

BL 4

Business Plan

2008-2013

**Innovation for product
development in disease
endemic countries**



Special Programme for Research & Training
in Tropical Diseases (TDR) sponsored by
UNICEF / UNDP / World Bank / WHO

Draft Business Plan for JCB

May, 2007

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EXECUTIVE SUMMARY

Needs and Opportunities

There is a growing need expressed by many developing countries for the capacity to discover, develop and produce pharmaceutical products, so that they are not solely dependent on innovation from outside sources to meet their needs. There is also a desire by many countries to better access and utilize indigenous knowledge for pharmaceutical products. These needs have been recognized most recently in the report of the Commission for Intellectual Property and Innovation in Health and the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property. There are increasing instances of DEC and their institutions focusing on product innovation driven R&D, mainly in emergent economies such as Brazil, India and South Africa. However, the application of innovation on neglected diseases remains a challenge to both the public and the private sector of developing countries. Internationally there is a greater level of understanding about how to develop public private partnerships for product development. Opportunities exist to coordinate existing academic networks and research groups in DEC into internationally competitive R&D teams, linking them to appropriate private sector contacts, and brokering access to technologies and practices that would empower them to competitively develop products and obtain funding from national and regional sources as well as the larger international community. An area that could be particularly capitalized on is that of indigenous knowledge and its potential application to new treatments.

Overall Objective

To foster the discovery and development of novel drugs, diagnostic tests and other products by institutions in DEC.

Specific Objectives

- Develop projects leading to the discovery and development of novel diagnostic tests, drugs and other products for tropical diseases carried out by teams of collaborating investigators and institutions in DEC
- Provide a platform and framework for scientific, legal and ethical support to facilitate DEC leadership of projects and partnerships for the discovery and development of pharmaceutical products
- Facilitate creation of south based 'spin-offs' (e.g. public private partnerships, networks of academic institutions and not-for profit foundations) focusing on and dedicated to innovation for discovery and development of drugs and diagnostic tests in DEC

Activities

Through establishing some successful product R&D partnerships in DEC it is anticipated that broader interest and support for this area can be leveraged. The business line will define gaps and opportunities for innovative R&D in DEC by generating a database of projects, institutions and investigators. It will facilitate both exploratory early stage discovery projects and mature development projects through competitive calls for proposals and will facilitate collaborative partnership development. The business line will work with other agencies to

provide support for the evaluation, transfer and development of emerging technologies and projects for centres in DEC. Special attention will be paid to projects and technologies building on and utilizing indigenous knowledge, including those associated with traditional medicines. Centres of excellence will be developed for key activities e.g. screening and to support partnerships and broader networks. Once strong projects are established, TDR will broker collaborations e.g. with the private sector and product development public private partnerships, to facilitate their progress. The business line will also assist centres and partners in the establishment of best management practices. Great emphasis will be placed on using TDR funds to enable projects to get to a stage where they can leverage other sources of funding and investment.

End-Products

At the end of seven years this business line plans to deliver the following end-products

- Up to 9 partnership R&D projects established with leadership from DEC institutions
- At least 3 new centres established in Africa, Asia and / or Latin America with internationally renowned capacity for screening and identification of lead compounds for the development of novel drugs for TDR diseases.
- Transfer and establishment of technologies necessary for target validation, lead optimization and toxicology studies in at least 5 centres.
- 'Spin-off' for further development and sustainability of at least 4 project partnerships based in developing countries, either as individual public private partnership projects, self-standing not for profit organizations, or activities taken on by companies
- DEC led partnerships to have developed 2 rapid diagnostic tests and transitioned 2 drug candidates into development.

