

TDR Business Plan 2008-2013

Endorsed by the Joint Coordinating Board, June 2007

“Fostering an effective global research effort on infectious diseases of poverty in which disease endemic countries play a pivotal role.”



Special Programme for Research & Training
in Tropical Diseases (TDR) sponsored by
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TABLE OF CONTENTS

1. EXECUTIVE SUMMARY	2
2. BACKGROUND.....	4
POVERTY, HUMAN DEVELOPMENT AND HEALTH RESEARCH.....	4
TDR - A SPECIAL PROGRAMME.....	4
CHANGED LANDSCAPE AND NEW STRATEGIC CHALLENGES	4
3. TDR VISION AND STRATEGY	7
CONTEXT	7
VISION	7
STRATEGY.....	8
4. BUSINESS LINES.....	10
BUSINESS LINE OVERVIEW.....	10
SCOPE OF BUSINESS LINES	11
MANAGEMENT OF BUSINESS LINES.....	13
BUSINESS LINE 1: STEWARDSHIP	18
BUSINESS LINE 2: EMPOWERMENT.....	20
BUSINESS LINE 3: LEAD DISCOVERY FOR DRUGS	22
BUSINESS LINE 4: INNOVATION FOR PRODUCT DEVELOPMENT IN DISEASE ENDEMIC COUNTRIES (DECS).....	24
BUSINESS LINE 5: INNOVATIVE VECTOR CONTROL INTERVENTIONS	26
BUSINESS LINE 6: DRUG DEVELOPMENT AND EVALUATION FOR HELMINTHS AND OTHER NEGLECTED TROPICAL DISEASES	28
BUSINESS LINE 7: ACCESSIBLE QUALITY ASSURED DIAGNOSTICS	30
BUSINESS LINE 8: EVIDENCE FOR TREATMENT POLICY OF HIV AND TB CO-INFECTION	32
BUSINESS LINE 9: EVIDENCE FOR ANTIMALARIAL POLICY AND ACCESS	34
BUSINESS LINE 10: VISCERAL LEISHMANIASIS ELIMINATION.....	36
BUSINESS LINE 11: INTEGRATED COMMUNITY-BASED INTERVENTIONS	38
5. TDR IMPACT MONITORING AND MEASUREMENT.....	40
OVERALL APPROACH.....	40
TDR LONG TERM IMPACT MEASUREMENT	41
TDR INTERIM IMPACT MEASUREMENT.....	41
BUSINESS LINE MONITORING	45
6. FUNDING	46
RESOURCE REQUIREMENTS	46
RESOURCE MOBILIZATION.....	48
RESOURCE JUSTIFICATION	49
7. OPERATING MODEL.....	51
ORGANIZATION STRUCTURE	51
GOVERNANCE STRUCTURE.....	52
CHANGE MANAGEMENT	54
8. KEY RISKS AND MITIGATING MECHANISMS.....	58
9. CONCLUSION	60

1. EXECUTIVE SUMMARY

Background

Health research is increasingly seen as critical for poverty alleviation and achieving the Millennium Development Goals. The Special Programme for Research and Training in Tropical Diseases (TDR) created in 1975 to support the development of new tools to fight tropical diseases of poverty and to strengthen the research capacity of affected developing countries, has made a significant contribution to this goal. However, the research environment has changed significantly over the last decades: (i) the epidemiology of infectious diseases is changing with some diseases moving to elimination and others emerging or re-emerging, (ii) there are many new initiatives and actors in the field providing new momentum but also leading to a more complex environment; (iii) disease endemic countries have greater research capability but are increasingly left behind in global research planning and priority setting; (iv) priority research needs are unequally covered with several research areas neglected despite their critical nature. In order to respond to these opportunities and challenges, TDR, through consultations with its stakeholders has developed a renewed vision and strategy.

Vision and Strategy

TDR's renewed vision for the next 10 years is to foster: **“An effective global research effort on infectious diseases of poverty, in which disease endemic countries play a pivotal role”**. In order to achieve the new vision, TDR will use a three-pronged strategy to: provide a collaborative framework and information service for research partners; empower scientists from Disease Endemic Countries (DECs) as research leaders; and support research on neglected priority needs. This implies three major strategic functions for TDR:

1. **Stewardship** for research on infectious diseases of poor populations: a major new role as facilitator and knowledge manager to support needs assessment, priority setting, progress analysis and advocacy, and to provide a neutral platform for partners to discuss and harmonize their activities.
2. **Empowerment** of researchers and public health professionals from DECs moving beyond traditional research training to build leadership at individual, institutional and national levels so countries can better initiate and lead research activities, develop a stronger presence in international health research and effectively use research results to inform national/ regional policy and practice.
3. **Research on neglected priority needs** that are not adequately addressed by other partners. This will focus on three research functions:
 - a) Foster innovation for product discovery and development
 - b) Foster research on development and evaluation of interventions in real life settings
 - c) Foster research for access to interventions

Business Lines

In order to implement this strategy, TDR will restructure its operations to a limited number of business lines (BLs), each supported by a robust business plan that details deliverables, timelines, milestones and partnerships. Gender will be mainstreamed into these plans. Their introduction will provide the necessary focus to achieve TDR's objectives and also ensure the desired accountability. Specifically, TDR proposes to introduce eleven business lines in the 2008-2009 biennium based on stakeholder consultations, scientific opportunities in the field and opportunities arising from TDR's current portfolio. Two correspond to the strategic functions of Stewardship (BL1) and Empowerment (BL2) that are core to the TDR strategy. The other nine correspond to the strategic function of Research on Neglected Priority Needs and may change over time. These include Lead discovery for drugs (BL3), Innovation for product development in DECs (BL4), Innovative vector control interventions (BL5), Drug development and evaluation for helminths and other Neglected Tropical Diseases (BL6), Accessible quality assured diagnostics (BL7), Evidence for treatment policy of HIV and TB co-infection (BL8), Evidence for antimalarial policy and access (BL9), Visceral leishmaniasis elimination (BL10), and Integrated community-based interventions (BL11). While Stewardship and Empowerment business lines span across all upstream and downstream research areas, the other nine, supporting Research on Neglected Priority

Needs, have varying levels of upstream/downstream focus with an increasing overall emphasis on downstream research. Some are functionally specific, while others are focussed on specific diseases. From a geographic perspective there will be a strengthened focus on research in DECAs with an emphasis on Africa. The scope of the business lines will be reviewed annually by TDR's Scientific and Technical Advisory Committee using clearly defined criteria to ensure optimal use of resources and continued relevance. This review will also allow different business lines to enter and exit the portfolio.

TDR Impact Monitoring and Evaluation

TDR will be evaluated on the impact it creates against each of its three strategic functions. Given the long term nature of its research activities, it is proposed that the impact created by TDR be evaluated over two horizons. In 5 years time (2012), TDR would be evaluated on the overall impact it has created on three specific dimensions, namely (i) Harmonization of research efforts as an indicator of Stewardship (ii) Disease endemic country leadership in health research as an indicator of Empowerment and (iii) Enhanced access to superior interventions as an indicator of Research for Neglected Priority Needs. This evaluation would entail a qualitative survey of key TDR stakeholders and a comprehensive quantitative review of all research outputs produced by TDR. In the interim, TDR would be evaluated annually on fifteen supporting quantitative impact indicators, which relate to the long term overall impact, and link to business line project milestones. Thus the system will cascade to the eleven business lines and can also be used to monitor their respective progress.

Operating Model

Operationalizing the strategy will require TDR to increase its annual budget of US\$ 50 million in 2007 to US\$ 80 million in 2013, an increase of ~8% per year which is modest but necessary if TDR is to meet its vision statement and foster effective global research and empowerment efforts in a professional manner. While TDR will attempt to proactively seek greater funding from the private, philanthropy and non governmental organization sectors, it is planned that the governmental and international public sector will still provide the majority of resources (70%). Should TDR be unable to mobilize the targeted resources, it plans to prioritize activities both across and within business lines. TDR will operationally restructure its organization to establish clear responsibilities and accountabilities and also foster a sense of entrepreneurship. Under the revised structure, four functional areas report to the director's office including: (i) Stewardship (BL1), (ii) Empowerment (BL2), (iii) Research on Neglected Priority Needs (BLs 3 to 11) plus, as, an integral part of the organization (iv) a small Portfolio Policy and Development team which will be responsible for metric monitoring and management of an 'innovation fund'. To adequately support these activities, TDR will have to grow its personnel headcount at an annualized rate of 6% from current levels of ~85 to ~120 in 2013. TDR will also strengthen and improve collaboration with all co-sponsoring agencies, notably WHO, including their regional offices. Properly positioned, TDR could become the infectious disease research arm of WHO and its other co-sponsoring agencies. As TDR transitions to this revised operating model, it will ensure adequate emphasis on (i) coordination and control processes, (ii) mechanisms to ensure accountability, (iii) enhancing capability and (iv) maintaining motivation of its staff and scientific committees. TDR recognizes the financial, scientific, human resources, external environment and project execution related risks to achieving this business plan and is proactively planning to mitigate them as it transitions to this new model.

The overall emphasis on focussed objectives based on analysis and stakeholder consultation, accountability for end-products, optimization of resource requirements, establishment of monitoring mechanisms and an operationalization plan is indicative of TDR's commitment to move towards a more business-like operational model. The anticipated cost-effective research-driven public health impact, with disease endemic countries playing a pivotal role, compares favourably with, and complements, other internationally directed research efforts. TDR believes that this business plan meets the challenges of its exciting new vision and represents a compelling opportunity for investment in research on infectious diseases of poverty.

2. BACKGROUND

POVERTY, HUMAN DEVELOPMENT AND HEALTH RESEARCH¹

Poverty creates conditions that favour the spread of infectious diseases and it prevents affected populations from obtaining adequate prevention and care. Conversely, infectious diseases predominantly affect poor populations and are a major cause of poverty. This message has been strongly promoted by WHO and others and there has been increasing recognition that poor health is an obstacle to development and that the control of infectious diseases is a prerequisite for poverty alleviation and the achievement of the Millennium Development Goals (MDGs). All MDGs are related to infectious diseases, whether directly as for HIV/AIDS, malaria and other infectious diseases (MDG 6), child mortality (MDG 4) and maternal health (MDG 5), or indirectly as infectious diseases affect productivity and learning, stigmatize and burden women, and proliferate in urban slums and among poor populations who lack access to essential drugs.

