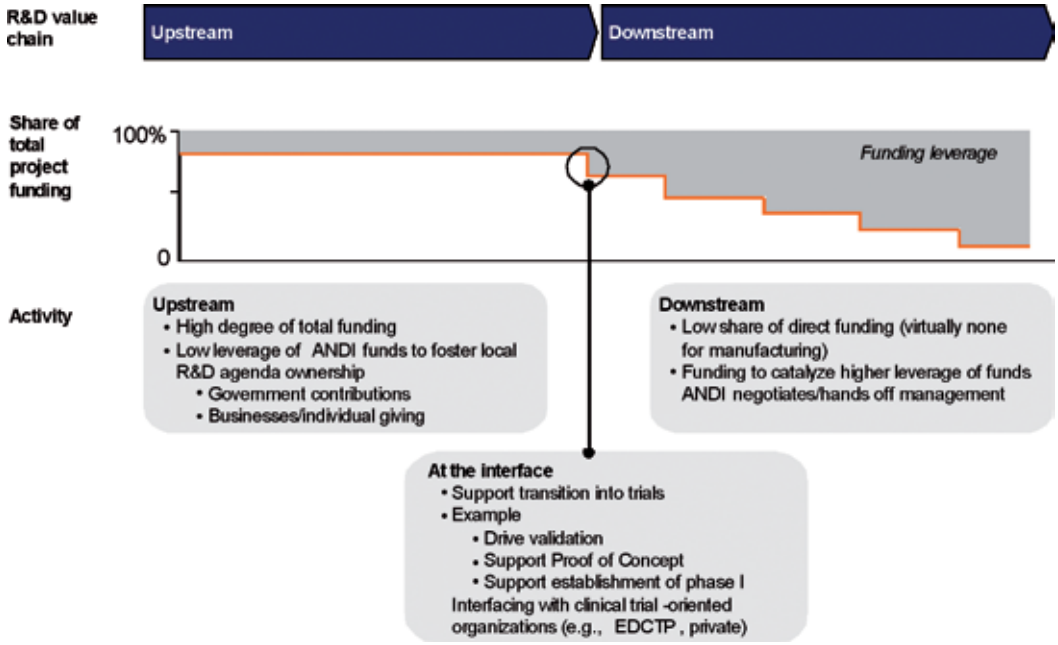


Exhibit 32 – Funds leverage approach

with private companies, ANDI needs to consider their goals. While some may be purely interested in market potential, others may include elements of social responsibility to guide their activities. Logically, products with uncertain or little market potential will require a different model, with ANDI trying to broker risk-sharing agreements between private partners, governments and ANDI itself. Such agreements can include tax incentives, advanced market commitments, grants, or benefit from corporate social responsibility. On the other hand, products with more promising market perspective may require less financial involvement from ANDI or other public sector stakeholders. This scenario could, however, use ANDI and local government financial contributions to develop much needed local manufacturing capacity or to engage local manufacturers, currently concentrated solely on final formulation and production[72], to venture further down into the R&D value chain, for example, into API synthesis/bulk manufacturing, clinical trial support, and lead optimization. Importantly, ANDI must ensure that public resources are not used to support private interests.

BUILDING AFRICAN R&D CAPABILITIES

Through its functions ANDI will leverage the existing capabilities and capacities for drug discovery and development in Africa. A key element of the projects is the networking of complementary centers with emphasis on developing "medium/small" centers with the support of "strong centers". In that sense, the support actions of ANDI will play differently across the network, depending on the type of center (Exhibit 33). The focus will be on optimizing existing "strong" centers and on transfer of technology (capacity) and knowledge (capability) to "medium/small" centers so that they too can develop into key R&D players. In addition, the fact that not only research workstreams are funded, but that there is investment in equipment and infrastructure across different centers is key. Developed technology platforms can be leveraged by the centers that hold them as shared services to

72. Country visit and interviews – Pharmaceutical manufacturers and industy associations (Kenya, Egypt, 2009)

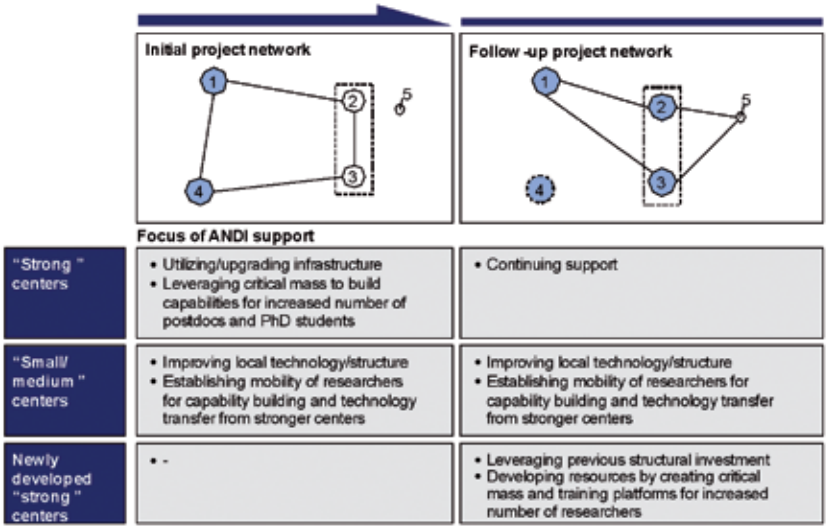


Exhibit 33 – The approach of ANDI to building research excellence across Africa

the portfolio of ANDI networks. The upgraded infrastructures, in turn, allow centers to drive excellence and become stronger. This pull mechanism is fundamental if world-class research excellence is to be developed. It will also help ANDI to identify and accredit health R&D centers of competence and excellence in Africa. One corollary of this approach is the creation of sustainable long-term options for scientific careers in Africa. Currently, an estimated 1/3 of African researchers are outside the Continent[73]. Only by creating an attractive research environment can top researchers be enticed

to continue their work in Africa and young scientists be brought to the mix. This is key to avoiding the current African brain drain. In addition, only by creating significant value for Africans in the Diaspora to bring back their expertise and technology to the Continent can the brain drain actually be reverted. Today, the few labs, few jobs and unattractive research packages limit the value proposition of building a career in Africa. In addition, there are limited or no opportunities for scientific entrepreneurship. In a first wave, ANDI is expected to contribute, directly and indirectly (via partnerships), to an increased number of research centers and of research jobs. For example, considering funding of 5 ANDI projects involving 5 centers each (25 in total) in which 4-5 scientists are involved in a project, ANDI will rapidly develop 100-125 scientists in the first few years. These researchers will be skilled in proposal design and project management, well trained and focused on product discovery and development and will take advantage of new and improved research centers and new technologies. This is important to create the leading groups that will attract more people and are able to compete for other funding beyond ANDI's. As the number of projects grows, so will the cadre of future research leadership develop (e.g., if running 15 projects, ANDI will be impacting an estimated 300-400 researchers).

With time this should result in a second wave, wherein researchers can not only join industry but progressively start taking advantage of newly developed products to launch their own entrepreneurial activities (e.g., CROs, biotechs, etc.). In this case the support of ANDI, both directly or indirectly via fund leveraging, will be key to form the right partnerships and create the right financial and strategic platforms.

73. Network of African Science Academies (NASAC) – Statement June 11 (2009)

5. THE OPERATING MODEL IS THE VEHICLE TO ACHIEVE ANDI'S VISION

ANDI'S VISION

The vision defines the desired evolution of an organization. It is essential to articulate targets and to define the operating model that would be best suited to advance the organization towards those targets. Hence, the visions statement of ANDI is:

> *"To create a sustainable platform for R&D innovation in Africa to address Africa's health needs"*

STRUCTURE BEHIND ANDI'S OPERATING MODEL

The organizational structure behind ANDI's operating model is the enabler to achieve ANDI's vision. For that reason, special attention was placed on making ANDI an organization that will ultimately operate in Africa. In addition, to achieve high impact on health research for Africa, the structure should acknowledge the substantial geographical, cultural, and epidemiological differences within the Continent. As such, ANDI will have a decentralized structure with regional hubs distributed in Africa's regions, and a central office to coordinate hub activities, centralize data, and provide adequate support (Exhibit 34). Ideally, the local hubs would obtain their legal status through the ANDI host organization. This is important to ensure that there are no unnecessary duplication of administrative functions across all hubs but also that the hubs are closely coordinated, maintain a close link and do not operate in isolation.

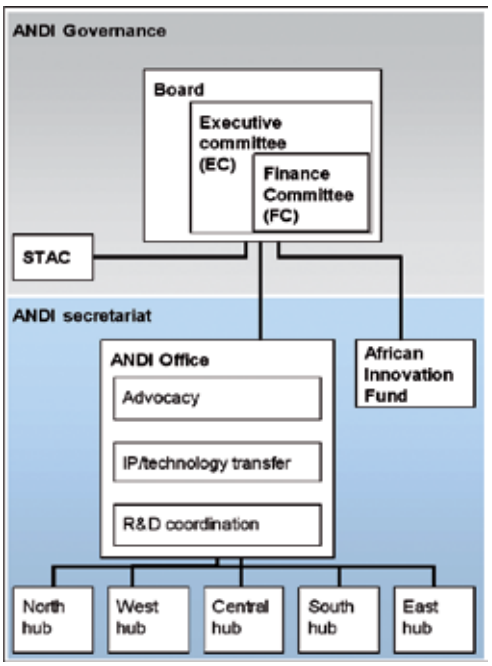


Exhibit 34 – ANDI's organizational model

ANDI SECRETARIAT

Legal status

Staffing the elements of ANDI's operational structure involves decisions around the legal entity under which associates are employed, which in turn defines their employee status, the salary scales used, and the immigration status in the countries in which they work and reside.

To select the best legal set-up, it is necessary to consider what it will take for ANDI to succeed as an organization. On one hand, it is essential that ANDI operates as independently as possible. This is key to ensure that it can set its own oversight strategy, and that it can take decisions on its budget and on talent hiring, retention and development. In addition, it is also important that ANDI operates in the least bureaucratic context possible. This allows ANDI to take rapid decisions and implement them without delay, with full responsibility and accountability, including the quick distribution of funds or personnel appointments. However, ANDI should be in a position where it is credible before donors and other stakeholders within and outside of Africa.