Comparative Advantage

Over the past 30 years, TDR has supported a number of networks of institutions and investigators in DEC like Brazil, Columbia, Nigeria, Thailand, India and South Africa to develop new bioinformatics and other biotechnologies that can assist the discovery of novel interventions for tropical diseases. Networks have also been established, mainly in developed countries, to specifically facilitate drug and diagnostics discovery and evaluation. These can be linked to provide an important source of innovation for technology transfer and development for DEC. TDR has supported capacity building in best practices (GLP, GCP, ethics) and published guidelines on many product development related activities including the clinical evaluation of herbal products and evaluation of diagnostics. TDR has also established successful public private development projects and discovery networks. It has a convening power with institutions in DEC and industrialized countries which will facilitate the building of effective north-south and south-south collaborations. TDR can also build on its previous very successful public private partnership start up experiences (e.g. MMV, FIND).

1. OBJECTIVES

1.1. OVERALL OBJECTIVE

To foster the discovery and development of novel drugs, diagnostic tests and other products by institutions in DEC.

1.2. SPECIFIC OBJECTIVES

- Develop projects leading to the discovery and development of novel diagnostic tests, drugs and other products for tropical diseases carried out by teams of collaborating investigators and institutions in DEC.
- Provide a platform and framework for scientific, legal and ethical support to facilitate DEC leadership of projects and partnerships for the discovery and development of pharmaceutical products.
- Facilitate creation of south based 'spin-offs' (e.g. public private partnerships, networks of academic institutions and not-for profit foundations) focusing on and dedicated to innovation for discovery and development of drugs and diagnostic tests in DEC.

2. NEEDS AND OPPORTUNITIES

2.1. NEEDS

There is a growing need expressed by many developing countries for the capacity to discover, develop and produce pharmaceutical products, so that they are not solely dependent on innovation from outside sources to meet their needs. There is also a desire by many countries to better access and utilize indigenous knowledge for pharmaceutical products. This capacity for innovation is seen as a critical element in contributing to both the sustainability of future product development and the appropriate use of the resultant products. It will also allow the development of equitable international partnerships in this area. Capacity for innovation is increasingly seen as a crucial component of future economic development and has been specifically recognized in the report of the Commission for Intellectual Property and Innovation in Health and the recently established Intergovernmental Working Group on this topic.

There is evidence that health innovation biotechnology for discovery and development of interventions could more likely become sustainable in developing countries as economic and other factors make such innovation competitive (Nature Biotechnology, vol. 22 Suppl. Dec. 2004, 1). The potential to sustain this capacity is exemplified by an increasing number of instances of technology transfer from major pharmaceutical companies to smaller manufacturers in disease endemic countries (DEC). Thus the need for countries to become contributors to innovation as well as recipients of innovation can increasingly be met.

Technology for discovery and development of interventions can become sustainable in developing countries, particularly where there is a strong academic base and where cost factors are such that public and / or private investment in innovation is competitive. Thus there is a growing desire for countries to capitalize on science and technology innovations for developing national capacity, based on indigenous, transferred and learned knowledge and skills, for local manufacture of pharmaceuticals.

2.2. OPPORTUNITIES

There is a groundswell of interest in further developing science and technology capabilities in many developing countries. There are also instances of institutions focusing on the innovation components of pharmaceutical product development activities in DEC (mainly in emergent economies such as India, Brazil and South Africa). The Bioscience eastern and central Africa (<http://www.biosciencesafrica.org/>) program was recently launched focusing on applications of biotechnology for agriculture in east and central Africa and with support from CIDA, Canada. NEPAD is also setting up centres of excellence for science and technology in Africa. This effort brought about the launching of three science-related initiatives, the African Institute of Space Science (AISS), Bioscience facility for Eastern and Central Africa, and the African Laser Centre (ALC). The ICGEB in India and FARMANGUINHOS in Brazil are specific examples of efforts on applications of technology

for interventions research with potential for product innovation for human health in disease endemic countries.

However, the application of innovation to neglected diseases remains a challenge to both the public and the private sector of developing countries. A major opportunity to address this challenge lies in funding and coordinating existing academic networks and research groups in DEC to become internationally competitive R&D teams. These can then be linked to appropriate private sector contacts and other partners. Access to technologies would be brokered that would empower them to further develop themselves and competitively access sustainable funding from national and regional sources as well as the larger international community. Developing expertise in product development activity in the neglected diseases area could have potential spin-off benefits for countries keen to develop such technologies more generally.