The vicious cycle of infectious diseases and poverty is difficult to break. Research is urgently needed to develop more effective tools and strategies to fight the infectious diseases of the poor and help attain the MDGs. Research, especially through research capability and research leadership in developing countries, is increasingly seen as a critical component, not only for improvements in health, but also for economic and human development.

TDR - A SPECIAL PROGRAMME

The UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) was created in 1975 within WHO as its Executing Agency to marshal the power of research and capacity building in the fight against infectious diseases of the poor, with the goal to improve the health of poor populations and to eliminate these diseases as obstacles to social and economic development. TDR has done this effectively and developed tools and strategies through effective partnerships. A SWOT analysis concluded that TDR is built on a solid and proven foundation of scientific expertise and effective international networks, that it must address weaknesses such as over-administration, and that the Programme can play a major international role in realizing opportunities and addressing challenges that are resulting from changes in the research landscape.²

CHANGED LANDSCAPE AND NEW STRATEGIC CHALLENGES

The research landscape of infectious diseases of poverty has evolved significantly over the last decades. This evolution has brought significant new opportunities but also new challenges that limit the effectiveness of the global research effort. Four key aspects of this changing landscape are:

¹ Poverty, Human Development And Health Research description summarized from 'TDR 10 Year Vision and Strategy'

² SWOT analysis for TDR outlined in 'TDR 10 Year Vision and Strategy'

1. Epidemiological changes

The epidemiology and control of infectious diseases of poverty have evolved significantly since TDR's inception, partly as a result of TDR research. Five of the original eight TDR diseases are now targeted for global (Chagas disease, leprosy, lymphatic filariasis, onchocerciasis) or regional (visceral leishmaniasis) elimination as public health problems. None of these diseases can be fully eradicated with the current tools and much research is still needed to achieve and sustain their elimination, but the research needs of these diseases have evolved significantly. In the case of diseases like malaria, while important new intervention tools and strategies have been developed (e.g. insecticide treated bednets, artemisinin combination therapies), large scale implementation lags behind and the burden remains terribly high. In other cases like TB, the epidemiology of the diseases has radically changed and is increasingly driven by the HIV epidemic. Similarly for other infectious diseases of the tropics, that were not originally included in TDR, e.g. certain helminthic infections and Buruli ulcer, the burden of disease, if known at all, persists and there are no adequate tools available for their control. Separating the current ten TDR diseases from other neglected infectious diseases of poor populations is increasingly artificial and there is a need for a more appropriate, more broadly scoped response to the priority research needs in disease endemic countries.

2. Increased activity and new actors

The organizational environment for infectious diseases research has changed dramatically. There is one major new organization, the Bill and Melinda Gates Foundation, and many new public-private partnerships (PPPs - 34 in product development), single disease control initiatives, academic consortia and others. This increase in the number of actors has been accompanied by a significant increase in resources for the development of new tools from various sources and further increases in budgets are expected for product development through public-private partnerships. This increase in actors and resources is a very positive development for infectious diseases research, but it has also resulted in a fragmentation of efforts and resources. Multilateral and bilateral donors, philanthropies and governments would therefore welcome greater coordination in agenda setting, harmonization in research funding, and more reliable information on investments in infectious disease research³. This would facilitate a better alignment of funding with priority research needs in disease endemic countries, and make donor actions more collectively effective in line with the Paris Declaration on Aid Effectiveness⁴.

3. Limited role of disease endemic countries

Despite the efforts of TDR and many other organizations, disease endemic countries are increasingly left behind in planning and priority setting for research on infectious diseases that are endemic in their countries. The technology gap is widening for many countries. They feel excluded from important debates and decisions, and are concerned that research is not properly targeting the public health problems that are of most significance to their populations. Disease

³ Fourth External Review of TDR. *Towards evolution and growth*. Geneva, TDR, 2006

⁴ High Level Forum on Aid Effectiveness, Paris, March 2005. *Paris Declaration on Aid Effectiveness*
www1.worldbank.org/harmonization/paris/FinalParisDeclaration.pdf

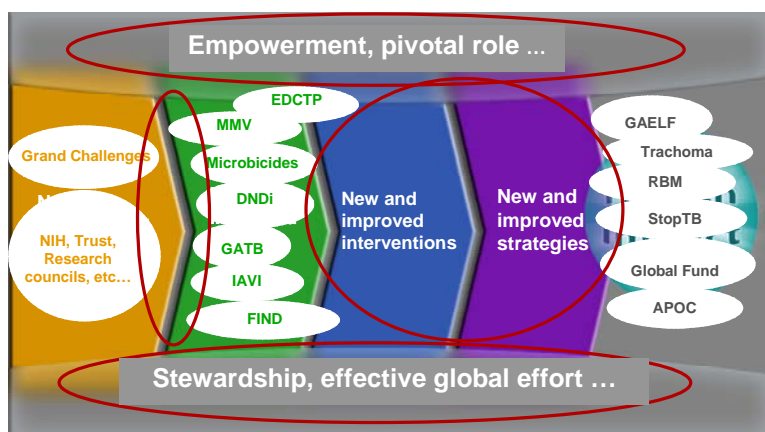
endemic countries have expressed the need for more direct participation in research priority-setting and other consultations that shape decision-making, and for the establishment of mechanisms through which their voices can be heard and where their public health research needs are publicized and better understood.

The research capacity in disease endemic countries has grown over the last decades and several countries are committing more of their own resources to health research. However, there remains a major need for further capacity strengthening, especially at a more strategic level in support of priority setting and research planning. Research capacity is still largely academic based, and disease endemic countries are still heavily reliant on north-south technology transfer. There is a great need to enhance capacity for innovation and product development in disease endemic countries, to build national capacities for policy and implementation research, and to enhance research capacity in control programmes and strengthen national commitment to health research.

4. Neglected research areas



Activity of other research and control organizations and major gaps (in red) informing the basis of TDR strategy.



The global research effort on infectious diseases of the poor is diverse and fragmented. Some areas are well covered, e.g. drug development for malaria and TB, and there is little need for TDR to support research in these areas. But other areas are neglected even though they are critical for the overall impact of the global research effort. Among these neglected areas are interfaces between major research domains, e.g. translational research between basic research and product development, research on the effectiveness of interventions between product development and intervention policy, and implementation research between research and large scale disease control. Research on each of these interfaces is absolutely critical: translational research to

feed the product development pipeline, intervention effectiveness research to inform policy of use and implementation research to help ensure that interventions reach the poor. The need for implementation research is especially great given the problems that health systems and disease control programmes have in achieving adequate coverage with available health interventions. Without significant research activities in these interfaces, the overall global research effort will fail to deliver the intended public health impact.

3. TDR VISION AND STRATEGY

CONTEXT

Given the change in the research environment over the last decades described in the previous chapter, TDR undertook a significant exercise to revisit its vision and strategy in 2005-2006. As part of the process an External Review was commissioned by its Joint Coordinating Board (JCB). Subsequent to the review, the JCB and TDR's Scientific and Technical Advisory Committee (STAC) provided broad direction and guidance. This led in turn to further wide ranging and active consultation with TDR's core governance constituents and stakeholders including experts in disease control, resource contributors, researchers from disease endemic countries and non-disease endemic countries, public private partnerships, the private sector and WHO (HQ and regional offices).

The resulting renewed vision and strategy responds to the new opportunities and challenges for infectious diseases research and the urgency to make the collective global research effort more effective and aligned to the needs of disease control in disease endemic countries. It also recognizes the need for disease endemic countries to play a leading role in research and priority setting to guarantee relevance, sustainability and optimal health impact for the poor. This strategy was discussed with TDR's Joint Coordinating Board during a special thematic session in October 2006, was approved, and is summarized in the rest of the chapter.⁵

VISION

TDR's vision for the next 10 years is to foster:

**An effective global research effort on infectious diseases of poverty,
in which disease endemic countries play a pivotal role**

TDR is uniquely placed to make this vision a reality in collaboration with other partners in the global research effort, but it will involve a new way of working for TDR. Increasingly, TDR needs to be a facilitator that supports all partners in optimizing their collective research effort against infectious diseases of the poor and that assists disease endemic countries in playing a leading role in this effort. TDR can play such a stewardship role because of its close links with disease endemic countries, the scientific community and all its co-sponsoring agencies and because it is established within WHO. TDR is seen as a programme that combines scientific competency, networking and experience, with a governance system that provides for equal participation of disease endemic countries at decision-making level.

TDR is also well placed to address neglected research on priority needs for disease control. A major strength of TDR over the last 30 years has been its impact-oriented research and capacity building activities that have yielded many tangible successes, have changed how disease control is managed, have reduced disease burden and have saved lives. The Programme has unique

⁵ Detailed description of TDR's vision and strategy outlined in 'TDR-10 Year Vision and Strategy' Document

experience, expertise and research networks in the relevant research domains, and its breadth of scope in terms of disease and functional expertise facilitates integrated, multidisciplinary approaches to problems. Increasingly, TDR is integrating its research and capacity building activities to ensure that scientists from disease endemic countries take a leading role in the research that it funds and coordinates.

STRATEGY

In order to achieve the new vision, TDR will use a three-pronged strategy with the following objectives:

- To provide a collaborative framework and information service on global research needs and activities for partners at global, regional and national levels
- To strengthen the scientific and management skills of researchers from disease endemic countries to empower them as leaders in research and to take a leading role in research priority setting and translation of research findings into health policy
- To support research on priority needs for disease control that are not adequately addressed

These objectives imply three major strategic functions for TDR:

1. **Stewardship** constitutes a major new role as facilitator and knowledge manager to: provide a neutral platform for partners to discuss and harmonize their research activities; provide up-to-date analysis and an online information service on global research needs, activities and progress; facilitate the identification of evidence-based research priorities through a process in which disease endemic countries play a leading role and that specifically addresses gender issues; advocate for research on infectious diseases of the poor; and help focus the global research effort on priority needs in disease endemic countries.
2. **Empowerment** of researchers and public health professionals from disease endemic countries, moving beyond traditional research training to build leadership at individual, institutional and national levels so disease endemic countries can better initiate and lead research activities, develop a stronger presence in international health research and effectively use research results to inform policy and practice.
3. **Research on neglected priorities** with focused support for innovative research on priority needs that are not adequately addressed by other partners, with a broad functional scope from discovery research to implementation research, but with a significant increase in support for implementation research. The stewardship and empowerment roles will permeate these research support activities and TDR will also facilitate entry of other partners into these neglected research areas.