Bearing the above in mind, an institutional arrangement premised on the provision of hosting servcies provided by a credibile multilateral organizationt based in Africa is particulalry attractive. In this regard, hosting ANDI at the African Development Bank (AfDB) appears highly interesting. The Bank has a significant history of legally hosting several initiatives and projects[74]. In doing so, it follows flexible hosting models, which guarantee both the necessary fiduciary involvement of the Bank and the required independence of the different hosted initiatives (e.g., ADEA[75]). This includes the possibility of having a fully separate governance structure, to leverage existing services (e.g., HR, payroll, accounting etc.), and accommodate employees under the employment structure of the Bank (salaries, immunities, etc.). The conditions of employment extended by the AfDB are very attractive and it is a well recognized employer, which would favor hiring of top people. At the same time, the fact that current initiatives at the Bank can autonomously hire and develop their staff is an indication that ANDI would be able to select the candidates it sees fit. In addition, legal hosting does not confine physical hosting to the AfDB itself but rather allows organizations to place their employees in other locations in Africa, as would be required for ANDI. This guarantees organizational cohesion and seamless mobility for the staff. Importantly, the credibility of the AfDB is ideal not only to secure funding in general but also to favor the recruitment of financial support from African and non-African governments, as it ensures recognized financial control and oversight.

In view of the time (6-8 months) requried to put in place the necessary hosting and governance arangements, discussion with AfDB should commence rapidly[76]. In the interim, the incubation potential of WHO/TDR would drive the preparatory work leading up to the formation of ANDI within Africa.

Independently from its legal status or actual location, the fully functional ANDI secretariat is expected to be small and lean.These will either serve the organization in its central office or in its regional hubs (Exhibit 35).

Central Office

The central office houses ANDI's administrative and support functions. The central office fulfills an important coordinating and oversight role for ANDI's networks and regional hubs and at the same time avoids the functional duplication required to place secretariat functions in each hub. Furthermore, to fulfill ANDI's vision, the ideal location of the central office would be in Africa. Given the time needed to carefully choose the location of the central office in Africa, to hire personnel,

74. African Development Bank – Annual Report (2008) and News and Events reports (2009)
75. ADEA – L'association pour le développement de l'éducation en Afrique
76. ANDI – 3rd Task Force meeting (2009)

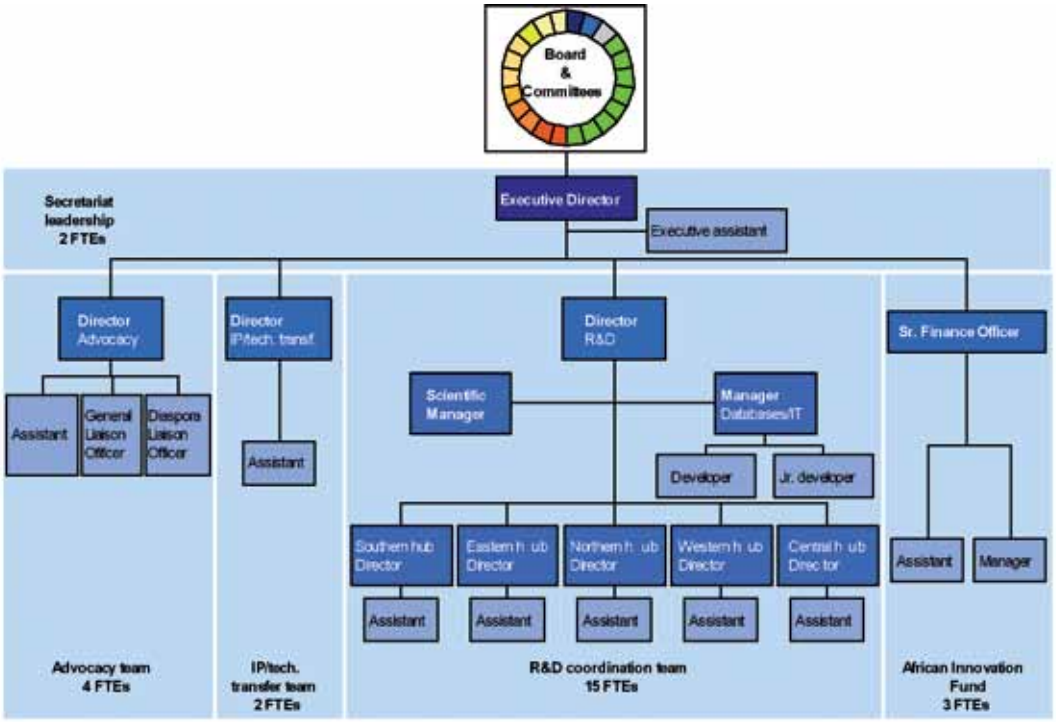


Exhibit 35 – ANDI's organizational model

to acquire the required space, and to negotiate the terms of agreement with the African Development Bank, preparatory work relating to the launch of ANDI in Africa will be managed through WHO/TDR, in Geneva. For the avoidance of doubt, ANDI activities such as for example grant making, the staffing of ANDI personnel, the entering into agreements with third parties in the name of ANDI, will not be undertaken by WHO/TDR. However, WHO/TDR will prepare for such activities and lay the groundwork for their implementation pending the formal implementation of ANDI as a network in Africa. It is critical that ANDI's central office is in a location that ensures not only proper infrastructure and local support but also that is can attract the best talent.

Hence, the criteria to select the ultimate location of ANDI's Secretariat are:

- In Africa, in a space offered by a host country, or in an African organization such as the African Development Bank.
- Degree of support offered by the host country or African organization
  - Space
  - Tax benefits and diplomatic immunity for ANDI and its personnel
  - Salaries for the support staff hired by ANDI (ANDI or legal host sets salary scale)
  - Utilities subsidy
- Reliable communications infrastructure
  - Telephone lines Computer networking
  - Access to international courier services
- Reliable electrical supply
- Convenient air travel to the cities where regional hubs are located and to overseas (Europe, North America and Asia)
- Good quality of life for the families of ANDI's employees[77]

77. For example, resorting to the Mercer Quality of Living Survey (2009)

Regardless of its final location, the central office will house an advocacy team, IP/technology transfer team, and R&D coordination team, which ultimately drive key functions of ANDI as well as related finance and governance functions.

Advocacy team

The advocacy team engages with local stakeholders to increase investment in health R&D and to set research agendas in line with local priorities. It also involves international stakeholders, to support ANDI and, more broadly, African-led and based health research. To specifically link the Africans in the Diaspora with ANDI and support Diaspora-led activities (e.g., ANDI promotion, fund-raising, etc) the advocacy team will have a dedicated person, organizing and liaising this key group. In addition, it collaborates with the R&D coordination team and the African Innovation Fund (see ANDI Governance section below) to forecast financial needs for health research and create fact-based arguments for governments and other stakeholders (Exhibit 36). It is important to note that such documentation is aimed at informing and promoting key discussions rather than at being normative. The advocacy team is composed of a Director, two Liaison Officers and an assistant.

IP/technology transfer team

The IP/technology transfer team is composed of a Director with the help of an assistant (team to grow as ANDI's scale increases). The objective of this team is to protect the intellectual property generated by ANDI's project grantees and to facilitate technology and materials transfer across African borders (Exhibit 36).

R&D coordination team

This team oversees ANDI's projects and drives project portfolio management to ensure efficient progress, help troubleshoot bottlenecks together with the local hub Directors, and facilitate the transition from one phase of the projects to the next across different network members (Exhibit 36). It is composed of a Director with the help of a manager (e.g., linking to the STAC) an IT team composed of a database/IT manager and 2 developers (one of which a junior).

Regional hubs

Regional hubs maintain ANDI's presence at the regional and country level. The legal status of such regional hubs should be assured through the host organization. They report to the R&D coordination team and are in constant communication with the research community, with local governments, and with the leadership of other health-related initiatives ongoing in the region. Hubs are also in charge of collecting local data and surveying the R&D landscape to relay information to the advocacy team. Hubs are lean structures composed of a Director and an assistant. The specific roles of hub Directors are to:

- Regularly visit research centers in the region of influence
  - Surveying local capacity
  - Evaluating technological needs
  - Promoting ANDI's activities
- Serve as the local contact point for network members to solve project issues and access ANDI's support

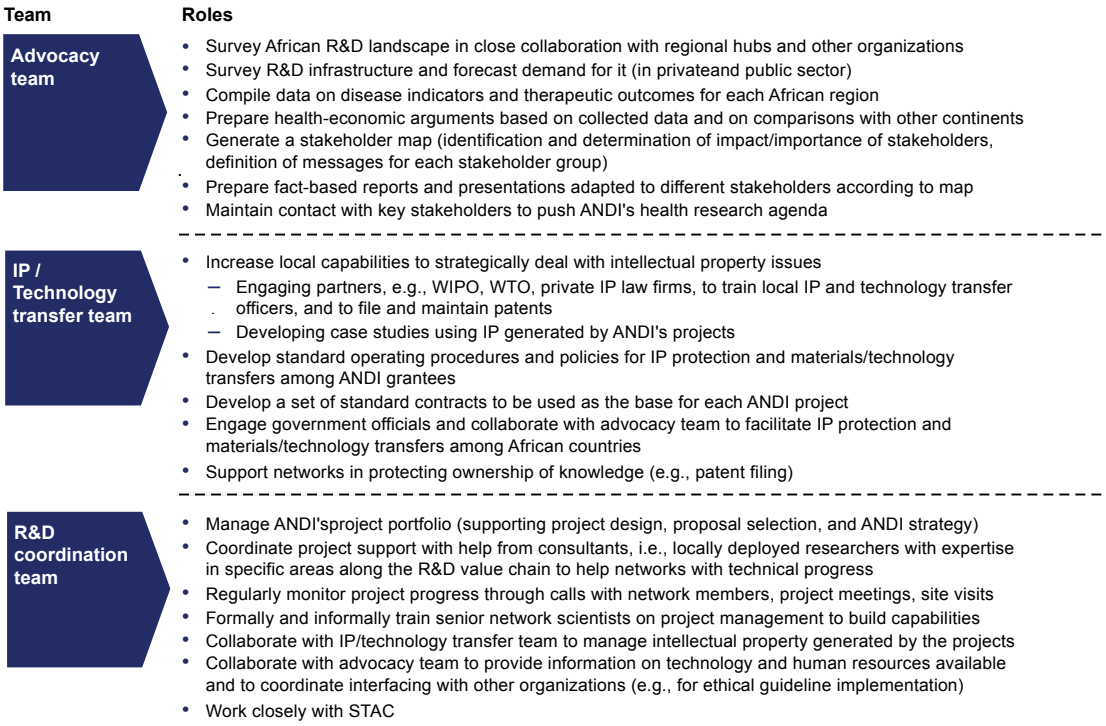


Exhibit 36 – ANDI central office teams

- Contact government officials to locally push ANDI's agenda with the help of the advocacy team
- Serve as the local contact point for scientists outside ANDI's networks
  - Supporting them with proposal development
  - Ensuring they access ANDI's African research database to find potential collaborators The physical location of regional hubs should aim to cover all African regions while preserving an efficient and lean ANDI structure. Due to the size of the Continent and the sub-optimal transportation and communication routes, it is not realistic to envision coverage from a single location. In addition, ANDI needs to be able to deliver its support at the regional level. This is important since health needs are often specific to regions (e.g., HIV/AIDS in the south and eastern regions, Malaria in the eastern, central and western regions, some helminthiasis more prevalent in western countries). Furthermore, African countries are organized into regional economical and trade groups. With the goal of not having more than five hubs, the UN regions of Africa were evaluated as a possible way to group countries into five discrete and non-overlapping sets. Importantly, the different country groups participating in trade, economic, development, and customs agreements[78] align quite well with the division of Africa into 5 regions as proposed by the Unit-

