Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases

African Network for Drugs and Diagnostics Innovation (ANDI), China Tropical Diseases Drugs and Diagnostics Innovation Network (China NDI), et al.

Contact:

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**Project title:** Development for Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases

**Project summary:**

Schistosomiasis, echinococcosis, vivax malaria and sleeping sickness are among the most Neglected Tropical Diseases (NTDs) in China or Africa today. Lack of simple, affordable, sensitive, and specific assays for field diagnosis make the prevention and control program for these diseases face many challenges. Landscape analysis showed that novel technologies and new tools are urgently needed in the diseases diagnosis.

This project will leverage a well-established high-throughput screening platform based on OMICS technologies developed by China NDI research group, which will be applied to discover novel biomarkers and process them to development. For better understanding of humoral immunity to clinical schistosomiasis, echinococcosis, vivax malaria and sleeping sickness as well as comprehensive analysis of humoral immuno-epidemiology, we will screen biomarkers of the four different parasitic diseases with genome-wide scales of 8000-10,000 proteins, using the samples from 2,000-4,000 human subjects. The biomarkers associated with these parasite infections will be indentified as well. The diagnostic kits identified by high-throughput platform will be translated into field and population based use. This will be the first time to develop such sensitive, specific and affordable new tools into the control and elimination of Neglected Tropical Diseases program.

Specific aims of the project, 1) Development of protein microarrays containing 8000-10,000 selected antigens for individual diseases. 2) Probe well-characterized infected human sera from China and Africa and identify serodiagnostic antigens. 3) Develop, evaluate, validate and optimize field deployable tests for each agent applicable to each region. 4) Seek regulatory approval and promote use of products in endemic area.

The key deliverables of the project in first five years include the following:
1. 8000-10,000 gene clones of 4 parasitic diseases;
2. 8000-10,000 recombinant proteins of 4 parasitic diseases;
3. Four kinds of biochips of parasitic diseases;
4. 4-7 diagnostic kits which can meet the current challenges in diseases control and prevention;
5. 4 registered diagnostic products based on multicentre evaluation and registration.

*As taken from original proposal template, question 5.*
1.* **Title of the project:**

Development of Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases

2.* **Submitted by:**

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3.* **Target disease or health condition:**

*(Focus on type II and III diseases and special R&D needs of developing countries in type I diseases where there is an identified health technology gap.)*

The project will initially focus on type II and III diseases, exemplified by helminths and protozoan such as schistosomiasis, echinococcosis, vivax malaria and sleeping sickness. Simple, affordable, sensitive, and specific assays for field diagnosis of schistosomiasis, echinococcosis, vivax malaria and sleeping sickness are not yet available, but they are urgently needed for these diseases. Biomarkers identified by high-throughput screening system and used to make recombinant antigen diagnostic reagents will provide a vital tool for the prevention and control of these diseases.

4.* **The suggested health technology that project seeks to develop:**

*(e.g. medicine; diagnostic test; medical device; vaccine etc.)*

The project will develop diagnostics tools that are easy to use and affordable in rural communities of disease endemic countries. The project is based on a well-established high-throughput screening platform based on genomics, proteomics and transcriptomics technologies (so called OMICS technologies) developed by CNDI research groups will be applied for this novel biomarkers discovery. This high-tech
platform enables biomarker screening on a genome-wide scale to be successfully realized. A multi-center evaluation in the field and clinical trial of the developed diagnostic products will be implemented in Africa and China. Additionally, a reference lab, product registration and QA/QC quality control of the product by manufacturer will be an important part of this project. The developed diagnostic will be incorporated into modern devices i.e. remote/mobile control system with data transfer to enable easy and real time access to information and test results. This will make bulk procurement and delivery of the final product to rural communities very easy. The resultant products will further support the development of m/e-Health system in developing countries.