Specifically within research on neglected priorities, TDR will emphasize on three research functions:

3a. Foster innovation for product discovery and development, emphasizing disease endemic country engagement

While product development partnerships focus on the development of control tools,

especially drugs, there remains a need for more effective "translation research" to feed "leads" into development pipelines; and greater engagement scientists from disease endemic countries in product R&D. TDR will work with and complement other research agencies and partnership activities by further developing networks between pharmaceutical companies, academia and institutions in disease endemic countries for the discovery of new leads for drugs. Promising leads will be transferred to other organizations as appropriate and if not adequately taken up by others, TDR might also pursue them. There will be a new focus on strengthening innovation and product R&D in disease endemic countries and TDR will seek to establish and support innovative initiatives within product R&D institutions in those countries. Building on previous success, TDR will further partner and leverage global efforts on discovery and development of vector control tools through convening, brokering, and focused funding of research and support activities.

3b. Foster research on development and evaluation of interventions in real life settings

One of the most neglected research areas is the development, evaluation and improvement of new interventions and intervention strategies in real life settings, and within a public health context. This critical aspect of research provides disease endemic countries with the evidence needed to make informed policy decisions and is becoming increasingly important given the growing pipeline of intervention tools. As TDR reduces its emphasis on product development per se, it will expand its research activities and partnerships in this area with greater focus on product evaluation (diagnostics, drug combinations and novel therapeutic strategies) and evaluation in vulnerable populations (e.g. pregnant women) where others are reluctant to do research. It will include research to develop improved intervention/ elimination/surveillance strategies and to establish cost-effectiveness in real-life conditions.

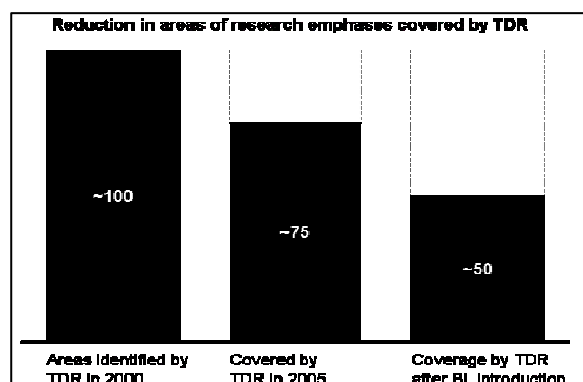
3c. Foster implementation research for access to interventions

Many products that have successfully completed the classical R&D process, have failed to achieve their full potential impact because of implementation problems that impeded access. Experience has shown that implementation research results in innovative strategies for getting interventions to the people who need them (e.g. Community Directed Treatment for onchocerciasis control). TDR research will focus initially on community-based interventions and integrated delivery strategies (covering both proven available products as well as new products), which are currently a priority need for disease control programmes and Ministries of Health, and address critical issues for scale-up. Implementation research will be undertaken in the context of national health systems and control programmes and involve leveraging of support for related research activities in countries (e.g. through the Global Fund to Fight AIDS, TB and Malaria). The social sciences will play a central role in implementation research by not only providing key research methodologies but also for undertaking related fundamental research on determinants of effective implementation of interventions such as the role of gender in access and health care delivery.

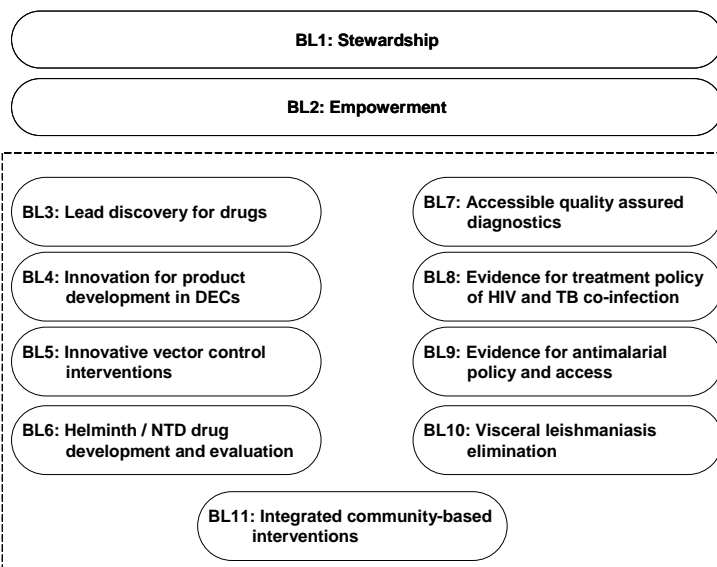
4. BUSINESS LINES

BUSINESS LINE OVERVIEW

To effectively deliver on its strategy and realize the objectives of the strategic functions of stewardship, empowerment and research on neglected priorities, TDR will restructure its operations to a limited number of clearly delineated business lines. Business lines represent a discrete set of coherent activities that lie at the heart of the new strategy. Each business line is inherently end-product oriented with a supporting business plan that details deliverables, milestones, timelines, funding requirements and partnerships, thus ensuring accountability. Two of the business lines correspond to the strategic functions of Stewardship and Empowerment that are core to the strategy and that require TDR to play a global cross-cutting role to bring greater cohesion and relevance to the international research effort. The other business lines fall under the strategic function of Research on Neglected Priorities. Each of them addresses an objective that caters to an unmet priority need for infectious disease control that TDR is well placed to address. The introduction of these latter business lines provides the necessary focus and business-like way of operating to the research activities supported by TDR. The figures (below) illustrate a focus on fewer areas of research under the new strategy and outline the specific business lines to be introduced in 2008-2009.



BUSINESS LINES TO BE INTRODUCED IN 2008-2009 BIENNIUM



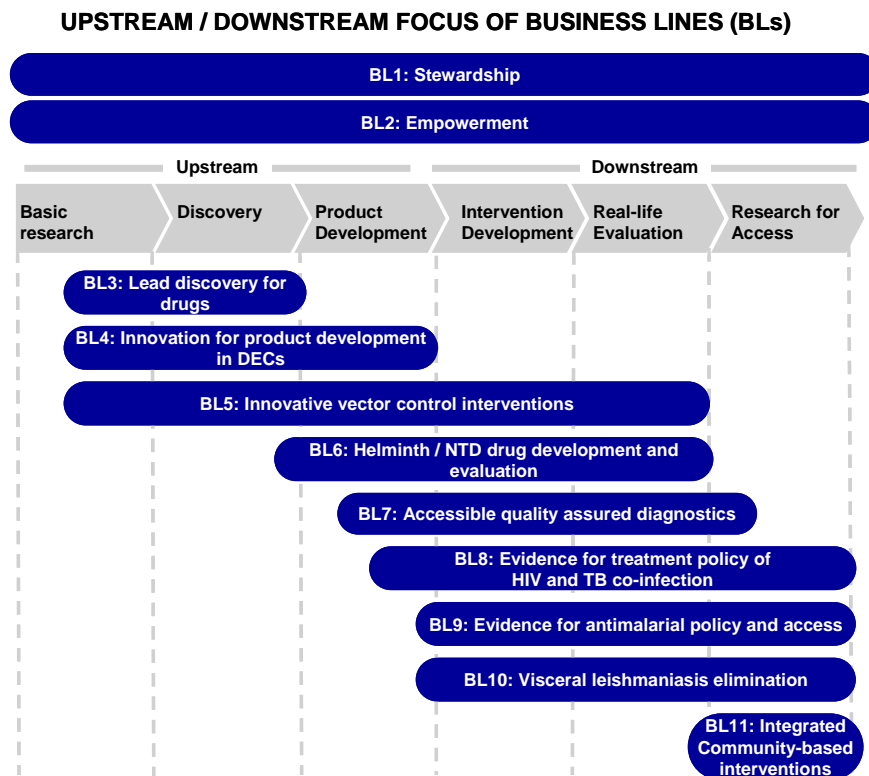
The clear objectives for the business lines, identification of deliverables and determination of metrics for monitoring progress are expected to: (i) ensure organizational alignment against the overall TDR strategy (ii) facilitate superior execution and achievement of objectives, and (iii) enhance attractiveness to potential donors.

The 9 research business lines planned as a starting point for the strategy are based on combined input from recommendations of recent scientific working groups that were managed in collaboration with the relevant technical departments of WHO, other stakeholder consultations on research needs and priorities, plus an assessment of opportunities arising from TDR's current portfolio. Whereas the two business lines corresponding to the strategic functions of stewardship and empowerment will be permanent features of the 10 year strategy, the research business lines will change over time. The criteria and processes by which this would happen are described later in this section under 'management of business lines'.

SCOPE OF BUSINESS LINES

Upstream vs. downstream research focus

Projects being undertaken by TDR under the purview of its business lines can be viewed in six categories of research. These are Basic Research, Discovery, Product Development, Intervention Development, Real-life Evaluation and Research for Access. While Stewardship and Empowerment business lines span across all these categories, the nine business lines operating under the Research on Neglected Priority Needs function have varying levels of focus on upstream and downstream projects as shown in the illustration below. Business lines 3 and 4 have an upstream focus while business lines 7, 8, 9 10 and 11 have more emphasis on downstream issues.