78. ECOWAS – Economic Community Of West African States; EAC – East African Community; ECCAS – Economic Community of Central African States; SADC – Southern Africa Development Community; AMU – Arab Maghreb Union; COMESA – Common Market for Eastern and Southern Africa; IGAD – Intergovernmental Authority on Development; CEN-SAD – Community of Sahel-Saharan States; UEMOA – West African Economic and Monetary Union; CEMAC – Economic and Monetary Community of Central Africa; SACU – Southern Africa Customs Union; CAEU – Council of Arab Economic Unity

ed Nations (Appendix Exhibit 13). This suggests the 5 region breakdown does indeed reflect a true practical grouping of the African countries. Therefore, it is suggested to use the UN regional division and place, ideally, one hub in each region. Such a model would benefit from an established regional definition and from the previous history of cooperation among the countries in each region.

An additional criterion for hub placement is to maximize proximity to the existing research community. This indicates that the preferred location for a hub would be a research center or university. With that in mind, an analysis of Africa's research output was conducted to point towards potential host countries in each African region. Exhibit 37 shows potential candidates as regional hubs. Similarly to the location of the central office, the regional hubs will, in close consultation with the ANDI host organization, be chosen based on the following indicative criteria:

- Sustained research output by the candidate country and proposed city Available space in a research institution, center or university that has shown scientific leadership
- Reliable communications infrastructure
  - Telephone lines Computer networking
  - Access to international courier services
- Reliable electrical supply
- Convenient air travel to the cities where the other regional hubs and the central office are located, and to Europe, the US and Asia
- Good quality of life for the families of ANDI's employees

It is worth noting that although ANDI would have an ideal number of five hubs, initial operation could start with a smaller number, one or two for example, reflecting the geographical distribution of research centers involved in the first ANDI projects.

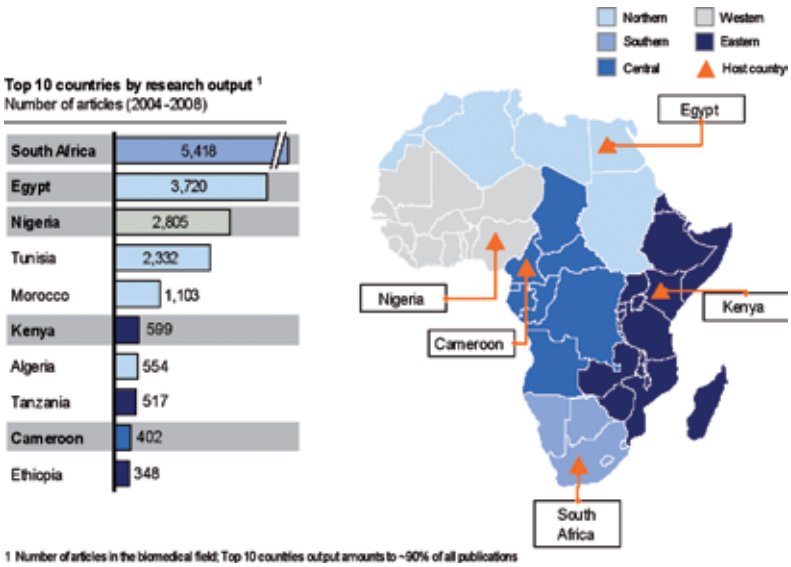


Exhibit 37 – Potential host countries for the 5 regional hubs (source: McKinsey & Co.)

ANDI GOVERNANCE

There are four structures playing different roles in ANDI's governance. These are the Board, the Executive Committee (EC), which is a subset of ANDI's Board, the Scientific and Technical Advisory Committee (STAC), and the Finance Committee (FC) (Exhibit 34).

ANDI's Board

The Board is the highest governing body of ANDI. It drives strategic design and policy making, which in turn is implemented and operationalized by the secretariat, namely through the Executive Director (ED). The responsibilities of the Board are three-fold. One, it determines ANDI's scientific priorities and recommends strategic project support, in consultation with the STAC. This guides the secretariat in establishing and sustaining project networks, namely through its R&D and IP teams. In turn, this allows the Board to suggest remedial actions in case of underperformance and guarantees direct accountability of the Executive Director (ED). Two, it defines the advocacy strategy and supports its implementation by engaging with governments, businesses and individuals through concerted efforts but also through personal relationships. This guides the operational work of the secretariat through the advocacy team. Three, through the Finance Committee, it oversees the flow of funds in and out of the AIF and approves annual budget, ensuring alignment between the financial and R&D activities of ANDI. ANDI's Board ensures wide stakeholder representation. It is propsed that it should be composed of around 20 members that meet annually (Exhibit 38). There would be 10 regional representatives (2 from each region, one on the technical side and one on the policy/political side), which include the Chair and Vice-Chair. In addition there should be some representation from OECD partner governments as well as some eminent African researchers, including representation from the African diaspora with expertise aligned with ANDI's scope. Furthermore, there should be representation from the international and African pharmaceutical/medical product industry and from non-governmental organizations (NGO). Finally there should be some representation from International organizations (e.g.WHO, AU). The AfDB, as host organization, will have a permanent seat on the ANDI Board. In appointing its members, the Board should strive to maintain gender balance.

The Board, in turn, is expected to be supported by a group of observers that will lend their perspective during the Board meetings. In addition to the aforementioned Board members, ANDI's ED as well as the Chair of the STAC (see below), also participate in Board meetings, albeit in an *ex-officio* role.

Notably, the ANDI Board is truly representative in that at least 70% of its members are African, while around half have specific heath R&D expertise. Apart from its credibility within the Continent, resulting from its true intergovernmental nature, the Board will also enjoy high recognition by the international community, both through its members (e.g., OECD representatives) and also through its observers. It is proposed that members are regularly selected by ANDI's Board[79] with the input of each constituency to act for a period of 3 years, renewable one time. The members are not only expected to collectively perform the roles of the Board, but also to

79. The initial Board of ANDI will be selected by the ANDI Task Force with the input of the constituencies

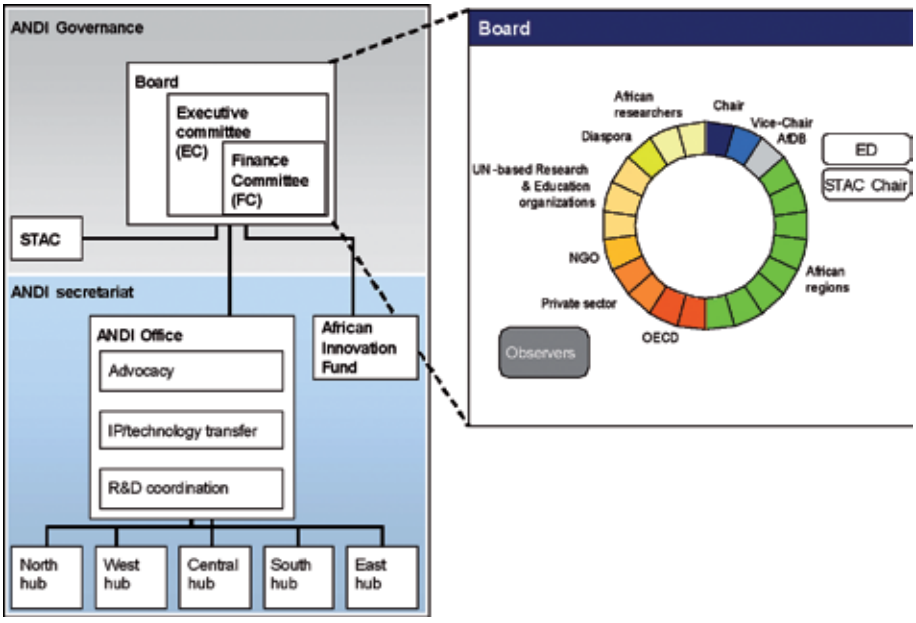


Exhibit 38 – Board structure

individually contribute their expertise on advocacy, health research, or financial management. The characteristics for each constituent member are as follows:

- The Chair and Vice-Chair, in their leadership position, represent ANDI and Africa as a whole
  - They are elected from the 10 regional representatives and can only be selected if they have served a first 3 year term as regional representatives
  - They will balance opinions among the group and, while representing their regions, will ensure impartiality in leading the Board to reach objective decisions This selection and transition process is compatible with the 3-year term of Board members and ensures continuity of ANDI's leadership Importantly, selection of the first Chair and Vice-Chair of the Board will result from a consultative process including the ANDI Task Force, the existing newly appointed members of the Board and the regions, to ensure leadership of this key governance body can be rapidly established while ensuring full alignment of all stakeholders
- AfDB delegate provides financial expertise and representation of overall Pan-African financial interests
- WHO delegate provides health and health research expertise and provides an international health perspective African regional delegates represent each of the 5 African regions
  - ANDI's Board consults with appropriate regional representative bodies for selection of regional representatives
  - An equal balance will be sought between representatives with a more marked health policy orientation (e.g., representatives of Ministries of Health or Higher Education) and with a more scientific orientation (e.g., representatives of Ministries of Science and Technology, or from public research institutions)
- OECD delegates ANDI's Board assembles a short-list of potential representatives from this constituency and individually invites candidates to become, or nominate, the respective Board members Private sector members represent the local and the global pharmaceutical/medical product arena