5. *Project summary:*

Schistosomiasis, echinococcosis, vivax malaria and sleeping sickness are among the most Neglected Tropical Diseases (NTDs) in China or Africa today. Lack of simple, affordable, sensitive, and specific assays for field diagnosis make the prevention and control program for these diseases difficult. Landscape analysis undertaken by ANDI and CNDI showed that novel technologies and new tools are urgently needed in the diseases diagnosis.

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4. 4-7 diagnostic kits which can meet the current challenges in diseases control and prevention;
5. 4 registered diagnostic products based on multicentre evaluation and registration.
6. 30 individuals trained and several institutions strengthened as part of this project.
6.* Public health need that the proposed project aims to address:
(Explain the public health need in terms of burden of disease; prevalence; incidence; fatality rate; geographical spread; current interventions and their limitations; and what proposed new technology would change in terms of disease prevention, control, diagnosis, treatment etc. If detailed information is not possible at present then please provide some basic level information)

Infectious diseases remain a significant contributor to the burden of disease in low- and middle-income countries. Schistosomiasis, vivax malaria, echinococcosis and sleeping sickness are among the most NTDs causing significant morbidity and mortality. In China, there is plan to eliminate schistosomiasis and malaria by 2020, but in Africa the timelines for possible elimination are increasingly being discussed. In China, approximately 68 million individuals are at risk of *schistosomiasis japonicum* infection and transmissions occurred in provinces along the Yangtze River and its southern areas in 2012. Schistosomiasis is still concentrated in sub-Saharan Africa where the bulk of the at-risk population, existing schistosome infections, mortality, morbidity and burden due to the disease reside. The schistosomiasis cases in Africa accounts for 85% of the number of people at-risk of the disease in the world. To date, schistosomiasis occurs at prevalence levels below 10% in about 12 countries and territories of Africa. National survey showed that 66 million individuals are at risk of *Echinococcus* infection and the average prevalence rate for populations in endemic areas was 1.08%; In Africa, patients with echinococcosis mainly reported in northern and eastern regions, the average prevalence of cyst echinococcosis of approximately 1-2% in the endemic areas. In year 2011, there were 4479 malaria cases reported through the infectious diseases reporting system from 27 Provinces in China. Although, Plasmodium vivax is not common in most parts of Africa, it has significant public health importance in east Africa, such as Ethiopia, and in some areas of the country the prevalence rate exceeds 70% of total malaria infections. A detailed gap analysis from CNDI and ANDI showed that diagnosis is one of the major limitations for the control of these diseases (Zheng et al. Infectious Diseases of poverty 2013). Traditional diagnosis methods of such parasitic infections like parasitological or clinical methods are neither simple nor convenient for population-based monitoring/surveillance. Improvement in diagnostic sensitivity and specificity of these diseases should focus on the investment in R&D, technology innovation and multilateral collaboration. This project is seeking to address this problem in a systematic and coherent way,. This Africa-China partnership presents a real opportunity to advance this area and build relevant capacity.

7.* Explain which new and innovative approaches and mechanisms to supporting financing and coordination of R&D this project would demonstrate?
(This is a very important part to be filled. The idea of these demonstrations projects is “to address identified gaps that disproportionately affect developing countries, particularly the poor, and for which immediate action can be taken” (WHA66.22). 66th WHA considered these demonstration projects as part of the efforts to “take forward action in relation to monitoring, coordination and financing for health
research and development”. The assembly decided to identify such projects that: “(a) address identified research and development gaps related to discovery, development and/or delivery, including promising product pipelines, for diseases that disproportionately affect developing countries, particularly the poor, and for which immediate action can be taken; (b) utilize collaborative approaches, including open-knowledge approaches, for research and development coordination; (c) promote the de-linkage of the cost of research and development from product price; and (d) propose and foster financing mechanisms including innovative, sustainable and pooled funding; (2) The demonstration projects should provide evidence for long-term sustainable solutions.”