Disease focus

Not all the business lines will have a uniform scope; some can be functionally specific but cover a wide range of diseases, while others can be disease specific and cover a range of functions as shown in the illustration (right). Stewardship (business line 1) and Empowerment (business line 2) will address the full scope of infectious diseases. Innovation for product development will be restricted to the most neglected diseases and critical areas which are not adequately covered by others (e.g. business line 6 will not cover malaria and TB development given

INITIAL PRIMARY DISEASE SCOPE OF BUSINESS LINES (BLs)

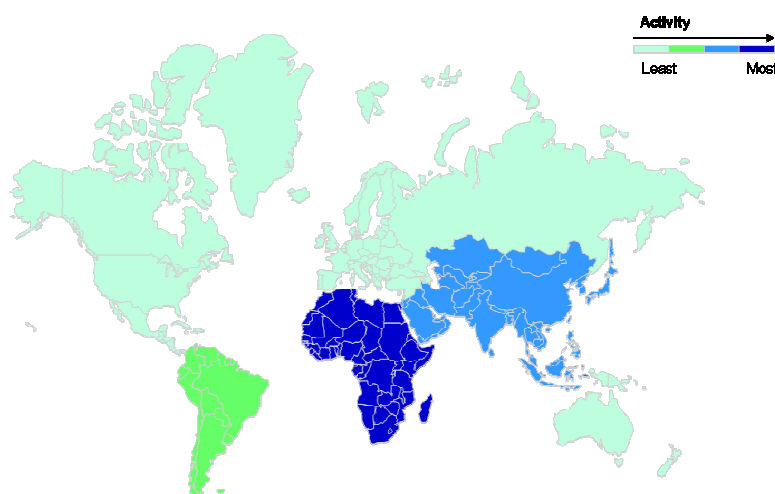
	Supporting BLs		Multi-Disease BLs						Single Disease BLs		
	BL 1	BL 2	BL 3	BL 4	BL 5	BL 6	EL 7	EL 11	BL 8	BL 9	BL 10
Malaria	✓	✓	✓	✓	✓		✓	✓		✓	
Tuberculosis	✓	✓	✓	✓			✓	✓	✓		
Dengue	✓	✓		✓	✓	✓	✓				
Kinetoplastids (Chagas, HAT, VL)	✓	✓	✓	✓	✓	✓	✓	✓			✓
Helminths (Schisto, Onco, LF)	✓	✓	✓	✓		✓	✓	✓			
Others (Leprosy, ST pneumonia)	✓	✓		✓		✓	✓	✓			

widespread efforts by public private partnerships (PPPs) but focus on helminths). Intervention and implementation research related business lines will focus on the TDR core set of neglected diseases, but with flexibility to respond to specific research needs of other diseases affecting the neediest populations. For example TDR’s emphasis on leprosy (one of the original ten diseases of focus for TDR) would be potentially restricted to business line 7 (Accessible quality assured diagnostics) and business line 11 (Integrated community-based interventions). At the same time, TDR plans to pursue emerging needs in sexually transmitted diseases (business line 7) and will pursue some limited research related to HIV (business line 8) and other illnesses experienced by children that especially link to malaria treatment including fever (business line 9). This proposed flexibility in disease focus will allow for a more appropriate response to the priority research needs in disease endemic countries.

Regional focus

From a regional perspective, the individual business lines will have varying activity levels e.g.

REGIONAL FOCUS OF ACTIVITIES ACROSS ALL BUSINESS LINES



business line 10 (visceral leishmaniasis elimination) will focus on the Indian sub-continent. Business line 5 (Innovative vector control interventions) will include Chagas' disease, which focuses on South America. Business line 9 (Evidence for anti-malarial policy and access) will lay emphasis primarily on Africa. Collectively, there will be a strong focus on research in disease endemic countries with

an overall emphasis on Africa. Where applicable, certain research activities will be regionally

based (e.g. business line 10 on visceral leishmaniasis elimination could be based in the Indian sub-continent), and in such cases TDR will facilitate and work towards local review, management and administration of activities. In line with current TDR trends, TDR-sponsored research will increasingly be undertaken and led by disease endemic country scientists and institutions with accompanying increased national and regional engagement. Additionally, TDR will enhance the responsiveness of its business lines to differences in regional needs through regional specific stewardship and empowerment initiatives, namely:

- Regional and national level institutions will be engaged to jointly assess regional research and capacity building needs and priorities, and to help develop solutions in collaboration with other organizations operating at the regional and country level. This process will fully utilize the regional and national structures of WHO (e.g. regional advisory committees for health research) and other co-sponsoring agencies.
- Coupled to the above there will be an enhanced emphasis on high level engagement in research discussions including ministries, regional political groupings and regional development banks.
- New regional initiatives will be established, such as the development of regional associations of tropical medicine and hygiene; and support will be given to develop best practices and processes for prioritizing and harmonizing infectious disease research within resource constrained countries.
- All TDR scientific committees will have regional representation from research and control communities, and will meet frequently in disease endemic countries.
- A concept is being developed under the Empowerment function, in which ‘satellite’ business lines will be operated and funded locally, but with technical support and quality assurance from TDR. This will be particularly valuable for continued TDR engagement with some middle income countries and can provide a mechanism to leverage their resources to support neighbouring countries that are more resource constrained.
- Regional networks focusing on specific issues, such as the Multilateral Initiative for Malaria, the Strategic Initiative for Developing Capacity for Ethical Review and the Forum for African Medical Editors will continue to be a focus of TDR activity.
- The above activities and many other regional activities will continue to be given added focus in TDR through its governance mechanisms, including the fact that two representatives from each of the six WHO regions sit on the Joint Coordinating Board.

MANAGEMENT OF BUSINESS LINES

The business lines will be reviewed regularly, at least annually, to ensure the optimal use of resources, the continued relevance of their activities and overall portfolio balance. Each business line will have its own scientific advisory committee to review technical progress, make recommendations on funding based on peer review, and advise on the strategic direction and workplan of the business line. On top of this, TDR's overarching Scientific and Technical Advisory Committee (STAC) will have the key role of reviewing progress of the full portfolio of

business lines at a higher strategic level and advising on the direction relevance and balance of the entire portfolio of TDR activities. In particular the entry or exit of a specific business line would require a proposal by the TDR secretariat, review by STAC and a subsequent decision by the Joint Coordinating Board.

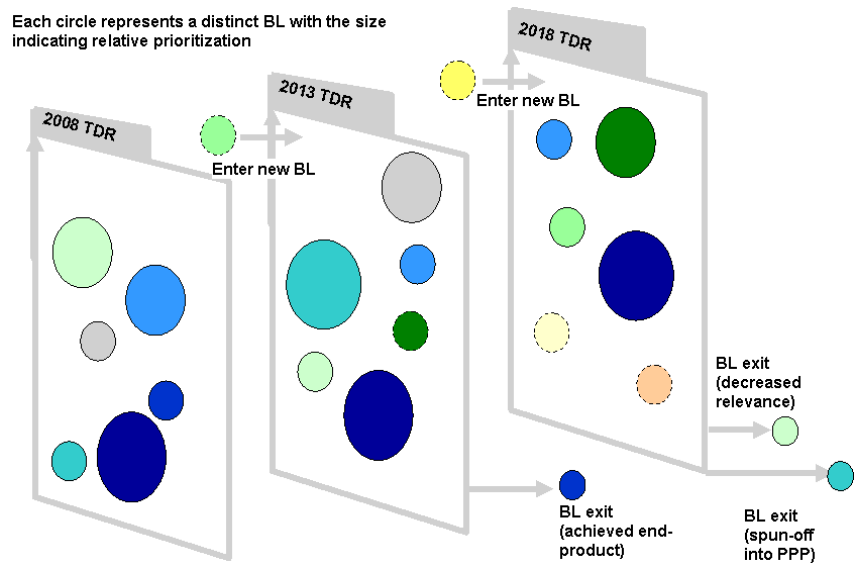
Entry - exit of business lines

While it is envisaged that the business lines associated with the strategic functions of Stewardship (BL 1) and Empowerment (BL 2) will remain throughout the duration of the strategy, business lines associated with the Research on Neglected Priorities function may change depending on need and circumstance over the next 10 years to provide added dynamism to the portfolio. The following criteria will be used to decide on portfolio entry of a new business line (all entry criteria to be met) or portfolio exit of an existing business line (when one of the exit criteria is met).

<p>Entry Criteria:</p> <ul style="list-style-type: none"> • Priority research need, demanded by countries, fitting within TDR strategy • Neglected research area not adequately covered and/or requiring DEC engagement • Expected high impact • Added value from TDR engagement • Potential for leveraging added benefit through partnering • Utilization and leverage of DEC research capacity and leadership • Adequate resources • Realistic business plan demonstrating the above and with risk/benefit assessment 	<p>Exit criteria:</p> <ul style="list-style-type: none"> • Deliverables met and goals achieved • Conclusive evidence that objectives cannot be met nor goals achieved • Relevance significantly reduced due to external factors or risk / benefit change • Inadequate performance, business line superseded by others, or activity better taken over by others • Spin-off: new partners effectively and sufficiently engaged with adequate resources and strategy to keep research sustainable without full TDR support • Lack of adequate resources
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In addition to the business lines an innovation fund of up to US\$ 1 million per year will be established to attract and promote novel research activities that may not currently be within the scope of TDR’s business lines. These research activities could potentially spur development of new externally driven programmes or future TDR business lines, if the research activities are scalable and fit with TDR’s strategic objectives. A subject area might arise for the establishment of a new business line in the following way: (i) analysis of critical areas of research undertaken through the Stewardship function might identify unmet research needs (e.g. vector borne diseases and climate change or impact of zoonoses); (ii) consultation with partners could further elaborate some pilot research usefully undertaken through TDR, which is accommodated and managed through the innovation fund; (iii) the pilot activity may result in not proceeding with further work, may lead to further activities best spun out for others to take on, or may lead to strategically important and substantive activities that justify development of a business plan and business line for TDR engagement.

Scenarios for business line exit are equally important. It may be possible to plan the exit of some business lines well ahead if they are specifically time limited. For example business line 10 should be completed by 2015, given the current target date of elimination of visceral leishmaniasis in the Indian sub-continent). However, exiting business lines in general is not so easy to predict as multiple issues justify exit. In some cases a business line may be exited if its stated objectives are no longer relevant due to changes in the external environment (e.g. emergence of other organizations adequately fulfilling the need). In contrast, some business lines could significantly enhance their scope and size (e.g.



business line 3: Lead discovery for drugs) leading to a spin-off as a stand-alone organization, as was done in the case of the Medicines for Malaria Venture (MMV) and Foundation for Innovative New Diagnostics (FIND). The work of some business lines might become closely linked so they need to merge (e.g. business line 9 on Evidence for antimalarial policy and access, and business line 11 on Integrated community directed interventions). Thus although this business plan indicates medium to long term activities for all nine business lines associated with the Research for neglected priorities function through to 2013, in practice one or two might yet exit, or require substantive modification before 2013. This would be managed with advice from the scientific advisory committees of the business lines and TDR's Scientific and Technical Advisory Committee (STAC).

The role of fundamental research

The move to the impact driven research defined by the business line approach and the focus on translational, intervention and implementation research does not imply a downgrading by TDR of the importance and significance of fundamental research. TDR firmly believes that scientific opportunity drives research across the entire research continuum. However, as demonstrated in the figure on page 6, there is less need for TDR to engage in the more open-ended basic research that is better handled, and better funded, by many national research agencies, and TDR's main comparative advantage lies more downstream.