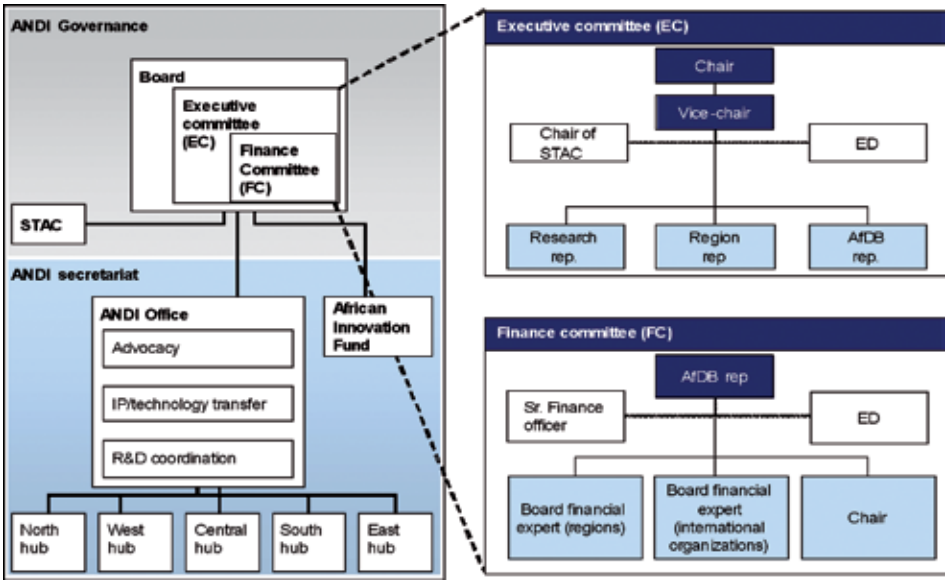
- Non-governmental organization (NGO) representative the local and the global NGO community
- African researchers and the diaspora researchers provide scientific expertise
  - ANDI's Board nominates the members for this constituency after assembling a short-list of potential candidates
  - In addition to their roles as Board members, the members of this constituency are expected to contribute their scientific expertise to ensure proper understanding, by the rest of the Board, of current health and research challenges in the different regions of Africa
  - ANDI's Board should guarantee that no conflict of interest with ANDI project selection and funding arises during the service of the selected researchers
- International observers support the Board
  - International agencies and foundations can apply to be observers and, if accepted by the Board, nominate their representative to ANDI.
  - Such agencies and foundations are selected as they develop direct links with ANDI, for example, through funding of ANDI, support of ANDI activities, etc.
  - While their observer role is expected to continue in the long term, the representatives should serve 3-year terms, similarly to those of Board members

In operating as the main governance structure, the Board might decide to structure itself into committees. These would be responsible for deeper understanding and analysis of specific issues of concern for ANDI's strategy, function and progress, and for making the policy making process more effective for the Board as a whole. (Appendix Exhibit 14).

Executive Committee (EC)

The Executive Committee consists of a small representation of the constituencies of the Board, meeting quarterly and geared to support and oversee strategy implementation and execution (Exhibit 39). The roles of the Executive Committee are to:

- Closely track the detailed progress of ANDI
- Review progress against set milestones and suggest remedial actions in case of underperformance
- Take immediate operational decisions, in consultation with the Board, on issues escalated by the ED. Major strategic decisions should only be taken by the full Board.
- Interact with the Scientific and Technical Advisory Committee (STAC) following up on the review process and keeping track of overall scientific quality of new and existing projects
- Oversee disbursements on a quarterly basis
- Contextualize decisions taken by the ED during the year in front of the Board
- Support preparation of annual Board meeting The Executive Committee is formed by Board members, which are elected to serve for 3 years, renewable one time. Direct representation of the Board at the EC ensures that execution oversight in always aligned with strategic oversight. As such, progress and issues experienced throughout the year are properly communicated to the Board during its annual meeting.



Exihibit 39: EC and FC structure

The Executive Committee is composed of 5 members, as follows: Chair and Vice-Chair of the Board, a selected African researchers in the Board, which can also be the Diaspora representative (scientific input), the representative of the AfDB (financial input) and a regional representative (advocacy input). The ED and Chair of the STAC (see below) also participate in EC meetings in an *ex-officio* role. The Executive Director (ED) reports to the Chair and Vice-Chair and answers to the Board. The ED is the ultimate responsible for ANDI's Secretariat and Hubs performance and hence for successful strategy implementation. As such, the ED must ensure the quality and success of calls for proposals, project milestone achievement, the development of fact-based advocacy materials, positive results of advocacy campaigns, IP capability building in the regions, efficient project support, etc.

Scientific and Technical Advisory Committee (STAC)

The STAC is composed of scientific experts of international reputation in the areas of concern to ANDI's projects. This specialist panel is chaired by a renowned African researcher that will also represent the STAC *ex-officio* at Board and EC meetings. It is expected from scientists in the Diaspora to contribute their expertise by becoming members of the STAC. The STAC will be established considering that, typically, three recognized scientists will be chosen for, and dedicated to, each project. Its members are selected *ad-hoc* to adjust the level of expertise to ongoing projects. They meet in person to evaluate projects and project proposals (1-2 times per year) and receive the progress reports from projects in their field of expertise to review. The mission of the STAC is to ensure scientific rigor in the project selection process, to uphold high quality standards for project reviews, and to evaluate the scientific impact of grants for critical equipment purchases and facility building or upgrades. Their roles are to:

- Advise Board, EC, and ED on scientific and technical aspects
- Evaluate grant proposals
- Recommend selected proposals to the ED and Board for funding
- Review ongoing projects
- Recommend grant renewal/withdrawal based on scientific progress
- Advise the Board on specific issues that require their scientific expertise

STAC members are appointed by the Board, including the Chair. The Chair of the STAC serves a 3-year term, renewable one time. Other STAC appointments occur when new ANDI call for proposals or new ANDI projects require expertise not already present in the STAC. STAC members can be replaced at the discretion of the Board.

Finance Committee (FC)

The Finance Committee as part of the EC will report to the Board on the financial activities of the African Innovation Fund that will be located with the AfDB. The FC will be responsible for providing advice on all policy and strategy issues relating to Finance. It would also review and provide advice on the ANDI's budget and operating expenses. In addition, the FC reviews the ANDI's and the AIF's Audited Financial Statements for each year, and make recommendations to the Board regarding the approval of the Financial Statements. Importantly, the FC will be tasked with providing advice to the Board on the ANDI's fiscal management policies and processes, including asset-liability coverage, financial forecasts, modalities of contributions and investment policies for the AIF's financial assets. Finally, the FC would serve as lead committee for conducting the AIF's replenishment process and eventual endowment activities.. Bearing in mind that it is envisaged that the AIF will be part of the AfDB accounting system and the AfDB will therefore act as trustee for funds deposited in the AIF. The operations of the AIF will also be subject to the oversight and accountability framework of the AfDB. However, decsions regarding, the flows of funds in and out of the AIF, would be made by the ANDI Secretariat. The ANDI Secretariat will appoint a dedicated Senior Financial Officer to manage this process. The operations of the AIF will be subject to the internal and external audit procedures of the AfDB. In addition, the Secretariat will be required to make periodic reports to the Board through the FC on the operations of the AIF.

KEY ELEMENTS OF ANDI'S PERFORMANCE MANAGEMENT

Performance management is essential to ensure ANDI's resources are properly utilized and that return on those resources is in line with ANDI's strategy, as set by its Board. Systems for performance management in ANDI are aimed to expose the Board and the Executive Committee to facts that allow them to evaluate the progress of ongoing projects, the impact of the activities undertaken by the central office and the hubs, and the evolution of the African Innovation Fund. The right set of Key Performance Indicators (KPIs) should encompass measurable outcomes. Specifically, KPIs need to be metrics relevant to ANDI, and which ANDI seeks to improve by operating in accordance to its mission. As such, the expected outcomes of ANDI, as well as the underlying KPIs, align with the operating principles of ANDI itself (Exhibit 40).

Operating principle	Expected outcome	KPIs
Collaborative R&D and capacity building	• Increased collaboration among African R&D centers	• No. of projects vs. budgeted target • Avg. no. of countries per project • Avg. no. of countries per article published by ANDIresearchers (historical, current)
	• Human capital development	• No. of researchers trained in ANDIprojects (MSc., Ph.D., postdoc) • No. of Ph.D./postodocsas first authors in an ANDIproject article • No. of individual travel allowances granted for international conferences • Share of researchers moving to next career step (within/outside Africa)

Operating principle	Expected outcome	KPIs
Research quality and translational drive	• Funding of high quality projects	• Share of proposals recommended for funding by the STAC • Share of proposals funded • No. of research articles in a peer-reviewed journal per project • No. of projects successfully finished
	• Successful product development	• Share of projects successfully reaching last progress report • No. of translational steps completed/project • Share of products transitioning to clinical trials/evaluation • No. of products at each stage of the R&D value chain • Share of products with granted market access

Operating principle	Expected outcome	KPIs
Project funding	• ANDI's financial sustainability	• Total ANDIyearly fund raising vs. target budget • Total endowment level • Fund rate of return
	• Degree of financial involvement of ANDI partners	• Total and avg. leverage from ex-ANDI sources for ANDI project • Share of country vs. non-country funding • No. of donors being leveraged per project
	• Increased R&D spend in health research in Africa	• Health R&D spend per capita per country • Share of health R&D dedicated to drug discovery and development • Share of R&D spend contributed by the public

Operating principle	Expected outcome	KPIs
Network support	• Improved technological platforms	• No. of applications for equipment and infrastructural funding • No. of times invested platforms are used by researchers external to the hosting institution • No. of users of ANDI'sopen access search engine • No. of full records on African researchers in ANDI's database
	• Improved technology transfer	• No. of evaluated inventions • Share of filled patents that are granted • No. of licensing deals • No. of times a partner is involved in a project • Share of ANDIresearchers trained in technical areas