These associated challenges and opportunities enable TDR to coordinate transfer of health innovation technologies while fostering the discovery and development of novel drugs and diagnostic tests in disease endemic countries.

An area that could be particularly capitalized on is that of indigenous knowledge and its potential application to new treatments.

This BL is designed to facilitate a stronger engagement of investigators and institutions in disease endemic countries in developing health innovations. It will focus on coordinating and providing support for projects on discovery and development of new diagnostic tests and drugs in disease endemic countries. Efforts will be dedicated to appropriate development and transfer of technologies necessary for target validation, lead optimization, toxicology studies and drug screening for new leads in support of the projects. Furthermore the goal will be to develop DEC led teams and partnerships that can subsequently build upon initial projects and sustain discovery and development of drugs and diagnostic tests in disease endemic countries.

With public and philanthropic assistance, combined with private sector partnership and investment, it is anticipated that capacity for tropical disease pharmaceutical innovation can be developed in selected developing countries where it is now absent or nascent. Successes emanating from these partnerships would act as a stimulus for enhanced activity in this area in many other disease endemic countries worldwide. It would stimulate other organizations to become engaged.

Many of the skills to manage such partnerships have been developed through the public private product development partnerships and these organizations may be able to play an assisting role with TDR in helping DEC partnerships develop. As DEC partnerships become internationally competitive PPP's and international philanthropic institutions, as well as regional and national organizations, may be future sources of funding and investment for such activities.

3. COMPARATIVE ADVANTAGE

3.1. TDR EXPERIENCE

In the past 30 years, national and international agencies have successfully trained individuals, and equipped and strengthened institutions in DEC to undertake basic research on diseases of poverty. Significant numbers of investigators and institutions have emerged, highly proficient in basic sciences research focusing on understanding the disease process and actively participating in clinical evaluation of new interventions for diseases of poverty. Collaborations between investigators and institutions in the disease endemic countries and industrialized countries of Australia, Japan, Europe and North America have also resulted in networks sharing technologies. These investigators, their institutions, infrastructures and the emerging networks represent a necessary prerequisite and important asset for successful introduction of health biotechnology innovation that can be used for discovery and development of drugs and diagnostic tests in DEC. TDR has been part of this development.

TDR is currently supporting a number of these networks of institutions and investigators (in Brazil, Columbia, Nigeria, Thailand, Australia, Netherlands, Portugal and USA) in developing new technologies for discovery of novel interventions for malaria, leishmaniasis, African sleeping sickness and Chagas disease including support for research on natural products. A program to evaluate the social, economic, legal and ethical implications (ELSI) of transfer of biotechnology innovation to resource poor settings has also been initiated.

TDR has over the last several years promoted capacity building in product development associated areas of expertise such as good laboratory practice, good clinical practice, project management and ethical review. It has formed several public private partnerships involving principle investigators as lead scientists from the countries in which the studies are being carried out. It has also published guidelines on the clinical evaluation of herbal products linked to traditional medicines and has supported capacity building activities for laboratory based assessment of the activity of natural products against parasites such as malaria.

TDR has experience of facilitating several product development activities where ownership fundamentally resides based disease endemic countries (notably vaccines in China and Iran, diagnostics in India and drugs in, Thailand).

Success in discovery and development of new drugs and diagnostics in disease endemic countries will depend on brokering successful partnerships between academic institutions in both developing and industrialized countries, biotechnology companies, large pharmaceutical companies, host governments in disease endemic countries, international PPPs and large funding organizations.