TDR's research will focus on the translation from basic research to innovation for product development and on the translation from product development to implementation and use. These activities however remain hypothesis driven and open to addressing fundamental questions:

- (i) the stewardship function will report on and advocate for basic research outputs and needs, in the context of its overall analysis of research needs and opportunities;

- (ii) empowerment will develop skills essential for translational research but will also seek to ensure that fundamental academic skill gaps are addressed, e.g. social science research;
- (iii) innovation research for products will include exploratory discovery research as appropriate and the relevant business lines each have a budget component for this activity;
- (iv) research on interventions and access will include hypothesis driven clinical research, or fundamental social research on issues such as determinants of compliance;
- (v) TDR will retain an 'innovation fund' for research of any nature that shows particular scientific promise.

Mainstreaming gender

TDR will mainstream gender in all its stewardship, empowerment and research activities. Each business line has identified in its business plan the gender dimension of its activities, which range from stewardship for gender equity in setting the research agenda and the role of gender as a key issue on the research agenda, gender equity as a major objective in empowerment for health research leadership, and the role of gender in the research activities supported by the research business lines. Gender is particularly important for business lines 7 to 11 which deal with evaluation and implementation research in which gender is a key determinant of the applicability and acceptability of interventions and of critical social processes in intervention delivery and access, and the corresponding business plans include a more detailed description of how these gender issues will be addressed. The advisory committee for each business line will track progress in addressing the defined gender issues, and identify new issues that will be incorporated into the business plan as appropriate. Each business line will be required to specifically address the gender dimension of its activities in its annual report to the Scientific and Technical Advisory Committee, which will then comprehensively assess TDR's progress in mainstreaming gender.

Ensuring disease endemic countries play a pivotal role

The business plan and strategy can only be successful if careful attention is paid to this critical element of the vision. Operationally it is critical at the outset that disease endemic country individuals, institutions and governments are at the heart of what TDR does from a governance, stewardship and technical perspective. It starts with appropriate representation on stewardship and empowerment consultations and is manifest in the manner in which individual research business lines are managed and operationalized through committees and investigators.

All TDR committees will continue to strive to have an appropriate geographic and gender balance. All research activities in disease endemic countries will seek to have national scientists as principal investigators, thus both developing and utilizing capacity through their research. TDR will seek to ensure that research activities in countries are aligned with national objectives and will further seek to work with and through national programmes, particularly for intervention and implementation research. In this way TDR will seek to put into practice the principles of the Paris declaration for its research. As well as retaining TDR's long standing promotion and utilization of disease endemic country expertise through its research, the stewardship and empowerment functions will seek to embed this further within the broader political context of research for health, including evidence for policy and capacity for innovation.

Ensuring synergies across strategic functions and business lines

The vision of fostering 'an effective global research effort on infectious diseases of poverty in which disease endemic countries play a pivotal role' should be at the heart of all that TDR does. TDR cannot help bring about enhanced coherence of global efforts if it is not working in a way that is internally coherent within the Programme and also within WHO. Managerial processes will ensure transparency of objectives and activities with comprehensive information exchange to help link relevant activities across functions and business lines. It will be particularly critical that the overlap of objectives within stewardship and empowerment lead to synergies of action. Both functions depend on outreach to the scientific community for success. Outreach, knowledge management and analysis leading to coherence of agendas (stewardship) and promotion of research leadership in disease endemic countries (empowerment) are separate, but related objectives. They both meet at the level of convening partners to assess needs and empowering those partners to deliver. These two processes are prominent across all TDR business lines. Cross-talk across the business lines to ensure that there is effective communication between different external networks, as well as within networks, will lead to significant synergies and movement for change. This will occur through appropriate web-based information on activities, appropriate planning of advisory committee meetings and regular internal secretariat meetings to monitor and assess both progress against defined objectives and opportunities for achieving TDR objectives. Collaborative working across strategic functions and business lines will be one of the competencies against which staff will be assessed.

Summary description of Business Lines

In the next sections each of the business lines will be summarized to illustrate the needs and opportunities, objectives, activities, end-products and comparative TDR advantage associated with their operation.

BUSINESS LINE 1: STEWARDSHIP

Needs and Opportunities

In recent years, there has been considerable new momentum and increased financial support for research and control of infectious diseases of poverty. While this is a positive development, it has also resulted in fragmentation of efforts and greater scientific inequality between developing and developed countries. There is little coordination among different research initiatives and it is becoming increasingly difficult for all stakeholders to know what research is being undertaken and to what extent current research efforts meet priority needs for infectious disease control. Knowledge on priority needs is becoming blurred as different constituencies define priorities from their own perspective and the role of disease endemic countries in research priority setting remains extremely limited. Furthermore, limited access to relevant research evidence continues to hamper effective utilization of research results for disease control efforts in developing countries. Efforts to bring better coherence and harmonization of the various activities are now much needed. As the only United Nations-based Programme dedicated to infectious diseases research, the TDR Programme is uniquely positioned to assume this global facilitating role, in close collaboration with its many co-sponsors, stakeholders and partners, including at regional and country level.

Overall Objective

To facilitate and foster knowledge management, needs assessment, priority setting and progress analysis for health research on infectious diseases of poverty, and to provide a neutral platform for stakeholders to discuss and harmonize their activities with disease endemic countries playing a pivotal role in the agenda setting.

Specific Objectives

1. Provide a global information platform on health research needs, opportunities and activities on infectious diseases of poverty.
2. Develop an evidence and analysis-driven forum for the identification of priority needs and major research gaps through stakeholder consultations and to enhance the relevance of infectious disease research priorities to control needs.
3. Provide a neutral platform for partners to discuss their activities, reach the highest possible level of consensus and enhance their collective efficiency and advocacy for infectious diseases of the poor with active involvement of disease endemic countries.
4. Advocate for support of health research and effective utilization of its results in control of infectious diseases of poverty at international policy level.
5. Foster research networks and kick-start innovative research initiatives.

Activities

The business line will organize broad consultations with partners from the research, disease control and donor communities in order to review the analysis of research needs and priorities, and to facilitate greater harmonization of the activities of different partners. Scientific working group meetings will be organized to undertake an in-depth and authoritative review of research progress, needs and priorities for individual diseases or cross disease issues. With support from consultants and virtual reference groups of experts, especially with active participation of

endemic countries, the business line will undertake systematic analysis of research opportunities and needs, and publish every two years a global update on infectious diseases research. The business line will also operate and improve an online knowledge platform on tropical diseases research that will be launched by mid-2007 and managed through BIREME, a well-respected WHO centre for health sciences information in Brazil, in collaboration with the Health Internetwork Access to Research Initiative (HINARI) and other key partners.

End-Products

- On-line global knowledge platform for infectious diseases research with equitable access to comprehensive information on research needs, activities and achievements; highlights of scientific publications; access to published articles; news and review articles on critical issues, discussion forums, resources, multimedia (launch 06/2007).
- Disease or thematic reference groups of global experts in specific diseases or cross-disease issues who continuously review research progress, identify scientific opportunities and control needs, and publish high-impact annual updates including in peer reviewed journals.
- Up-to-date published reports on research opportunities, needs and priorities, and research achievements for individual infectious diseases or cross-disease issues that are widely accepted and promote DEC research.
- Comprehensive analyses of regional or global research needs, science opportunities and challenges in health systems that stimulate high level fora and action.
- Biennial report on infectious diseases research: priority research needs, gaps and global progress (first publication by 12/2009).
- Collective advocacy for new opportunities in infectious diseases research, with evidence of activities initiated or enhanced, and with DEC institutions playing a pivotal role.

Comparative Advantage

Historically, TDR is the global leader in priority setting for tropical diseases research. It has developed a systematic method to analyse priority needs and research opportunities for tropical diseases, and results of a comprehensive analysis for 10 tropical diseases have been widely used as a reference for global priorities for tropical diseases research. TDR has a culture of consultation, networking and consensus building that is essential for objective analysis and inclusive priority setting. It is a programme that is built on the principles of science and is deeply committed to the generation of objective evidence as the basis for public health action. TDR, operating within WHO, has earned the trust of ministries of health of disease endemic countries and the programme has extensive networks in endemic countries that greatly facilitate the analysis of research needs. TDR has a strong track record in publishing high-quality publications and electronic media products on infectious diseases, and in making these available in disease endemic countries. TDR has surveyed the knowledge needs of researchers and health professionals, and has already taken the lead in developing an on-line global knowledge platform for tropical diseases research.

BUSINESS LINE 2: EMPOWERMENT

Needs and Opportunities

Research capacity in disease endemic countries has grown over the last decades and several countries are committing more of their own resources to health research. However, there remains a major need for further capacity strengthening, especially at a more strategic level and in support of priority setting and research planning. Strong health research leadership is needed in DEC's to inspire innovation and direct high quality research programmes that address national and regional priorities. Such leadership requires competent individual leaders, as well as a facilitating environment and interaction with health decision makers. Increasingly the international research community seeks the development of partnerships with local, national and regional institutions in DEC's. To be effective, these partnerships require strong and competent leadership within the DEC health research communities. There is a great need to enhance capacity for innovation and product development in DEC's, to build national capacities for basic, clinical, and implementation research, and to enhance research capacity in control programmes and strengthen national commitment to health research.

Overall Objective

To develop excellence and leadership in health research and decision making so that high quality institutional and national systems can identify and manage research priorities.

Specific Objectives

1. To support the development of responsible health research leadership in DEC's at individual, institutional, and national levels
2. To enhance the quality and relevance of health research in developing countries within the context of institutional and national frameworks by:
 - a. promoting interfaces between research academia and control institutions;
 - b. promoting best practices for research and associated decision making.
3. To leverage TDR's role in health research by fostering national and regional initiatives to promote and empower local researchers to meet their own health research priorities

Activities

The activities will support both individual researchers and institutions through a variety of mechanisms. Individuals will have access to research grants, scholarships, fellowships, re-entry grants and WHO regional office managed small grant schemes. Institutions will be encouraged to support their researchers and be provided with ongoing strategic advice and financial support. Databases on TDR researchers, institutions, research networks, ethics committees, research policies and methodologies will be set up as key linking resources. Special attention will be given to female researchers and to countries where English is not a primary language.