Exhibit 40 – Key performance indicators

6. FINANCIALS

BUDGETARY NEEDS

Initial funding

Having decided on the most appropriate organizational structure and financial model for ANDI, a detailed budget is required. This will help raise the necessary funds to turn ANDI operational, but also to design and set-up the African Innovation Fund. Calculating the required budget takes into consideration two major dimensions. One is the project financing cost, which includes workstream funding, equipment and facility support as well as other expenses such as travel, the STAC and the scientific consultants. The other is the running costs of ANDI, which includes, for example the different offices and its governance structures. It is estimated that ANDI will start the implementation of its business plan in the third quarter of 2009 (year 0) at TDR (Exhibit 41). There is an initial spend (USD 0.3 million) on the *ad interim* management team, which includes a manager and an assistant manager working with the leader of Innovation and Research at TDR, and on initial Board meetings, as this key governance structure starts to be set up. The first full year of operation is 2010 (Year 1) during which a series of activities are planned (see Implementation chapter), including the selection of the initial 5 projects. In this case the first costs associated to project networks are incurred (USD 0.4 million) for STAC activities and for the first ANDI annual meeting (i.e., 3rd ANDI stakeholders meeting). The recruitment of the ED is also initiated by the Board at the end of 2010. The first 5 selected projects are scheduled to start on Year 2 (2011) increasing project financing to a total cost of

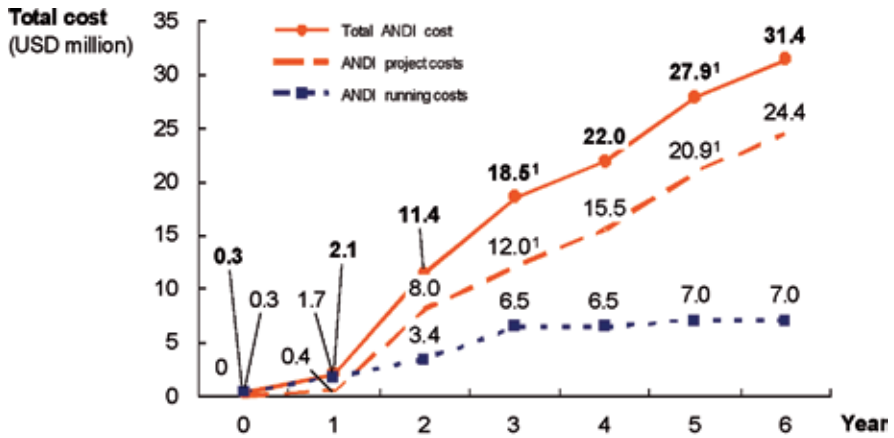


Exhibit 41 – Budget projections

USD 8 million. In addition, transition between TDR and the African central office location and between the *ad interim* management and the full ANDI team starts this year, as does the AIF, elevating the running cost to USD 3.4 million. In 2012 (Year 3), ANDI moves into full operation as all selected hubs are launched with the respective personnel and the central office itself is fully staffed. In addition, two more projects are added to the portfolio and the first IT investments are completed, elevating the total ANDI annual cost to USD 18.5 million (Exhibit 41, and see also Table 1 and 2 for detail). From then on and out to Year 6 of operation (2015) the direct investment in research networks keeps increasing at a steady pace, while running costs remain stable (see also Appendix Exhibit 15 for potential budget variations). This is possible because all the basic functions of the organization are implemented, allowing ANDI to rapidly launch and aggressively enlarge the project portfolio. In addition, by Year 4 specific investments in preclinical developments (USD 1.5 million per annum) are also planned to ensure products move into clinical trials. As such, it is expected that around 80% of the total ANDI budget will be dedicated to research by 2015. By year 7, each of the first 5 projects (started in 2011 and considering 5 years of funding) will have received a total USD 5 million for its research workstreams plus USD 1.5 million for critical equipment, USD 0.45 million for facility investments and USD 1.5 million for preclinical development. Thus, total investment for these initial projects will have been over USD 42 million.

Local contributions

To ensure immediate African ownership of the ANDI projects and of ANDI itself, it is crucial that local contributions are secured as soon as projects are selected. One form of local contribution expected is an equivalent investment of 10% of direct project cost by each of the centers in a project network. This is a clear mechanism to ensure local institutions are fully supportive and that local financing to ANDI is guaranteed, independently of individual governments wanting to contribute directly to ANDI's fund or not. Such contributions can be done in any form (e.g., in-kind, in-cash, in-place, as overhead replacement) to allow for smaller centers to participate in whichever form they can. Importantly, upon ensuring such local funding, the equivalent sums in ANDI's budget will be ring-fenced for investment in other activities, namely targeted financial support of downstream activities. This is important as such expenses are likely to be necessary to ensure any product arising from a project can be moved downstream (e.g., via a proof-of-concept study or support in accrediting a trial center). In addition, it is an indirect way to pool local support and leverage it across the Continent, wherever necessary. It is estimated that by year 3 USD 9.7 million are invested directly into network research centers (workstream, technology and facility support). Hence, the amount to be ring-fenced can reach up to ~USD 1 million at this time, and this sum would be applied to any product being developed with the scope of an ANDI project.

In addition, local contributions towards administrative cost are also expected from the institutions that host ANDI offices (central, hubs, fund office). This administration cost was estimated to be USD 0.5 million by year 3 or 10% of the total cost of the offices[80]. ANDI envisages that local hosts will be able to contribute half of the administrative costs (i.e., 5% of total secretariat cost).

80. A 10% share of administrative costs was deemed feasible and desirable when benchmarking against other similar organizations.

Table 1 – Budget estimation details for project financing base for year 3 (2012)

Line item	Estimated cost USD million	Personnel FTE	Key assumptions
• Work stream funding	7.00	-	• USD 1 million per project for 7 projects with 5 centers per project • USD 200k per center per year as estimated in country visits and using international benchmarks (for salaries, consumables etc.) • Includes investment in mobility also to bring researchers together for 2 day meeting to finalize proposals • Contributions to institutional overhead (if applicable) already included (to a maximum of 20%); Institutions also assure reporting of project accounting for auditing purposes • Expected leverage from local sources of 10% (USD 0.7 million)
• Equipment grants	2.10	-	• 1 critical piece of equipment (beyond cost addressable with workstream funding) per project • USD 300k per piece of equipment as estimated from country visits and vendor information • Expected leverage from local sources of 10% (USD 0.2million)
• Infrastructure g rants	0.83	-	• 2 research facility upgrades/construction per year in total of all 5 networks • Each upgrade/construction estimated at USD 225k as per HILW LLP • USD 200k for IT support infrastructure (USD 150k for maintenance of current system and USD 50k for system development) • Expected leverage from local sources of 10% (USD 0.05 million)
• Travel allowance	0.42	-	• USD 4k per person per year (3 people per center to a total of 75 people) • USD 2k air travel, USD 0.3k insurance, USD 0.8k lodging (4 days) • USD 0.6k per diem (4 days), USD 0.3k for meeting registration
• Annual meeting	0.30	-	• Same cost as Abuja meeting (October, 2008, around 250-300 people)
• STAC	0.19	-	• USD 7k per member per year assuming 3 members per project (total STAC panel with 15 members) • USD 1k proposal reviews • USD 6k for Annual meeting travelling (USD 3.5k air travel, USD 1.5k lodging for 5 days, USD 1k per diem (5 days)
• Scientific consultants	0.15	-	• Consultant panel formed by 6 members (servicing 5 projects) • USD 25k per consultant with multiple visits (as per TDR 's experience)
• **Total**	**10.99** [1]	-	

1 Excludes USD 1 million one-off costs to setup the IT platform

Table 2 – Budget estimation details for running costs base for year 3 (2012)

Line item	Estimated cost USD million	Personnel FTE	Key assumptions
• Hubs	1.75	10	• 5 hubs, each composed of: 1 Director (228/year), 1 assistant (121k/year) • Hubs is hosted by local institutions • 10% of admin cost (USD 0.15 million), half of which to be secured by local institution
• Central office	2.27	13	• 1 office, composed of: • **Leadership:** ED (279k/year) w/ executive assistant (140k/year) • **R&D team:** 1 Director (264k/year), 1 manager (120k/year total), 1 DB manager (228k/year), 1 developer (156k/year ea.), 1 Jr. Developer (140k/year) • **IP team:** 1 Director (228k/year); 1 assistant (121k/year total) • **Advocacy team;** 1 Director (228k/year), 1 assistant, 2 liaison officers (121k/year each) • Office is hosted by TDR or local institutions • 10% of admin costs to be supported locally (USD 0.2 million)
• African Innovation Fund	0.51	3	• Fund composed of: 1 SFO (264k/year), 1 assistant and 1 manager (121k/year each) Fund office location to be determined 10% of admin costs to be supported locally (USD 0.05 million)
• Governance	0.16	-	• Cost associated with Board, Executive and Finance Committee relates to meetings of these groups • Meeting travel for 10 Board members (other 10 expected to travel at own expense) – 1 meeting/year • Meeting travel for the 5 Executive Committee members – 2 meetings/year • USD 8k per member of Boeard or EC per meeting • USD 5.5k for air travel, • USD 1.5k for lodging (5 days) • USD 1k per diems (5 days)
• Hub IT training	0.15	-	• Delivered at hub/regional level and coordinated by the IT personnel of the R&D team
• Non-personnel cost	1.13	-	• 20% of total ANDI running cost associated with FTE (on a base of USD 4.2 million) • Includes travel (65%), professional services such as external auditing of the ANDI operation (20%) office maintenance (10%) and office consumables (5%)
• **Total**	**5.97** [1]	**26**	

1 Estimated Admin costs of USD 0.50 million including rent, parking, cleaning, admin support, staff development excluded from total (total is USD 6.47 million)