This project describes an innovative inter-and intra-regional cooperative approach for South-South cooperation. Analysis of the pan African Centres of Excellence undertaken by ANDI (Nwaka et al 2012) show that there is little or no South South collaboration for R&D and local production for neglected diseases including in the area of financing. The project emphasis capacity building, open source and knowledge sharing approaches in all elements of its implementation. A critical component of the project is the implementation of common platforms and protocols for all data evaluation and standardization. Shared databases will be used for data management but final results and conclusions will be made accessible.

Our integrated approach will reduce the cost of the final product by supporting R&D and access using different financing models. In line with ANDIs operational model, the R&D component will be financed through public financing mechanism while the large scale production of the final component will be financed through a combinational public financing, social venture and loan models. This approach will support the continued participation of the industry while at the same encourage technology transfer. The public financing can involve a variety of financing model including pooled funding by WHO member states, establishment of prizes to encourage innovation in the area of diagnostics and taxes. This approach is innovative and will ensure sustained access to the product and also to the development. It will also encourage countries or regional bodies to support its own financing mechanism.

A professional global or regional fund management structure can be implemented a regional Bank or international body to manage the fund.

8.* Evidence of market failure/research landscape:
(Explain why there has been no investment in this technology or why investment has not resulted in access to the health care product.)

While significant efforts and investment has been made by governments to support the development of genome sequences of pathogens that cause Type II and III Diseases, there has not been a systematic and integrated approach to leverage genomics to discover novel biomarkers and diagnostics products for type II and III diseases especially in Africa, China largely due to market failure. The Global Strategy and Plan of Action (GSPOA), outlined at the 61st World Health Assembly provides a framework to support this critical area of work and to solve the health problems of developing countries. A key element of this strategy is prioritization of critical R&D needs, capacity
building including in regulatory processes, R&D, technology transfer and sharing, as well as monitoring and evaluation. The strategy also emphasizes South South and North South collaboration, partnerships, establishment of collaborative networks all of which are embodied in this project.

A health R&D landscape analysis undertaken by ANDI, and CNDI show that there is significant research gap in R&D for these diseases. For example, only few products are being researched or in clinical trials for these prevalent diseases in the various areas. Second, there is a little or no South South collaboration to share lessons and address these problems in sustainable way. In Africa, for example, only 5% of peer-reviewed articles published from 2004-2008 involved institutions in more than one African country. Thirdly, there is insufficient investment in African R&D with overall yearly R&D spend of 0.3% of total African GDP, which is about USD 14 billion below the world median (Strategic Business Plan of ANDI 2009). Also important is a lack of coordination of ongoing efforts, including fragmented financing in the continent. This project will help in overcoming some of these challenges.

9. **The scientific and technical feasibility:**

   *(Describe the scientific and technical basis for the proposed technology in terms of the state of the art e.g. candidate molecules; biomarkers; pipeline; previous efforts, if any, to develop same or similar technology etc. Include some risk analysis)*

On the basis of previous parasite genome projects, we obtained a mass of parasite Omics (transcriptomics, proteomics, genomics and metabolomics) information and integrated them into ChinaPathDB (Figure 1, 22 genomes, 24 transcriptome and 7 proteomes) which covered Schistosoma, Plasmodium, Clonorchis, Echinococcus, Babesia and so on. A well-established high-throughput screening platform (Figure 2, 3) based on OMICS technologies and ChinaPathDB was developed by China NDI research group (Hu W et al., Nature Genetics, 2003; Liu F et al., Plos Pathogens, 2006; Liu F et al., Proteomics, 2007; Liu F et al., Mol Cell Proteomics, 2009; Zhou Y et al., Nature, 2009; Chen JH et al., J Proteome Res, 2010; Cai SJ et al., J Proteome Res, 2013). Hence, a robust platform discovering and evaluating new biomarkers for diagnosis of parasitic diseases are available. With this platform, we developed a series of the colloidal gold immunochromatography assay (GICA) strips for diagnosis of parasite infection (*C. sinensis*, *S. japonicum* and *E. multilocularis*) based on parasitic recombinant proteins in collaboration exist within China NDI and ANDI, and industry partner for commercialization exist too. China NDI through the National Institute for Parasitic Diseases (NIPD) established a national parasite diagnosis reference laboratory with provincial diseases control institutions in endemic area. This project will develop a pipeline of diagnostic products with utility in resource poor setting.
Figure 1 Structure of China PathDB