Health research management courses will emphasize the need for ethical and high quality in research and decision making, for both laboratory and clinical research. This will be backed up by a process that helps countries recognize and document the achievements of researchers and institutions and facilitates transition of research into practice. TDR will also support, through a networking approach, focused curriculum development required to sustain research in priority areas of neglected infectious diseases.

'Satellite' business lines for national and regional initiatives will be developed that are operated and funded locally. Technical support and quality assurance will be provided from TDR until such initiatives are self-sustaining.

End-Products

- Leadership by DEC researchers and research institutions:
 - Research leaders in DECs with internationally recognized research projects of high quality.
 - DEC universities effectively managing high impact research and generating high quality PhDs.
 - Inventory of TDR researchers and research institutions in DECs, including alumni, experts and recognized laboratories and institutions, so that their expertise can be utilized.
 - Short courses and masters courses established in research and management topics, maintained and sustained in DECs.
- Enhancing the quality and relevance of health research within national frameworks:
 - Networks of DEC researchers, research institutions and control partners involved in discussions on national research needs and facilitating transfer of research results into practice.
 - Guidelines and associated database developed on topics to inform the implementation and adoption of best practices. Internationally recognized standards increasingly being met by laboratories and researchers, human subjects protection programmes, ethics committees and data management centres.
 - Concept of health research quality systems established at national level and developed.
- Regionally based 'satellite' business lines/networks on specific research activities established to address unmet needs, operating under local ownership and with sustainable locally generated funding.

Comparative Advantage

TDR is a global leader in capacity strengthening for health research in DECs. It has partnered with many agencies, academic and non-academic institutions and networks to support human resources and research infrastructure development. It has fostered capacity building in biomedical and health research programmes for more than 30 years, and has a critical understanding of the needs of disease endemic countries and countries in transition regarding empowerment for health research leadership. TDR is itself engaged in all aspects of biomedical and clinical research, which provides it with a hands-on understanding of the need for research capacity, leadership and ethical decision-making. Since its inception, TDR has supported the training of 1,400 DEC scientists, 70% as PhDs and 20% at Masters level, with remaining 10% supported post-doctoral or short-term specialized training. Brain-drain has been minimal due to careful selection of candidates, long-term follow-up, and assistance to re-entry in the home institution. It has a track record of initiating self-sustainable regionally based activities, such as the Strategic Initiative in Developing Capacity for Ethical Review (SIDCER) and the Forum for African Medical Editors (FAME).

BUSINESS LINE 3: LEAD DISCOVERY FOR DRUGS

Needs and Opportunities

In recent years there has been an expansion of product development activities for tropical diseases through a number of new public-private partnerships (PPPs) for malaria, tuberculosis and certain neglected tropical diseases. However, there is a dearth of credible drug leads to feed the development pipeline of these PPPs and there is an urgent need for a vibrant drug discovery initiative to produce such leads. Furthermore, for helminth diseases there is currently no PPP for product development, and for the helminthiases there is a need to go beyond lead discovery and identify drug candidates that can be further developed by partners or within TDR.

Pharmaceutical and animal health companies often have relevant compounds that have not been assessed for their potential to treat tropical diseases. Experience shows that companies are willing to avail their compounds for testing but are unsure about an appropriate mechanism in view of the risk of exposing their intellectual property to competitors. TDR has played a pioneering role in establishing win-win agreements with industry in which they partner and contribute compounds for evaluation through the TDR coordinated network of compound assessment centres. Availability of parasite genome sequences also present opportunity for de novo discovery of new chemical entities.

International interest in, and WHO-promoted discussions on, public health, innovation and intellectual property continue to highlight the need for this activity and to link this to the development of innovation capacity in developing countries.

Overall Objective

To facilitate and support the discovery of new drug leads for tropical diseases through, networks and partnerships between pharmaceutical companies, academia and disease endemic country (DEC) institutions.

Specific Objectives

- Identify quality drug leads for tropical diseases and facilitate the transfer of those leads to PPPs, industry, and other innovative partnerships for further development.
- Identify drug candidates for helminth infections (initially focusing on schistosomiasis, lymphatic filariasis and onchocerciasis) through the Helminth Initiative and transfer the candidates to appropriate partners for development.
- Promote the global coordination of drug discovery activities through the network and partnership model.
- Promote technology transfer and innovative drug discovery in DECs through the North/South collaboration networks and partnerships.
- Support targeted fundamental research on generation of new tools to facilitate drug discovery.

Activities

The discovery of quality drug leads against infectious diseases associated with poverty will involve the establishment of a portfolio of prioritized targets, progressing validated targets through high throughput screening, *in vitro* and *in vivo* screening through the TDR compound assessment and pharmacological networks, as well as iterative medicinal chemistry and exploratory toxicology on promising leads. New partners for compound supply will be proactively identified, and transfer of leads to relevant development partners implemented. DEC researchers and institutions will be engaged in these partnerships.

End-Products

- 10 leads discovered by 2013, 1 lead transferred to a partner every other year
- Open access database of drug targets (starting 2007)
- Helminth Initiative fully functional by 2008
- 2 drug candidates for helminthiases identified by 2013
- Coordinated drug discovery strategy, based on networks and partnership
- DEC scientists and institutions participating in lead discovery
- Open access high-impact publications and standard operating procedures for lead discovery

Comparative Advantage

TDR is well positioned to play the leading role in the discovery of new leads based on its track record and current progress. TDR has considerable experience in virtual drug discovery and an understanding of the desired product profiles and needs of DECs. TDR has helped create some of the existing PPPs (e.g. MMV, DNDi, FIND) and also provided some of the lead series currently being progressed by them. TDR has the convening power to assemble global experts from academia and industry to review and select promising projects. It has unrivalled access to thousands of compounds through its unique network of compound assessment centres, and it has established win-win agreements with industry (e.g. with Pfizer, Serono, Chemtura) to enable them to contribute to the network. TDR has experience in creating networks between the North and South and in linking lead discovery with fellowships and capacity development in DECs. In fact, a new drug discovery strategy for tropical diseases based on networks between academia, industry in developed and developing countries is already in place and delivering leads.

BUSINESS LINE 4: INNOVATION FOR PRODUCT DEVELOPMENT IN DISEASE ENDEMIC COUNTRIES (DECS)

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 DECs 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 DECs 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 DECs.

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 DECs.
- 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 DECs.

Activities

Through establishing some successful product R&D partnerships in DECs 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 DECs 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

DECs. 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 DECs 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 DECs. 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 DECs 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).

BUSINESS LINE 5: INNOVATIVE VECTOR CONTROL INTERVENTIONS

Needs and Opportunities

Most neglected tropical diseases are transmitted by insect vectors, and there is a major need for research to develop improved vector control tools and strategies for prevention of these diseases. Genome sequencing of the main vectors of malaria, dengue, and Human African Trypanosomiasis (HAT) brings the promise of radically improved vector control methods, but their development will require careful coordination and field evaluation of the new approaches. Community-based vector control traps for HAT can effectively reduce the tsetse fly population. However the application of these traps has not been sustainable, partly because of technical constraints such as variations in their attractiveness for different species of tsetse flies. In the case of malaria, there is a need to generate new knowledge on vector biology, ecology and insecticides resistance in order to improve the implementation of existing vector control strategies. Elimination of transmission of Chagas disease was achieved in several countries in South America, but the vector control methods used are not appropriate for Central America where transmission is maintained by peridomestic and sylvatic triatomine vectors.

Overall Objective

To develop and evaluate improved and innovative vector control methods for the prevention of neglected diseases.

Specific Objectives

- To promote the development and testing of new methods for improving Human African Trypanosomiasis (HAT) vector mass-trapping systems, and support the generation and exploitation of Glossina genome sequence data.
- To advance the development and evaluation of new and improved integrated methods for malaria and dengue vector control.
- To progress the development and evaluation of alternative methods for the prevention of re-infestation and the control of Chagas disease vectors.

Activities

The activities of the business line will range from funding competitive research grants and supporting investigators to generate new knowledge on vector biology and to develop improved vector control methods; facilitating research activities undertaken by others to generate vector genome data; developing methodologies and criteria for field testing of new methods and approaches, including issues relating to ethical, legal and social implications (ELSI) of genetic modification of insect vectors, and supporting capacity building and ensuring active involvement of DEC researchers in the different research activities. The facilitating and coordinating role will build on the current TDR activities in this area, which are highly appreciated by all key partners.

End-Products

- Improved odour baits and odour release system for tsetse traps by 2011
- New and improved large-scale tsetse mass-trapping methods by 2012
- Glossina genome sequence data generated by 2010
- Criteria for biosafety and efficacy evaluation of GM vectors established by 2013
- Improved methods for integrated malaria vector control approaches by 2012
- Improved methods for targeted and integrated dengue vector control by 2012
- Methods for identification of the origin of triatomine re-infestation by 2010
- Improved methods for preventing Chagas disease vector re-infestation by 2012
- New methods for Chagas disease vector control developed and evaluated by 2013

Comparative Advantage

TDR has demonstrated research leadership as indicated by the multiple reviews it has published on vector control and the scientific working group meeting convened in 2002 where it defined the issues and challenges of vector control and recommended new research directions. TDR's catalytic role in vector research is expressed through examples such as the malaria vectors genetic transformation network and the International Glossina Genomics Initiative (IGGI) consortium. TDR is currently / in the process of collaborating with multiple partners in the area of vector research including entities like the Sanger Centre (UK), Genoscope and IRD (France), Riken Genomic Sciences Centre (Japan), Yale University School of Medicine (USA), Liverpool School of Tropical Medicine (UK), the SANBI (South Africa) and the Wellcome Trust. The Gates Foundation and the NIH Foundation have agreed to collaborate with TDR for malaria and dengue. Much of this interest relates to TDR leadership in promoting the debate on, and pragmatic research response to, Ethical, legal and social issues (ELSI) of genetically modified disease vectors in public health through a publication in 2003. This is of critical importance for the potential testing and delivery of innovative genetically modified organisms. Operating under the auspices of WHO greatly facilitates the ability to link research into policy and practice, for example there is already a long-standing collaboration between PAHO and TDR for Chagas. Finally TDR is also renowned for its achievements in capacity building and networking as illustrated by its support for the bioinformatics and functional genomics training centres in Thailand (for Asia) and Mali (for Africa) and its strong engagement of DEC institutions in the ELSI debate.