Long-term perspectives

The level of direct funding provided by ANDI is of around USD 8.5 million over 5 years for each of its initial projects (finishing in 2016). This is appropriate considering the R&D costing benchmarks[81] for both fixed dose combinations (FDC) and new chemical entities (NCE) developed in PPP projects. For example, lead identification programs cost around USD 2.5 million, while inclusion of preclinical work is costed at around USD 4.5 million. In addition, the development of an anti-malarial NCE (from discovery to 6 months into phase I) costed USD 11.5 million while an FDC development from preclinical to registration was costed at around USD 15-20 million. However, the range is highly variable for projects including significant downstream efforts. This is illustrated by the example of a TB NCE that costed USD 86 million to take from preclinical up to end of phase III. While ANDI funding appears well aligned with the needs of projects aimed at bringing products into clinical trials, leverage from other sources will be necessary for downstream R&D. Depending on the required funding, this can easily be equivalent to 5 times ANDI's funding and it can be significantly higher if manufacturing capacity investments are required. As is, the budget of ANDI needs to be leveraged to significantly address the drug discovery and development R&D investment gap (see Exhibit 4). This clearly points out to the fundamental role ANDI can play to broker the involvement of other partners. Encouragingly, several recent projects yielding promising products have found significant downstream support, including that of pharmaceutical companies (e.g., DNDi/Merck collaboration, Wyeth/TDR collaboration, TB Alliance/J&J collaboration). However, it also indicates that ANDI will need to ensure some flexibility as it defines its activities and its budgetary needs every year. This is important to guarantee that, where needed, ANDI can focus more efforts in a specific activity. An example would be a project showing great promise but needing more support in downstream sections such as clinical trials. In this case ANDI would need to proactively work to get partners on board ahead of time while potentially also focusing on raising its own funds to enable such project financing. Ultimately, this means that it will be key for ANDI to continuously monitor the R&D funding needs so as to adjust its budget growth model. In that sense, it is expected that by year 6 of operation (2015) an analysis of the achievements and gaps of ANDI will instruct strategic decisions for the following 5 year period (to 2020, see Appendix Exhibit 16). Potential scenarios include maintaining the course, in case the number of funded projects and partnership leverage is adequate to effectively move products forward (predicted budget would raise to USD 33 million), or growing the portfolio in case not enough opportunities are created to move products into downstream development (up to 20 projects, with a budget of USD 39 million). In addition, ANDI might, at that point, decide to play a more direct role in supporting investments downstream if that is required to ensure ANDI's strategy is successful. In such a scenario the annual budget could double to USD 61 million if ANDI would support one compound Phase I and one compound Phase II study per year.

81. Wellcome Trust – The New Landscape of Neglected Disease Drug Development (2005)

POTENTIAL MODELS FOR THE AFRICAN INNOVATION FUND

In the section discussing governance structures, the African Innovation Fund and its relationship with ANDI's Board were introduced. There, emphasis was placed on accountability and oversight of the AIF to ensure a healthy balance between ANDI's operational needs and the sustainability necessary for long-term support of projects aimed at drugs and diagnostics development. With that in mind, three key elements are pivotal to define the ultimate shape that the African Innovation Fund should take:

- Accountability and oversight of the AIF
- Sustainability to ensure ANDI's activities can endure in the long term
- Constancy of funding streams to maintain adequate project support

Accountability and Oversight

As mentioned above, the African Innovation Fund will be part of the ANDI host organization accounting system and the ANDI host organization will act as trustee for the AIF. The operations of the AIF will be subject to the oversight and accountability framework of the ANDI host organization. Decsions regarding, the flows of funds in and out of the AIF, would be made by the ANDI Secretariat. The ANDI Secretariat will appoint a dedicated Senior Financial Officer to manage this process. The operations of the AIF will be subject to the internal and external audit procedures of the ANDI host organization. In addition, the Secretariat will be required to make periodic reports to the Board through the FC on the operations of the AIF. Such arrangements will ensure that an appropriate accountability and fiduciary framework is in place. The Global Fund is an example of a similar setup. The funds are hosted at the World Bank, which acts as a trustee disbursing funds directly to the recipients upon approval by the Fund Board.

A fund that not only collects, but also invests the available assets involves taking investment decisions and establishing a risk-return strategy that is compatible with ANDI's mission. This inherently more complicated task implies a more complex setup and, therefore, more elements to guarantee efficient operation and higher oversight to ensure accountability. It is worth noting that investment of ANDI's assets does not imply an aggressive return strategy. Investment objectives range from obtaining enough returns to sustain complete operations, to simply keeping up with inflation or hedging against large currency fluctuations. In this regard, the role of the Senior Financial Officer in an accountability framework that is overseen by the FC is critical.

Sustainability and constancy of funding streams

Achieving a sustainable financial position and a constant stream of funds to support the long-term running of ANDI's operations is directly tied to the sources of funds. Current models of funds sourcing at international organizations and health research-focused institutions can be divided in traditional donor-based funding, innovative public health funding, and endowment fund.

Traditional donor-based funding

This option relies on periodic (annual/biannual) campaigns to raise funds. These campaigns target potential donors by showing past successes, future plans, and how responsibly funds previously donated to the organization have been used. Target donors tend to be public institutions like governments or institutes of health, and large private foundations.

In this context the AIF would function well at exisiting organizations, such as the African Development Bank (or the World Bank). These institutions are familiar with this type of funding model and have all the mechanisms in place to manage them. The advantage of such a funding scheme is that, being the most prevalent, it benefits from donor trust. Large and recognized organizations like the WHO and the Global Fund use this mechanism to secure the funds for their activities.

On the other hand, repetitive reliance on donors entails serious risks to sustainability. Donor priorities change over time as their objectives evolve and their economic situation fluctuates. The Global Fund, for example, is experiencing this risk first hand, currently counting a USD 3 billion shortfall for their current replenishment campaign. This is due to several reasons including the decision of the American Government to fund certain priorities directly rather than through the Global Fund and the current economic downturn[82]. These examples show that uncertainty around donor-based funding may end up compromising the sustainability and constancy of funding streams for ANDI.

Innovative public health funding

Responding to donor volatility, recent innovative sources of funds are becoming more popular. These innovative sources do not depend directly on donor objectives. Instead, they rely on mechanisms believed to be more stable. Work on defining and documenting such innovative financing mechanisms has been recently completed by the Taskforce on International Innovative Financing for Health Systems[83] and is currently under way by the WHO Expert Working Group on R&D Financing[84]. Some of these mechanisms include:

- Government-controlled streams, e.g., indirect taxes to airline travel, currency transaction taxes, debt swaps such as Debt2Help, and government backed bonds schemes like IFFIm[85]
- Commitments from the private sector, e.g., Advanced Market Commitments for Vaccines
- Performance-based commitments from public and private donors, e.g., cash on delivery schemes such as paying a fixed amount for every child vaccinated as done by GAVI's Immunization Services Support (ISS)
- Consumer awareness, e.g., blended value products like (PRODUCT)RED Existing organizations like the African Development Bank have experience with this type of funding models, and could therefore be suited to hold the funds.

The advantage of such mechanisms is that they generate recurrent income. At the same time, they are more long-term focused and, therefore, more suited to achieve sustainability. Unfortunately, high economic exposure is still an issue for these sources. Economic downturns damage

82. Interviews - Global Fund members (2009)
83. Taskforce on International Innovative Financing for Health Systems – Report (2009)
84. http://www.who.int/phi/R_Dfinancing/en/

tax and product revenues, and make long-term commitments from the private sector more difficult to obtain. Furthermore, the relative novelty of some of these funding mechanisms implies multiple negotiations with many different parties. In summary, although improving sustainability, innovative public health funding still suffers from uncertain constancy of streams and complicated management of a diverse portfolio of funding sources. While clearly not to be excluded as a source of funding, this type of stream will require significant and long-term efforts to engage multiple stakeholders (e.g., different governments) and progressively increase its associated contribution.

Endowment fund

Proven to achieve sustainability and with the capacity to be managed in a "through cycle" approach, the establishment of an endowment fund has been the prevalent model for research institutions and private foundations. These funds require the maintenance of capital with projected returns in line with the budget of the organization. After the initial setup using an adequate amount of seed capital, sustainability and a constant return stream can be achieved through professional management with clear incentives to ensure performance. Endowments do face the risk of poor management, and market volatility. These risks are, however, manageable. Fund managers, as employees of the organization or servivce providers, can be properly incentivized to achieve high performance or replaced in case of poor management. Market volatility can be better managed in an endowment due to the flexibility to quickly reallocate assets to manage that risk. In the case of donor-based funding and innovative mechanisms, the fund cannot take measures to limit its exposure to ongoing economic conditions.

Although it is unclear to what extent such a model could be fully implemented in the frame of the African Development Bank, there are encouraging examples. ADEA[86] holds its funds at the African Development Bank in a relatively independent unit with its own governing Board. The organization was capable of setting the fund in that manner due to the alignment of its mission with the goals of the Bank. Such a solution benefits from the credibility of the Bank, its ties to Africa, and the available infrastructure. The costs, operational details, types of asset classes available for investment, and performance of such independent funds held at the African Development Bank need still to be explored in further detail. Data from the Global Fund, however, indicates that World Bank investment returns are well below what other educational and non-profit endowments achieve[87]. Another possibility is to use the services of any established private bank, as these institutions have experience with this type of holdings. There is also a wide array of providers that deal with private foundations and public endowment funds. These private solutions have the disadvantage of not being the norm in the international organization arena, and may therefore create a falsely high perception of risk in the eyes of donors. On the other hand, the actual risk profile of the investment portfolio can be fully governed by ANDI's Board through its EC, FC and the ANDI Secretariat Senior Financial Officer. Another major advantage of an endowment is that it can accept funds from any source big or small, traditional or innovative.