Figure 2 Platform-components by China NDI
10. **Reasons for proposing:**

*(Provide details if any priority setting and/or selection criteria that has underpinned the consideration to take up this area of technology for development.)*

Diagnosis is central to control and elimination of neglected tropical diseases. Landscape analysis undertaken in Africa, China and other developing countries show a clear need and comparative advantage in investing in developing diagnosis products that accessible in rural communities for neglected diseases. Our main reason for proposing the project is based on the need in China, other Asian region and Africa. This assessment is based on available mapping data and government priority in the various regions. The technology and capacity for the project is available within our network and the project will leverage these. The project will also foster South-South collaboration and capacity building coupled with inter/intra-regional cooperation involving public and private partnerships.

11. **Who could potentially develop the technology/carry out the research?**

*(Provide known details: individual researcher? Group of researchers? Research/coordination organization including PDPs? Group of research organizations working together? Combination of these; What would be the process of selection of developers?)*
The project proposing institutions have a number of existing institutions in China and Africa with clear expertise and understanding of diagnostics and type II and III disease issues. The project will also establish a multidisciplinary network of experts and teams to tackle the specific areas of the projects. From the African side, ANDI is presently working with a network of 38 pan African Centres of Excellence in health innovation (Nwaka et al. BMC Int Health Hum Rights, 2012), and a subset of these CoEs is a network of institutions with expertise and track record in biomarker and diagnostic product development. Some these institutions include the Theodor Bilharz Research Institute (TBRI) Egypt, Kenya Medical Research Institute KEMRI, University of Lagos Nigeria, Makerere University Ugandan and others. Furthermore, ANDI can implement new calls to identify any missing capacity both locally and globally. On the China side, network of centers working in this area already exist including R&D centers focusing on biomarker and diagnostic products. In addition, ANDI is working with leading diagnostic development and manufacturing companies in South Korea including SD Diagnostic and Bioneer.

12. **Who could potentially manufacture the final product?**
   *Multinational company? Local production? Joint venture? How the decision will be made about the producer?*

   A number of companies that can support the manufacture of the products exist including EASE-Medtrend Biotech. China as well as companies in South Korea that are working with ANDI to implement technology transfer for local production in Africa such as SD Diagnostics, Infopia and Bioneer. In addition a technical committee of the project will identify additional local manufacturers in China and Africa to manufacture and locally distribute the products.

13. **What could be the role of WHO, if any, in this demonstration project to bring this venture to fruition?**

   WHO essential medicines department will be involved in project at different levels: i) support for regulatory capacity building, ii) prequalification products.

14. **Please outline a timeframe and projected milestones for the project covering the first 5 years. This should also highlight the immediate actions that need to be taken?**

   Year 1-2: Sample collection and novel diagnostic biomarkers discovery using biochip approach:
   1. Collection of well-characterized infected and control sera in China and Africa;
   2. Selection of interested antigens on a genome-wide scale by various criteria;
   3. High throughout cloning and in vitro expression of selected genes;
   4. Fabrication parasites protein microarrays using expressed parasitic proteins;
5. Identify reactive antigens through immune screening by microarrays.

Year 3: Rapid diagnostic test and rapid molecular test development.

Approach:
1. Large scale expression and purification of recombinant diagnostic markers;
2. Development of use friendly immunostrips of different parasitic disease.

Year 4-5: Filed evaluation and mark development of the productions.