TDR has established successful partnerships and convening power with academic institutions in DEC as well as in industrialized countries through its grants programs and committee activities. These networks of centres and investigators currently collaborating with TDR, combined with TDR's experience of incubating larger public private partnership organizations that can become stand-alone and sustainable such as the MMV and FIND, provides an important asset and source of innovation for technology transfer and innovation development in DEC.

3.2. SYNERGIES WITH OTHER ORGANIZATIONS

International Public Private Partnerships (PPPs) including MMV, TB Alliance, FIND and DNDi currently assess more projects having potential for development into interventions than they have capacity to manage or support financially. TDR also has several project leads that could be further developed. Such projects, in addition to projects initiated already in DEC, represent possible starting points for the development of drug and diagnostic tests projects for groups and teams in DEC.

Several Institutions in DEC have acquired necessary capabilities for participating in innovative drug discovery activities but could benefit from further partnership, coordination or international funding support. These institutions including FIOCRUZ, Brazil, BIOTEC, Thailand; ICGEB & CDRI, India; Noguchi, Ghana; NIPRD, Nigeria; SANBI, South Africa provide opportunities for rapid take off of project activities on the BL. Efforts will also be focused to use the strength of these group of countries to develop projects in less developed countries facilitated through south-south collaborations. Proposals will be developed with network institutions to seek funding support from international organizations and governments.

The activities proposed in this BL provide unique opportunity for TDR to build on its previous very successful PPP start up experiences (such as the MMV, FIND) and its collaborations with the PPPs to foster introduction of innovation through projects that will help to develop a new generation of innovative research scientists capable of driving entrepreneurial activity for discovery and development of biopharmaceuticals in situ. TDR's bridge to governments that are increasingly interested in nationally promoting innovation allow the activities of this BL to be reinforced and serve as part of a broader establishment of innovative capacity in DEC.

4. ACTIVITIES AND END PRODUCTS

4.1. KEY ACTIVITIES

Specific objective 1: Projects led by DEC institutions leading to innovative products

- Define gaps and opportunities for innovative R&D in DEC through mapping (create a database of projects, institutions and investigators). This could be achieved within 12 months, sustained and further developed.
- Facilitate, through competitive calls for proposals and the development of these proposals into coherent projects, the establishment of partnership R&D projects, with leadership from an institution in DEC. These projects would be a mix of exploratory and mature R&D projects. Special attention will be paid to projects building on and utilizing indigenous knowledge and clinical issues associated with evaluation of traditional medicines.
- Once projects are successfully established, collaborations will be brokered to facilitate further development phases between DEC project teams and other organizations (e.g. PPPs) as appropriate.

Specific Objective 2: Platform to support DEC leadership in product development

- Establish a support infrastructure to assist in the evaluation and transfer of emerging technologies for discovery of novel diagnostic tests and drugs to centres in DEC – this could be carried out in partnership with other organizations e.g. MIHR and be well established within 2 years, maintained and further developed.
- Provide particular support related to development of, and issues associated with, indigenous knowledge
- Facilitate through calls for proposals and meetings the establishment of reference centres of excellence for specific activities and networks to support discovery projects on drugs and diagnostic tests as appropriate.
- Link successful teams identified through projects to other projects as appropriate in order to continue to contribute to network activities and serve as reference groups.

Specific Objective 3: Facilitate creation of south based 'spin-offs'.

- Support the 'spin-off' for further development and sustainability of at least 4 project partnerships based in developing countries and regions, either self-standing not for profit (PPP) organizations, or business-focused support organizations. It may even be that some of these activities obtain investment funding from other sources and are taken on by new

companies. Emphasis will be placed on leveraging funding from other sources to ensure sustainability for the activities and to build on and maximize TDR impact.

- Establish courses and capacity to develop business plans and manage complex projects in key geographical segments.

In all activities attention will be paid to gender issues. Attempts will be made to redress the under-representation of women in this field of research by offering - wherever appropriate and through designated funding mechanisms - special opportunities to female researchers. Attention will be paid to regional and national initiatives to help address structural factors inhibiting women scientists in advancing their careers or making best use of their acquired leadership capacities. Attention will also be given to least developing countries (LDCs) and to countries for which the first language of operation is not English.