BUSINESS LINE 6: DRUG DEVELOPMENT AND EVALUATION FOR HELMINTHS AND OTHER NEGLECTED TROPICAL DISEASES

Needs and Opportunities

Helminthiasis are responsible for an enormous burden of disease in developing countries. This has been highlighted in recent years through WHO's development and promotion of an integrated strategy to address neglected tropical diseases. Although many new PPPs have been established for the development of drugs against certain neglected infectious diseases, none of them addresses the drug needs for human helminths and a variety of other diseases. The control of helminthiasis is based on preventive mass chemotherapy of populations at risk. Effective drugs are available, but they are few, and their extended use carries the risk of drug resistance development. Further research is also required to support their scaled-up use in combinations. The situation is particularly critical for onchocerciasis for which annual mass treatment with ivermectin has brought the disease under control but has not eliminated the adult parasites. The development of a safe macrofilaricide that would allow onchocerciasis eradication is therefore a top research priority. The drugs for lymphatic filariasis and schistosomiasis control have also limited effect on the adult or immature stages of the parasites, and more potent drugs would be of immense value for more effective control or elimination of these diseases.

Overall Objective

To develop new and optimize the use of currently available drugs for helminths and other neglected tropical diseases (NTDs).

Specific Objectives

- Development and registration of new drugs for onchocerciasis, lymphatic filariasis, schistosomiasis and other helminthiasis and field evaluation of their effectiveness to achieve the control programme objectives they are being developed for.
- Generation of evidence for improved use of currently available drugs to support disease control, elimination or eradication strategies for NTDs with emphasis on integrated disease management or prophylactic chemotherapy including:
 - Evaluation of the efficacy and safety of modifications of currently used doses or treatment regimens
 - Evaluation of efficacy and safety of combinations of currently available drugs
 - Assessment of safety and efficacy of co-administration of drugs
 - Evaluation of product safety and efficacy in children and pregnant women
- Development of products for other neglected diseases when an opportunity emerges and no other organization is available or has the know-how to do so.

Activities

The activities of the business line will involve the identification of development drug candidates and their progression into development, building on the work of BL 3. Product development will be undertaken according to a development strategy and plan, and legal agreement between WHO and Pharmaceutical partners, to generate evidence on efficacy and safety for drug registration by partners. Once a new drug is registered, the business line will proceed with field studies to determine the safety and effectiveness of the drugs in real-life settings, and their operational

value for disease control and/or elimination. Clinical studies will be undertaken to provide data for improved use of currently available drugs for diseases targeted in integrated intervention strategies in line with WHO strategy. To optimize the effectiveness and relevance of the research activities, there will be close interaction with disease control programmes and with Bio/Pharma companies in the North and South, while expounding and utilizing capacity and infrastructure in disease endemic countries.

End-Products

- Pre-clinical and clinical evidence of efficacy and safety of new drugs against helminths that support registration by pharmaceutical partners (e.g. registration of moxidectin by 2013).
- Evidence that the registered drugs are safe for large scale use and more effective than currently used drugs in the control of onchocerciasis, lymphatic filariasis, schistosomiasis and other helminthic diseases (e.g. impact of moxidectin on onchocerciasis transmission).
- New information for the utilization of drugs for diseases targeted for the integrated approach and multi intervention packages for disease control (e.g. combined use of praziquantel and oxamniquine).
- Evidence for improved use of currently available drugs to support disease control, elimination or eradication strategies (e.g. effect of benznidazole on chronic Chagas' disease).
- Capacity in centres in developing countries for conducting clinical trials and capacity of developing country regulatory authorities to review and approve clinical trial exemptions and new drug applications.

Comparative Advantage

TDR has around 25 years of experience and track record in discovery, development and operational evaluation of drugs for onchocerciasis, lymphatic filariasis and schistosomiasis; it has provided the evidence on which the global control and elimination strategies for these diseases are based. TDR has been supporting research on drug resistance and has clinically evaluated 5 drug candidates for onchocerciasis in the last 8 years. TDR has a track record of motivating pharmaceutical companies to provide their drug compounds for development for tropical diseases and to collaborate in and co-fund the development of these compounds TDR has conducted key clinical research of the safety and efficacy of concomitant administration of key drugs for integrated disease control. It has a track record in building, strengthening and utilizing capacity for Good Clinical Practices, Good Laboratory Practices, and Ethical review in disease endemic countries and conducting clinical trials according to internationally accepted standards. Finally, TDR has particularly close links with the African Onchocerciasis Control Programme (APOC), the Lymphatic Filariasis Elimination programmes and Schistosomiasis Control programmes which consider TDR to be their research arm. TDR works very closely with WHO's Neglected Tropical Diseases department in this area and responds to, informs and builds on its strategies for NTD control and elimination.

BUSINESS LINE 7: ACCESSIBLE QUALITY ASSURED DIAGNOSTICS

Needs and Opportunities

Diagnostics are a critical component of efforts to reduce disease burden and help countries realize their health-related Millennium Development Goals and their use and need is increasingly promoted in WHO policies and strategies. Unfortunately, although many high-quality diagnostic tests for infectious diseases are available, they are neither affordable nor accessible to patients in developing countries. For example, 500,000 babies die in sub-Saharan Africa every year from congenital syphilis because women lack access to a screening test for syphilis in pregnancy, and only 16% of TB cases are reported with a laboratory-confirmed diagnosis. The few existing tests that may be appropriate for use in primary health care settings in developing countries are sold and used with little evidence on their effectiveness because diagnostics are not subject to strict regulatory approval standards. There is an urgent need for accessible quality-assured diagnostics for infectious diseases of poverty, and for research to gather objective evidence on the cost-effectiveness of these tests in real-life settings.

Overall Objective

To promote and facilitate the development, evaluation and application of diagnostic tests appropriate for use in primary health care settings in developing countries.

Specific Objectives

- To define diagnostic needs for diseases of poverty and to set standards for diagnostics quality
- To facilitate test development
- To assess and assure diagnostic performance and quality
- To increase access to diagnostics in the developing world, taking into account socioeconomic factors and issues of gender equity

Activities

The activities that will be undertaken by this business line range from convening expert consultations to define diagnostic needs and product specifications, facilitating test development and test evaluation to test introduction for case management and disease control in DECs. The focus of research activities along the path from development to introduction vary between diseases according to needs, e.g. HAT, VL, and TB require intensive investment in test development as existing diagnostics are neither sensitive nor accessible. For other diseases such as malaria, VL and sexually transmitted infections (STIs), diagnostics are available but require a rigorous evaluation, or if evaluated and found to have acceptable performance, countries may need assistance with development of training materials, quality assurance programmes and formulation of policy for sustainable adoption. The business line will promote standards for diagnostic research and advocate for regulatory control of diagnostics in DECs. A network of biobanks will be established to provide well-characterized reagents, strains and specimens to facilitate test development and evaluation. Diagnostic trial sites will be provided with training in Good Clinical Laboratory Practice (GCLP) and capacity building modules will be designed with the ultimate goal of DECs leading their own diagnostics R&D, evaluations and quality assurance programmes.

End-Products

- Diagnostic needs and product specifications defined for each priority disease.
- International standards and guidelines for the design and conduct of diagnostic evaluations published for each priority disease.
- Novel diagnostic targets identified for HAT, schistosomiasis and tuberculosis (in collaboration with BL 3).
- Data on performance and operational characteristics of tests for priority diseases, with the publication of at least ten evaluations of diagnostics for primary health care settings in developing countries by 2012.
- Pre-qualification evaluation schemes established for all priority diseases.
- Preferential pricing and bulk procurement of new diagnostics, with at least 2 diagnostics included in the WHO Bulk Procurement Scheme for each priority disease.
- A validated framework and roadmap to accelerate the introduction and sustainable adoption of promising diagnostics into the developing world (in collaboration with BL 8 - 11).
- Templates for Quality assurance schemes for diagnostics with accepted performance.

Comparative Advantage

In the past few years, the diagnostics group within WHO/TDR has developed a strategic workplan based on WHO's comparative advantage which includes global convening power, setting norms and standards, and a strong network of regional offices that work closely with country disease control programmes. Specifically, the diagnostics group has convened global technical consultations to define diagnostic needs, and are developing quality standards for diagnostic evaluations, conducting diagnostic evaluations, working with countries to identify barriers to access to diagnostics and to conduct research to provide evidence for policy and sustainable adoption. It has also utilized TDR's extensive research networks and relationships with developing country control programmes to build capacity in diagnostic research, evaluation and test introduction. TDR has created a mechanism for diagnostic tests with acceptable performance and operational characteristics to be included in the WHO Bulk Procurement Scheme so that they can be available to all UN member states at negotiated pricing. This BL will build on this foundation and work closely with major test developers such as the Foundation for Innovative New Diagnostics (FIND) and the Program for Appropriate Technology in Health (PATH) to evaluate the tests developed. It will also work with WHO partners, country disease control programmes, research institutions, NGOs such as Médecins Sans Frontiers to conduct policy-driven test introduction and implementation research.

BUSINESS LINE 8: EVIDENCE FOR TREATMENT POLICY OF HIV AND TB CO-INFECTION

Needs and Opportunities

Resource limited countries are constrained in their ability to cope with the rising burden of HIV driven TB due to the limited evidence on strategies to optimize treatment and case management. For example, TB occurs concomitantly with HIV and, given the recent WHO - promoted scale-up of ARV therapy, there is an increasing need to define optimal timing of ARV therapy during TB treatment and to find better alternatives to current drug regimens (particularly rifampicin) that minimize drug interactions and side-effects. Independent of HIV status, the long duration of treatment required with the current regimens is an obstacle to effective TB control. Drugs like fluoroquinolones may allow for simpler, shorter regimens; these regimens must be tested, developed and registered. We also need to better understand and address the frequent occurrence of IRIS (immune reconstitution inflammatory syndrome). Identifying biological or pathogen surrogate markers will facilitate monitoring disease activity and treatment response, with the potential to accelerate treatment evaluation and drug registration. Lastly, there is a compelling need to identify constraints in accessing diagnosis and care of individuals suffering from TB and/or HIV co-infection and successfully addressing 'real-life' factors affecting adherence to treatment (including issues related to gender). While these challenges are enormous there is strong momentum to address these issues through the stop TB partnership, a global alliance of over 400 organizations, which aims to halve TB prevalence and deaths by 2015, partly through investment in R&D.