Approach:
1. Organization of a multi-center evaluation in the field and the validation of the diagnostic productions in the center.
2. Commercialization and manufacture of the immunostrips
3. Registration of the products in China and Africa
4. Development of remote/mobile control system with data transfer in bulk procurement
5. Development of appropriate m/e Health platform and advocacy.

Capacity building will span all parts of the project.

15. What is the intellectual property (IP) landscape relative to this project? Is there any IP, e.g. patents that need to be licensed in to be able to develop and market the product in developing countries? How would IP and related intellectual assets, including knowhow, proposed to be managed in this project?

For the Biomarkers: IP will reside by any institutions that produces or owns them but the project network through China NDI and ANDI will seek a license (exclusive or non-exclusive in nature) to facilitate access to final product in developing countries. Where IP is required to facilitate access the network will implement such need.

16.* What would be the strategy to ensure access to the product once it is developed?

(Access is an important dimension of these demonstration projects, it is important for the projects to begin with the end in mind, explain how this project would deliver the technologies to the needy patients i.e. price and affordability; modes of supply; storage; prescription; dispensing; and compliance; WHO will develop guiding principles for ensuring access to any products coming out of the demonstration projects)

Project will follow any guidelines agreed with WHO. In addition, the network will ensure that any product that results from the project will be publicly available under preferential pricing terms. This will be included in specific manufacturing agreements with companies.

In addition, the following modalities will be considered as part of the project agreements to ensure access: i) the project will engage African and Chinese governments, development agencies, international organizations, NGOs and Foundations to secure procurement of the products resulting from this project for the poor populations of Africa and developing countries; ii) appropriate pricing for the
products that result from this project will be agreed ahead of time and that products sold through the public and private sector market meet these pricing guidelines.

17. **How could the project be financed paying particular attention to the need to demonstrate new and innovative forms of financing? Also provide an estimated cost of the project.**

We hope that initial financing for the project will be provided by WHO member states through this application. A variety of financing model including pooled funds by government, taxes, special loan through government guarantees would be appropriate mechanisms. Such pooled funds can be hosted at regional development banks, for example, ANDI has ongoing collaboration with African Development Bank and an African innovation has been proposed. The fund can provide grant money for this and other demonstration projects, and also promote various venture approaches or government guaranteed loan for manufacturing and access. This approach will promote technology transfer, South South and North South collaboration to support sustained local production and access of finished product.

Estimated cost: USD3.5 million per year for 5 years.

18. **How could the project be governed and coordinated paying particular attention to the need to demonstrate better way of coordination?**

A technical committee of ANDI and China NDI will be established. However, the existing governance of ANDI (Figure 4) and NIPD will be used for the overnight. The ANDI structure is outlined below:

**ANDI Board:** The Board is a ministerial currently consists of 12 members from among its key stakeholders including representatives of ministries of health, science and technology and finance from the five regions of Africa. WHO, AfDB and host agency also sit on the Board among other members.

**ANDI Secretariat:** The Secretariat includes the central office of ANDI, its sub-regional hubs and staff responsible for the implementation of all ANDI activities under the leadership of the ANDI Executive Director.

**Host agency in Africa:** United Nations office for Project Services (UNOPS) has been selected by the ANDI Board as the new host agency for ANDI and contractual arrangement between WHO and UNOPS is being finalised to this effect. In the time being ANDI is temporarily hosted within TDR as a project.

**STAC:** The STAC is comprised of experts with a track record in various aspects of health product innovation and the R&D value chain. STAC members are independent experts acting in an individual and personal capacity. They provide independent technical advice to the ANDI Board and the ANDI Secretariat, in accordance with its terms of reference.
19. Have any donor agencies/governments already indicated interest in supporting the project?