4.2. END-PRODUCTS

At the end of seven years this business line plans to deliver the following end-products

Specific objective 1: Projects led by DEC institutions leading to innovative products

- Up to 9 partnership R&D projects established with leadership from DEC institutions
- DEC led partnerships to have developed 2 rapid diagnostic tests and transitioned 2 drug candidates into development.

Specific Objective 2: Platform to support DEC leadership in product development

- At least 3 new centres established in Africa, Asia and / or Latin America with internationally renowned capacity for screening and identification of lead compounds for the development of novel drugs for TDR diseases.
- Transfer and establishment of technologies necessary for target validation, lead optimization and toxicology studies in at least 5 centres.

Specific Objective 3: Facilitate creation of south based 'spin-offs'.

- 'Spin-off' for further development and sustainability of at least 4 project partnerships based in developing countries, either as individual public private partnership projects, self-standing not for profit organizations, or activities taken on by companies

4.3. INTERIM IMPLEMENTATION MILESTONES

The implementation plan is based on a 2009 start as per the TDR business plan. The plan and milestones are represented in the GANTT chart attached as follows:

- Initiation of project: A database of activities, institutions, investigators emerging technologies and projects will be established and updated regularly in order to be current. Gaps, opportunities and priority areas for innovative R&D projects in disease endemic areas and relevant diseases will be defined through consultation meetings and establishment of an advisory board by second quarter 2009.
- A call and competitive selection of preliminary projects and support centres (e.g. screening centres) will be completed by end 2009. Two levels of projects (exploratory and full projects) will be selected.
- Constitute Project development team(s) and negotiate MoUs/agreements as appropriate to assist in selection and monitoring of projects by 2010.
- Transition existing TDR advisory expertise in this area to an expert scientific advisory committee by June 2008. Milestones: Workplan for translation research and product development committee. Review and funding of projects.
- Provide funding, establish technical support and develop business plans for 5 teams focusing on priority areas in discovery and development of interventions for neglected diseases by mid 2010.
- Facilitate development of tools for monitoring and evaluating projects, validating centres and deploy the tools by 2009 Milestones: two to three teams established by 2009; Monitoring and evaluation tools and practices developed by 2009; Tools and procedure validated by 2011

To be developed in collaboration with appropriate teams in TDR

- Provide program and facilities for training in Good Clinical and Laboratory Practices and Project Management.
- Assist in development of academic courses on product development through BL 2.
- Assist in developing programs in Ethical, Legal and Social implications (ELSI) of technology development and transfer.

Business plan: Business line 4 – Innovation for product development in DEC

| Activities | Years | | | | | | |
|----------------------------------|-------|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Mapping, updates and maintenance | | | | | | | |
| Calls for projects 1 | | | | | | | |
| Calls for projects 2 | | | | | | | |
| Calls for projects 3 | | | | | | | |
| Support Center Call 1 | | | | | | | |
| Support Center Call 2 | | | | | | | |
| Support Center Call 3 | | | | | | | |
| IPR Network Activities | | | | | | | |
| | | | | | | | |

¹ Calls for projects activities include letters of intent, short lists, selection and negotiation of MoUs

² Support Center activities will be designed to meet the needs of ongoing projects in specific activities such as chemistry, detail *in vivo in vitro* evaluations and toxicology studies. This will also include training and workshops on good practices, project management and ELSI

³ IPR issues on biology, chemistry and testing will be conducted in partnership with other organisations