85. IFFm (International Finance Facility for Immunization) – Programme overview (2006)
86. ADEA – L'association pour le développement de l'éducation en Afrique
87. From inception until the end of fiscal year 2004 the Global Fund averaged 2.5% of investment income derived from contributions (Trustee Reports); during the same period, professionally managed US educational endowments averaged 7%

Unlike traditional donor-based funding, an endowment does not need to only focus on institutional donors through elaborate campaigns. The Stanford University case shows that, contrary to popular belief, small gifts do make a difference. Most donations to the university are under USD 1,000, but combined add several million to the fund each year. In fact, Stanford received USD 911 million in gifts in 2006, each gift averaging less than USD 13,000. The possibility to tap into smaller sources of funds does not preclude traditional sources. Stanford and many other research institutions in the US receive major sums from government and private foundations in the form of donations and grants. This donor flexibility maintains the ability to receive funds from the sources typical for other health-focused organizations. However, it also opens the possibility to tap into non-conventional funding options such as debt swaps with African governments, while opening a channel for Africans in the Diaspora and, in fact, all people of African descent, to participate as donors. A disadvantage of an endowment-based mechanism could be that some donors may be unwilling to support endowments, as they are not traditionally used in the context of international organizations. Donors might feel contributions to an endowment as directly funding the organization itself rather than its objectives or projects. This is, however, the case with most research institutions too. In fact, not all donations to the institutions that do have endowments end up supporting the endowment. Some of those donations are restricted for current use or for specific projects. As endowments are independently managed, their presence do not preclude tapping into gifts, grants and donations destined for immediate use. In the case of ANDI, while every effort is to be made to highlight the fact that an endowment will allow sustainable funding for health research projects in Africa, it should not restrict access to other funding streams.

It is worth noting that endowment funds are becoming more common for non-profit organizations in the developing world, including in Africa. Moreover, it is not necessary to look for inspiration into star funds like the multi-billion dollar endowments from Harvard, Stanford or MIT. Endowment funds in the developing world illustrate the plausibility of the task and, despite their smaller scale, are also examples of sustained growth, innovative capital sourcing, quick setup and good performance. The endowment of the University of Cape Town, organized around an independent foundation and a trust located in the UK, for example, has grown to a significant size that at the end of 2007 reached USD 240 million[88]. The Foundation for Community Development in Mozambique is an example of successful local fund raising. Through personal contacts (mostly with mid-size businesses) and advocacy, they were able to locally source USD 300,000 to start building an endowment in the late 80s. A few years later, they participated in a debt swap with the Mozambican government that provided additional USD 3 million[89]. In Colombia, the Corona Foundation established its endowment fund in less than a year with donations from individuals. Ten years later, after reaching over USD 25 million, the fund provided almost 70% of the foundation's budget with 9% annual returns[90].

88. University of Cape Town – Annual Report (2008)
89. The Synergos Institute – Building Endowments (2000)
90. The Synergos Institute – Building an Endowment: A Case Study of the Corona Foundation (2000)

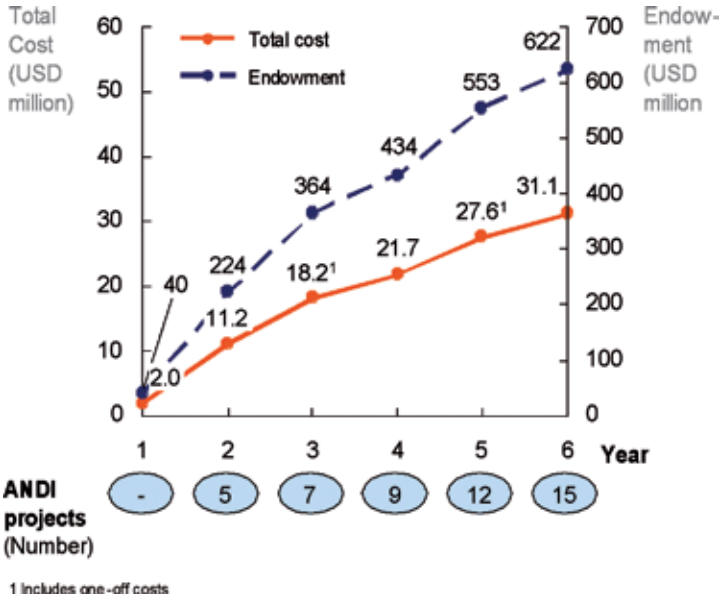


Exhibit 42 – Endowment size needed to fully support ANDI (considering local contribution for administrative costs)

ANDI's full budget calculated in the previous section for the full operational organization (Year 3) starts at around USD 18 million and reaches around USD 31 million by 2015 with 15 running projects. Assuming a conservative rate of return of 5%, the endowment should start operations in 2012 (Year 3) with USD 364 million to fully cover ANDI's costs. The endowment should grow to USD 622 million to fully support ANDI's 2015 operations (Exhibit 42). Although this sum may seem large it constitutes a medium-sized endowment fund in the universe of educational endowments and non-profit funds. Regarding the feasibility of reaching that ideal sum, it is worth noting that it represents only 0.2% of African public debt[91]. In other words, a debt swap at a 50% discount would only need to involve 0.4% of African public debt to fully support ANDI's operations in perpetuity. In summary, an endowment-based funding approach would be the best way for ANDI's financial model to operate. This approach is inherently sustainable, and the ability to manage it through economic downturns allows the highest possible constancy of funds streams. Implementing such a financial model for ANDI would constitute a true innovation and a pioneer effort for an international organization devoted to health research in the developing world.

91. CIA Factbook (sum of public debt of all African countries reached an estimated USD 218.5 billion in 2009)

7. RISK AND MITIGATION MECHANISMS

Financial risk

ANDI has set the target to initiate its activities with a full team geared to support the initial 5 projects and to grow the portfolio with minor organizational changes up to year 6. This means that the set-up cost for the operation itself is USD 6 million (including administrative cost) by year 3. However, this will allow the organization to increase its reach very significantly over the first 5 years. ANDI must clearly communicate this logic so as not to create the perception that its own costs will be increasing yearly as the initiative grows.

By year 6 total budget is to reach USD 31 million. As such, ANDI's target is to achieve ~20% annual growth. However, it is unclear whether ANDI will need to initiate immediate and large scale advocacy efforts to obtain funds from multiple donors or if some level of seed funding can be attained upfront. The latter would be ideal but few organizations are in a position to establish the African Innovation Fund rapidly (beyond the EU, World Bank/African Development Bank). In turn, obtaining funding from multiple donors might be hampered by the current economical downturn. Lack of support could greatly limit ANDI in achieving a successful launch. It is considered that this plan, based on key stakeholder views, as well as the position of ANDI within the African health R&D framework of activities, will be a positive influence to gather initial funding, from both large and small donors. In order to further mitigate this risk, ANDI and its members should pursue funding opportunities from other avenues like the private sector or large organizations such as the Bill and Melinda Gates Foundation. Research risk

ANDI's deliverables are intimately associated with moving new products through the R&D value chain and into clinical trials and manufacturing. Drug discovery and development has a high inherent risk on delivery. The attrition rate for the pharmaceutical industry is high, with only 1 out 10 or 20 drug candidates entering development actually reaching regulatory approval. ANDI will thus proactively monitor project progress so that resources are dedicated to projects more likely to deliver, while others are rapidly adjusted or even terminated as needed. By involving leading experts, both at the level of the STAC and as project consultants, and by extensive due diligence, ANDI will enhance the effectiveness of its investments as well as the chances of reaching the desired impact.

Contextual risk

ANDI is clearly a unique initiative in today's global and African health R&D landscape, in that it focuses on driving collaboration among different African stakeholders to develop products for Africa's own needs. However, other existing organizations could potentially see ANDI as disputing their activities. This could become an issue if ANDI is perceived to be developing new products for African needs alone. It will be important to clearly communicate that ANDI activities will focus on areas where there are significant gaps for product development in Africa (mostly on upstream R&D). However, it will also be important to communicate that it sees the successful introduction of new products in Africa as an effort involving different partners especially for downstream research.

These partnerships that ANDI will focus on brokering must also include the private sector and the local governments. The fact that the credibility and convening power of TDR can be leveraged to propel ANDI's target partnerships will be a major mechanism to mitigate this specific risk.

Organizational risk

As a truly African initiative, ANDI will drive the establishment of its hubs and its central office in the Continent. It is expected that countries and their key institutions will compete to provide hosting agreements with ANDI. However, the lack of adequate infrastructure in many areas of Africa could jeopardize the functioning of ANDI. A key action will be to scrutinize the potential locations for ANDI in great detail and bypass any political or scientific pressures that might be applied to locate hubs/office is less than optimal location. Still, operating in Africa will pose challenges including uncertainties associated with political and socioeconomic instability, disasters, and infrastructure-related challenges. These can all delay delivery. ANDI must, therefore, monitor its R&D and advocacy activities closely so that it can react creatively and rapidly to deliver against planned milestones. The implementation of the proposed business plan entails significant scientific, managerial and administrative capabilities to be collected across the ANDI team. In addition, it requires such team to be assembled quickly under the direction of a high performing ED. Hence, training and recruiting personnel with excellent research backgrounds and experience with project management and African public health expertise will be crucial. Such good talent is not abundant, especially in Africa, and tends to be competed out by other organizations, namely the UN. As such, ANDI must uphold its strategy to compensate its associates with high level packages, in line with those offered by other organizations.

8. IMPLEMENTATION PLAN

The activities involved in implementing ANDI can be divided into 3 large concurrent sections: (1) initiating the preparatory work in respect of the host agreement negotiations, project pipelines, governance structures (from 2009); (2) launching ANDI as fully operational in Africa and establishing the AIF as a collection fund (2012); (3) creating an endowment fund within the AIF and ramping-up and operationalizing of the R&D activities of ANDI (2012 - 2013).

Organization

Importantly, overall implementation success will require a few key critical steps to be taken quickly in 2009 and 2010, so as to start implementation. Preparatory work with respect to the lanuch of ANDI will start under the auspices of the WHO/TDR. WHO/TDR will support it financially and will appoint and support an *ad-interim* management team, until the ED is appointed and teams are fully staffed. This initial team will be responsible for preparing and managing the process for the selection of central office and regional hubs location, as well as the first calls for proposal. The *ad-interim* management will also support the ANDI Task Force in appointing the governing Board, which is expected to be fully functioning upon the launch of ANDI as a network hosted by the AfDB. At this point the ANDI Task Force will cease its functions. The *ad-interim* management will then support the newly appointed Board with the legal hosting agreements process with the

Secretariat ■ AIF	2009 (Q4)	2010	2011	2012
Central office hosting	• At TDR	• At TDR • Office selection process	• At TDR • Host country selected • Office staffing	• At AfDB • Office staffed and fully operational at final location
Hub hosting	• -	• Hub selection process	• Location of 5 hubs selected • Hub staffing	• 5 hubs staffed and fully operational at final location
Legal status/employment	• WHO[1]	• WHO[1]	• AfDB[2]	• AfDB/IGO[2]
Other activities	• *Ad-interim* team appointed • Start Board invitations • Prepare first project calls	• Board appointed • Task Force dissolved • Run first project call • Legal agreements • ED selection started	• ED appointed • Full team appointed • Run second project call	• Run third project call • Review process for projects from first call • ANDI databases fully operational
Fund type	• -	• Establish collection fund	• Collection fund	• Fully established endowment
Fund legal status	• -	• AfDB	• AfDB	• AfDBor independent
FTE Number	2	2	6	26
Total cost USD million	0.3	2.1	11.4	18.5
Projects Number	-	-	5	7

Exhibit 43 – Evolution of ANDI status during the implementation period ([1]As a project under the auspices of the WHO at TDR; [2] Project with intergovernmental organization (IGO) status at the AfDB)

AfDB. Once the hosting arrangements are finalized and the locations of ANDI's offices are determined, the Board can start the process of choosing and appointing an Executive Director. The culmination of the endeavor will mark the full start of ANDI in January 2012 with its central office at the final African location and the initial number of hubs running.