ANDI is presently supported by WHO, TDR, European Union, Nigeria government, African Development Bank through Korean and Brasil Trust Funds. China NDI has been supported by WHO/TDR and Chinese government. All efforts will be made to generate funds from china for this project.
Addendum: Development of Easy to Use and Affordable Biomarkers as Diagnostics for Types II and III Diseases

This addendum provides more information on how our project will address the following key elements of the call for demonstration projects:

1. Delink the price of the final product from the cost of R&D.
2. Utilizes collaborative approaches, including open knowledge innovation approaches.
3. Utilizes licensing approaches that secure access to research outputs and final products.
4. Proposes and fosters financing mechanisms including innovative, sustainable and pooled funding.
5. Fosters effective and efficient coordination mechanisms amongst existing organizations/initiatives.
6. Strengthens capacity for research, development and production, including through technology transfer, in developing countries.

1. As outlined in our proposal, the project intends to demonstrate a robust and verifiable delinkage of the price of final product(s) from the cost of R&D. Firstly, the starting point for our project is the availability of the sequence of relevant pathogen genomes, which the international community supported over the past years, and the cost of which will not influence price of product(s) resulting from this project. Secondly, our project have leveraged these sequences to obtain a mass of parasite transcriptomics, proteomics, genomics and metabolomics (OMICS) information and integrated them into a ChinaPathDB Biomarker Screening Platform (comprising 22 genomes, 24 transcriptome and 7 proteomes), covering different Types II and III diseases (see Fig 1, 2, 3 of our proposal). The potential of this innovative high-throughput screening platform vis-a-vis diagnostic development has been published in leading international journals such as Nature, Nature Genetics and others (see our proposal). Again the costs associated with developing this platform will not influence the cost of resultant product(s). Through this
publicly supported platform, a series of the colloidal gold immunochromatography assay (GICA) strips for diagnosis of parasite infection based on parasite recombinant proteins have been developed in collaboration with a small Chinese Biotech company which is a partner in this proposal. Through ANDI, several African institutions have engaged with their Chinese counterparts to advance this project, and we intend to engage other public and private partners. If selected as a demonstration project with appropriate financing, this project will demonstrate and ensure that the price of any resulting product is delinked from the cost of R&D. This approach is consistent with an integrated Push and Pull mechanism being developed by ANDI, which considers different financing models for both R&D and manufacture/access (Fig.1). Our project is geared to deliver quality assured, easy to use, accessible and affordable diagnostics that will support control and elimination programs for specific neglected diseases.

![Fig.1: proposed mechanisms for managing/financing R&D, transition to downstream manufacture/access. Illustration also demonstrate delinkage of R&D cost from price of final product.](image)

2. One objective of ANDI and other regional networks such as China and ASEAN networks is to utilize different collaborative approaches, to enhance the development of products for diseases that disproportionately affect developing countries. Such approaches include organized networks, consortia and public-private partnerships that promote South-South and North-South collaborations as well as open innovation and knowledge sharing. This proposal exemplifies the potential and power of such innovative
and inclusive inter-and intra-regional collaborative approaches to solve the health challenges of developing countries. Analysis of the Pan-African Centres of Excellence undertaken by ANDI (Nwaka et al 2012) shows that there is limited South-South collaboration for R&D and local production for neglected diseases including in the area of financing. Indeed, our unique diagnostics development platform for neglected diseases is a global open innovation resource that will be more widely accessible through this project. Furthermore, all relevant protocols and data will be shared through platform databases to be used for data management and knowledge exchange.

3. **The project will manage IP and licensing to secure research outputs and final products as follows**: i) ANDI and its Chinese partners are already working to document any background IP associated with this project. The project team has agreed that such background IP will reside by the institution(s) that developed them but must be made freely available to all partners for the purposes of R&D, manufacture and public access. This includes the platform and all technologies associated with it, ii) through the coordination framework for the project (see original proposal), all background and program IP will be implemented through appropriate licensing agreements that ensure public access to research results, unhindered manufacture and access to final products. This type of licensing modality is well known to the project partners. We will establish appropriate monitoring and evaluation mechanisms for all phases of the project to ensure that access is not hindered.