5. FUNDING

5.1. RESOURCE REQUIREMENTS

US \$ x 1000

| Activity | Description | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|----------|--------------------------------|------|--------------|--------------|--------------|--------------|--------------|
| 1 | Mapping (Database development) | | 100 | 100 | 100 | 100 | 100 |
| 2 | Funding for full projects | | 500 | 1,250 | 1,500 | 3,000 | 4,250 |
| 3 | Exploratory projects | | 250 | 500 | 500 | 500 | 500 |
| 4 | Support centers and networks | | 100 | 200 | 200 | 200 | 200 |
| 5 | Scientific Meetings | | 100 | 100 | 150 | 150 | 150 |
| | Activities | | 1,050 | 2,150 | 2,450 | 3,950 | 5,200 |
| | Personnel Costs | | 349 | 805 | 1,382 | 1,382 | 1,382 |
| | No. of professional staff | | 1 | 3 | 5 | 5 | 5 |
| | No. of support staff | | 1 | 1 | 2 | 2 | 2 |
| | Total | | 1,399 | 2,955 | 3,832 | 5,332 | 6,582 |

5.2. RATIONALE FOR RESOURCES REQUIRED

The starting budget for the first year of the BL will be US\$ 1.4 million, increasing gradually as more projects are developed and centres activities take off, to US\$ 6.6 million by the fifth year. TDR support for each project is estimated at US\$ 0.5 million per year for full drugs discovery and development projects, US\$ 0.25 million per year for diagnostic tests projects and US\$ 0.1 million per year for exploratory projects. It is anticipated that this support will be supplemented by cost sharing, gifts and in kind support from industry and national, regional and inter-national organizations including bilateral supports for the participating countries.

The funds provided through this business line, though significant, do not support the full costs of the R&D projects. This level of funding will however make a real impact on projects and help move them forward. The projects will require leveraged additional funding from other sources, especially as the projects move into late stage clinical development and manufacturing and production. TDR's added value, in addition to provision of funds is through managerial and mentoring support and leveraging other financial support. The goal of this BL is not to fully develop a product, but to initiate, facilitate, stimulate and empower individuals, institutions and countries to develop their capabilities and projects to a level where they can significantly sustain themselves.

Distribution of projects and activities for drug discovery and development projects

| Year | Exploratory projects | Discovery | Pre-clinical | Phase I | Phase II | Phase III |
|------|----------------------|-----------|--------------|---------|----------|-----------|
| 1 | 2 | | | | | |
| 2 | 3 | 1 | | | | |
| 3 | 3 | 1 | 1 | | | |
| 4 | 3 | 2 | 1 | 1 | | |
| 5 | 3 | 2 | 2 | 1 | 1 | |
| 6 | 3 | 2 | 2 | | 1 | 1 |
| 7 | 3 | 2 | 1 | | | 2 |

Distribution of projects and activities for diagnostic tests discovery and development projects

| Year | Exploratory Projects | Discovery and Laboratory | Clinical Field Evaluation |
|------|----------------------|--------------------------|---------------------------|
| 1 | 1 | 2 | |
| 2 | 2 | 2 | 1 |
| 3 | 2 | 1 | 1 |
| 4 | 2 | 2 | 2 |
| 5 | 2 | 3 | 2 |
| 6 | 2 | 2 | 2 |
| 7 | 2 | 2 | 2 |

6. RISKS

Health biotechnology innovation requires long term commitment and sustained financial as well as technical support. Despite such investment, there is no guarantee that new interventions will be delivered immediately. However, such investment well managed is guaranteed to deliver core infrastructure and human resources necessary for national and regional products R&D capabilities and could have further knock-on effects for innovation beyond tropical diseases for example providing biotech capabilities.

Some of the people we have discussed this with have doubt as to whether strong product R&D projects can be generated from developing countries. Our experience indicates that although this represented a significant challenge in the past, a lot has changed, the basic scientific expertise and 'desire' for developing countries to move into these activities is strong and the chances of success are high. It is our obligation to facilitate that process and help meet the needs expressed by DEC.

Some of the specific risks for the proposed BL are:

1. Failure of proposed projects to yield leads and products that can be further developed.
2. Reluctance to share or transfer technologies between partners that are necessary for innovation. Difficulty in obtaining multi-party agreements.