African Innovation Fund

The setup of the AIF needs to strike a balance between the immediate needs to start ANDI quickly to benefit from the current momentum, and the end goal of achieving financial sustainability to ensure long-term operation. To attain such a balance, the AIF implementation plan consists of two phases: collection AIF, and endowment AIF.

Collection AIF

This first phase can start quickly, with the goal to establish an operational account to receive contributions to start ANDI and to operate it during its inaugural years. The activities involve choosing a hosting institution for the collection fund. The African Development Bank is currently the preferred option for this activity, as well as hosting of an endowment. However, hosting arrangements need to be formalized and the endowment option at AfDB further explored.

Fund raising from initial donors, during this phase, should start to guarantee ANDI becomes financially stable as early as possible. During part of this phase, the recruitment effort should start with the aim of having a Senior Finance Officer in place by the end of 2010/mid 2011. The rest of the finance team can be staffed to develop the endowment option and decide on AIF's end-state.

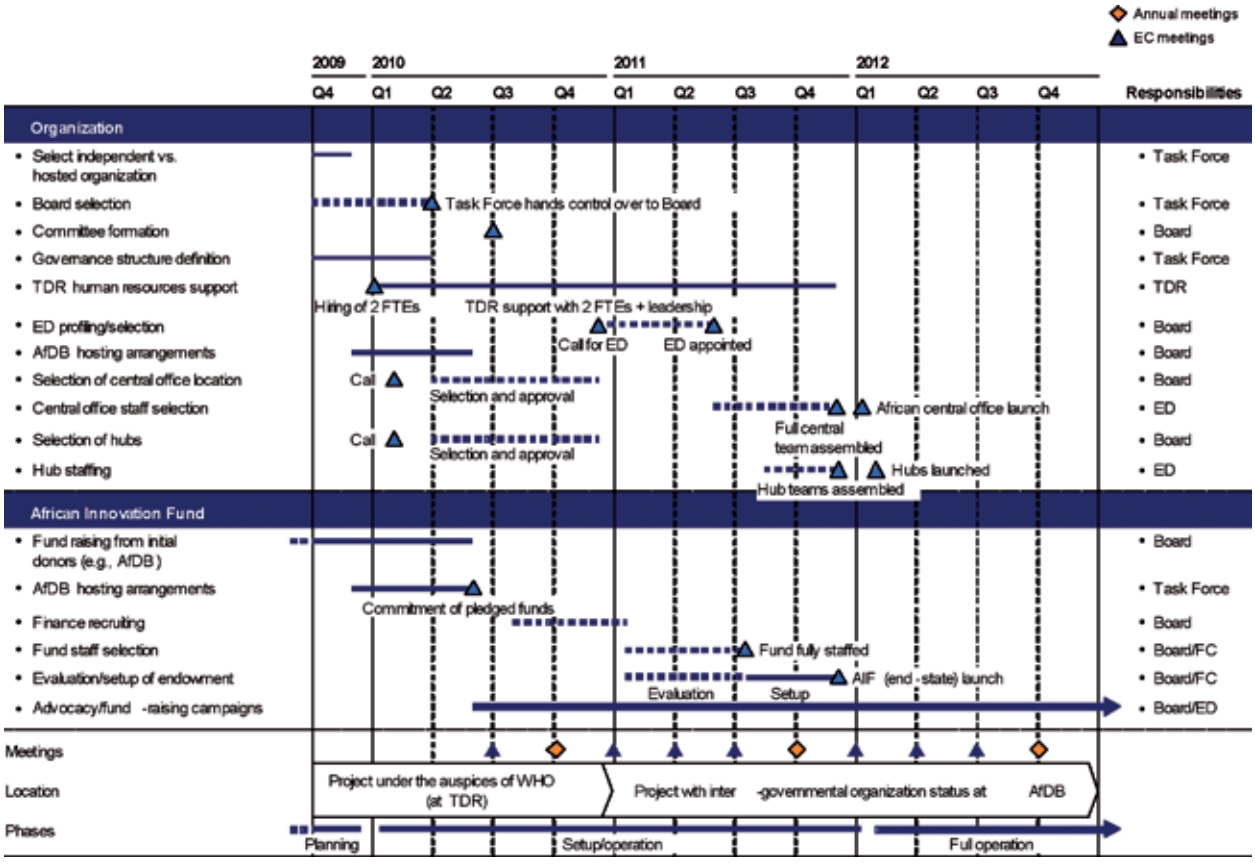


Exhibit 44 – Organization and AIF implementation plan

Finally, a major activity during this phase will be to setup the endowment, and start running the AIF by 2012 (estimated timeline and activities for setting up the fund is provided in Appendix Exhibits 17 to 20).

Endowment AIF

The setup of the AIF must have been completed during the previous phase, but much of the endowment seed will probably be collected during the initial years of this phase. The aim is to reach an endowment level that guarantees ANDI's sustainability and contributes as much as possible to its independence from donors.

R&D Activities

ANDI's R&D activities will have a quick start during the setup phase. The first call for scientists to submit letters of intent (LOI) for ANDI's network project grants will take place in January 2010. A process to select the STAC will be conducted in parallel to ensure the relevant expertise to judge those LOIs is present. During the first quarter of 2010, LOIs will be reviewed and about 10% of them pre-selected (based on criteria) to convene in a meeting. The objectives of such a meeting are to connect scientists expressing interest in participating in ANDI's network projects, and to coach them on proposal preparation. By September 2010, a second meeting will bring the same researchers together to finalize their proposals. Initially, these preparation meetings could be chaired by the STAC but, due to costs and STAC member availability, a fully functional and experienced R&D coordination team might take over in subsequent years. The STAC and the R&D coordination team will have already reviewed the finalized proposals. It is, therefore, expected that the final revision will take simply a week with the final discussion and selection made in person by the STAC during the Annual ANDI meeting in October.

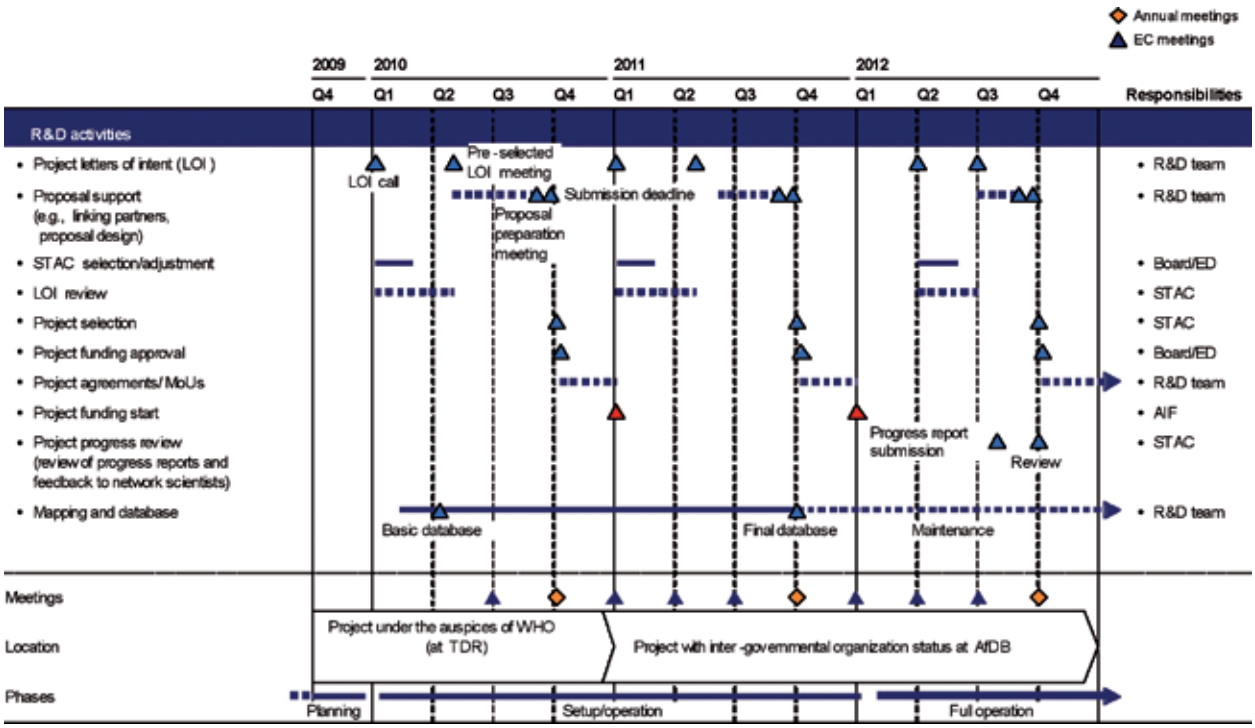


Exhibit 45 – R&D activities implementation plan

The call for LOI that will take place during 2011, will have extra time allocated for review and proposal support to ensure both scientists and the ANDI team learn during the process and adjust its timing and steps. By the 2012 call, it is expected that LOI review time and proposal support phase will be reduced. This will facilitate the task of the STAC and ensure highly qualified STAC members make themselves also available to start reviewing ongoing projects.

Acknowledgement

"The ANDI task force would like to thank McKinsey & Company for the support they provided in developing the strategic and business plan for ANDI. We also thank other stakeholders (individuals and institutions) who contributed in the preparation of this document"

"Creating a sustainable platform for R&D innovation in Africa"

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