4. **We propose an interlinked financing approach to support demonstration projects**: i) immediate implementation of voluntary pooled financing scheme by government and private entities, ii) implementation of government approved taxes on specific products/services in the medium-term to complement the pooled financing, and iii) to leverage the fund (pooled and/or taxes) to support R&D through grants and innovation award schemes, and at the same time support appropriate guaranteed loans or social venture initiatives or prizes to address unique R&D/manufacture and access issues. The combination of grants with guaranteed loans and social venture support is consistent
with delinkage of the cost of R&D from price of the final product. This approach will also promote technology transfer, South-South and North-South collaboration for sustained R&D, local production and access to finished product. Such fund can be established as a professionally managed, Trust Fund (TF) or Innovation Fund or Endowment Fund, through a regional and/or global body, such as a Development Bank/Work Bank/WHO/UN body. A number of developed and developing countries have TFs for various developmental issues, however, the concept of interlinked or integrated Fund as described here for R&D and access is innovative and can easily be implemented. The Fund host shall disburse funds under the directive of a coordinating body for approved project(s). This approach will promote sustainability, scalability, transparency and accountability. Our project covers the various parts of the diagnostics value chain and is well suited as a demonstration project to illustrate these financing approaches. We will establish a global advocacy/communications/fund-raising effort through our coordination machinery to support agreed financing mechanisms.

5. **Analysis undertaken by ANDI and others show that lack of coordination and financing (fragmentation of efforts) are major bottlenecks in the implementation of robust collaborative product R&D and access initiatives for diseases that affect developing countries.** The good news is that the issue of coordination and financing are recognized as important for the success of WHO demonstration projects. Through ANDI and partners, we intend to identify and work with other relevant global parties. This will be achieved proactively and through regular global calls for additional technologies/partners. ANDI has already reached out to PATH -Seattle US as potential partner, and discussions are ongoing with the EDCTP, SD Diagnostics (major producer of malaria RDTs) and Infopia in Seoul for R&D, manufacture and capacity building. Please note that our project platform can handle multiple Types III and II diseases, thereby presenting unique advantages in the context of demonstration projects than single disease/product focused projects. These advantages include: i) the opportunity to develop robust pipeline of products with better prospect for success, ii) our approach provides for learning and sharing of resources across diseases, with the prospect of
developing the much needed integrated/multiplexed diagnostics for several neglected diseases, iii) the opportunity for the project team to initiate regular open and global calls for complementary technologies/partners to join the project. This will promote coordination/linkages with other players and make it possible for interested parties such as PDPs/FIND, companies and institutions from developed and developing countries with relevant expertise to join the project. Please note that coordination includes direct management of the project(s), such as preparation/implementation of project budget, portfolio/pipeline management, approval/disbursement of funds to project partners, M&E and reporting. These will be effectively implemented through the project coordination mechanism.

6. **Strengthening capacity for research, development and production, including through technology transfer, in developing countries was highlighted in our original proposal and above.** We believe that this is critical in sustaining access to health products in the long-term. As a deliverable in our submission, we defined the approximate number of individuals/institutions that will be trained/strengthened as part of this project. Capacity building will span all parts of the project from R&D to regulatory to manufacture and access. This will include multi-center evaluation in the field and clinical trial of the developed diagnostic products. Reference laboratories, product registration and QA/QC of the product by manufacturer will be other areas for capacity building and technology transfer, especially in Africa. Our goal is to incorporate/integrate developed diagnostics into modern devices i.e. remote/mobile control system with data transfer capabilities to enable easy and real time access to information and test results. This will support m/e-Health system in developing countries.

Finally, our proposal is innovative, scalable and sustainable with potential transformational outcomes – it meets the key criteria for demonstration project as outlined in WHA66.22, and earlier resolutions on the Global Strategy and Plan of Action on Public Health Innovation and IP.