Overall Objective

To optimize treatment and case management/delivery of care for all patient populations with tuberculosis and tuberculosis/HIV co-infection, including patients with additional co-morbid diseases

Specific Objectives

- Develop the evidence for shortening and simplification of TB treatment in TB and HIV-infected TB patient populations.
- Develop the evidence for management of HIV-infected TB cases:
 - concomitant use of anti-TB and antiretroviral drugs
 - optimal timing of highly active antiretroviral therapy (HAART)
 - more effective anti-TB chemotherapy regimen for treatment with HAART
 - Role of bio/surrogate markers and immunomodulation for optimal care of patients presenting with IRIS and HIV-infected TB.
- Develop strategies for operational implementation of TB and HIV/AIDS case management and treatment strategies in resource-limited settings of high burden countries in Africa.

Activities

Activities will involve: (i) clinical trials to assess the safety and efficacy of better regimens for TB (including simplified/shortened regimens, treatments which can be given with ARVs and incorporate optimal timing of ARVs); (ii) clinical research on IRIS; and (iii) operational research on management of HIV-infected TB patients and scale-up of treatment strategies in resource-limited settings. These studies will be done in close collaboration with national TB and HIV control programmes in high-burden countries.

End-Products

- Simpler/shorter TB treatments, including; (i) registration and evidence for use of gatifloxacin-containing FDC for 4 months by TB Control Programmes (2013); (ii) evidence of safety and efficacy of 4-FDC TB therapy in HIV-infected and non-infected pulmonary TB patients (2011).
- Evidence for the optimal timing and concomitant use of TB treatment and HAART for improved management of HIV-infected TB patients (TB-HAART), (2013).
- Use of rifabutin-containing TB regimen (rifampicin-free regimen) for management of HIV-infected TB patients failing 1st line ARVs (2013).
- Evidence for the utility of bio/surrogate markers and immunomodulation for improved care of patients presenting with IRIS and HIV-infected TB (2013).
- Evidence to develop guidelines for improved access to care for HIV-infected TB patients.

Comparative Advantage

Many public and private health providers are involved in the field, but only few research programmes are as experienced and well placed as TDR to address the totality of issues surrounding the case management of TB, particularly in HIV high burden settings within National TB Control Programmes. TDR has longstanding networks of research institutions and cadres of nationals trained in the conduct of research in the countries where the burden of TB and HIV is most pronounced. TDR's links with National TB Control Programmes and its regionally based clinical coordination research support network will enable it to provide "real life" evaluation of the effectiveness and feasibility of the proposed interventions. This experience is demonstrated by the endorsement of TDR's strategy by the Stop TB partnership and the Stop TB department of WHO and its adoption of recommendations of the TDR's scientific working group (SWG) on TB. The partnership has asked TDR to contribute to the development of a research agenda⁶ and the operational deployment of new tools (drugs, vaccines and diagnostics) within National TB Control Programmes in conjunction with other key players.

⁶ Onyebujoh P, Rodriguez W and Mwaba P Priorities in TB research; Lancet. 2006;367:940-2

BUSINESS LINE 9: EVIDENCE FOR ANTIMALARIAL POLICY AND ACCESS

Needs and Opportunities

WHO estimates that malaria is responsible for over one million deaths per year. These deaths are avoidable using artemisinin-based combination therapies (ACTs), but most malarial fevers are not treated appropriately. Many patients seek treatment too late or do not reach public treatment facilities and obtain health care from the private or informal sector, where they often get inappropriate and poor quality treatment. If Millennium Development Goals 5, 8 and 17 (reducing childhood mortality, halt malaria and provide access to essential drugs) are to be met, there is an urgent need for research to complement existing malaria control policies and strategies through providing evidence for malaria treatment policy and for effective management of malaria at the community level. Several new antimalarial treatments are being developed and increased funds are being made available for DECs to deploy them. Countries need to make policy choices based on objective and comparative evidence on the safety and effectiveness of these antimalarial drugs, and to provide this evidence the different drugs need to be scientifically evaluated under real-life conditions. Research is also needed to determine the usefulness of diagnostics in different epidemiological settings, to improve diagnosis and treatment of malaria to community level and to determine effectiveness of integrated interventions against malaria and other childhood infections at the community level.

Overall Objective

To improve access to effective treatment for malaria and case-management of malaria and other childhood infections at all levels of the health system with the aim of reducing childhood mortality.

Specific Objectives

- To assess the safety and effectiveness of antimalarial drugs in "real-life" conditions of use, at different levels of the health care system, and in high-risk groups including pregnant women and persons infected with HIV.
- To develop a comprehensive package for the diagnosis and treatment of malaria episodes of various degrees of severity at the community level, determining its feasibility, acceptability, safety and cost-effectiveness.
- To develop an integrated diagnostic and treatment package to be delivered at the community level for the management of malaria and other childhood infections, and measure its impact to reduce mortality in children.

Activities

The studies to assess the safety and effectiveness of antimalarial drugs in real life conditions of use will be undertaken by an international consortium, built around the INDEPTH network where the field studies will be undertaken. TDR will be responsible for independent scientific oversight of the studies, and other partner institutions will provide technical support in their area of expertise. The implementation research on home management of malaria and fever will be managed by TDR, and involve multi-country studies to develop and test the effectiveness and health impact of improved home treatment methods and strategies. These studies will be

undertaken in close collaboration with national malaria control programmes to ensure optimal relevance of the research.

End-Products

- A research framework for the generation of information on safety and effectiveness of antimalarial drugs in "real-life" conditions of use (2008).
- Independent and objective evidence on the safety and effectiveness of new antimalarial drugs in real-life conditions of use (starting 2009).
- A field-tested, community-accepted, safe and effective treatment package for malaria episodes of various degrees of severity at the community level (2010).
- Evidence of the impact of the comprehensive diagnostic and treatment package to reduce severe malaria morbidity and mortality (2012).
- Guidance on how to scale up coverage with an effective diagnostic and treatment package for malaria made available to policy makers by 2013.
- Socially acceptable and operationally feasible treatment delivery model for prompt management of children with uncomplicated malaria, pneumonia and diarrhoea by community care providers (2009).
- Evidence on the impact of an integrated management package for malaria, pneumonia and diarrhoea at the community level on under-five mortality (2013).

Comparative Advantage

Over the last decade, TDR has been instrumental in developing strategies for community-level treatment of uncomplicated malaria episodes with oral drugs - it has conducted most of the original studies which led to the Home Management of Malaria strategy. TDR also undertook most of the studies that led to revised WHO recommendations for the treatment of malaria using ACTs. TDR has been instrumental in the development of several drugs against malaria such as Lapdap plus artesunate (in collaboration with MMV and GSK), rectal artesunate and the label extension of Coartem for paediatric use. It has experience in conducting post-registration studies, including multi-centre "Phase IV" trials and pharmacovigilance studies, and it has developed and refined a multi-country study model for this type of research. TDR is increasingly partnering in malaria research with research institutions and malaria control programmes, UN agencies (e.g. UNICEF), regulatory authorities, drug development agencies and other entities in affected African countries. By effectively combining research and capacity building, TDR has helped build a wide network of malaria researchers in Africa who can undertake the required research. TDR will work closely with WHO's Global Malaria Programme and the Roll Back Malaria Partnership to facilitate linkages between research and control.

BUSINESS LINE 10: VISCERAL LEISHMANIASIS ELIMINATION

Needs and Opportunities

Visceral Leishmaniasis (VL) is a fatal disease with an estimated incidence of 500,000 cases per year. Of those, 60% occur in the Indian subcontinent (India, Bangladesh and Nepal) mainly amongst the poorest population groups living in rural areas. Diagnosis and treatment of VL has always been very difficult, but the recent developments of new drugs (e.g. miltefosine - first oral drug for VL - ambisome and paromomycin) and diagnostics (rK39 - rapid diagnostic test for VL) has created a major new opportunity for improved control or even elimination of VL. Given the unique epidemiological features of the disease in the Indian sub-continent, namely (i) human beings are the only reservoir (ii) there is only one vector species which is amenable to control and (iii) the geographical distribution is limited, the elimination of VL is truly a realistic possibility. Furthermore, there is political commitment at the highest level with the Ministers of Health of Bangladesh, India and Nepal signing a Memorandum of Understanding at the World Health Assembly in 2005 for joint efforts to eliminate VL from the Indian Subcontinent by the year 2015. The elimination initiative has been facilitated by WHO as a whole and notably through its South East Asian Regional Office and has attracted the interest of several donors. However, to achieve elimination, major hurdles will have to be overcome and research is needed to further improve intervention tools and provide evidence on cost-effective and appropriate implementation strategies.

Overall Objective

To develop intervention tools and generate evidence for influencing policies for elimination of visceral leishmaniasis

Specific objectives

- Play a stewardship role to define needs, priorities and provide technical guidance to research for elimination of visceral leishmaniasis
- Generate evidence on most cost-effective elimination strategies using optimal interventions across treatment and vector control
- Develop and evaluate new and improved diagnostics, drugs and combination therapies

Activities

TDR will be the research arm of the Regional Technical Advisory Group (RTAG), convened by the WHO Regional Office for South-East Asia (SEARO), of the elimination initiative in the Indian subcontinent and will, through appropriate analysis, expert advice and consultation, advise the committee and other partners on the research aspects of the elimination initiative. TDR will expand its ongoing implementation research in the three countries, and increasingly integrate these research activities in the national elimination programmes. Research on the effect of implementation of case management and vector control will go in parallel with epidemiological modelling of the most effective strategy to achieve elimination. The development research on drug combinations and diagnostics will build on the established infrastructure and expertise in the

countries, especially in India and will be undertaken with partners in a way that maximizes its applicability for programmatic policy and action.

End-Products

- Ongoing functional link with the regional technical advisory group (RTAG), stakeholders and interested parties to assess and advise on tools and strategies for elimination (now till 2013).
- Consensus reached on VL elimination strategies (2013).
- Optimal and most cost-effective elimination strategy defined, combining case management and vector control:
 - Cost-effective and sustainable vector control strategy in the 3 countries (2011)
 - Evidence on real-life cost-effectiveness of the chosen drug combinations (2013)
 - Cost-effective strategy for case managements and optimal use of VL drugs and diagnostics in the health system and by the population
- Improved interventions: safe and affordable combination therapy (2013).

Comparative Advantage

TDR has a long and recognized experience in working with disease endemic countries and regions through WHO towards the development of cost effective intervention tools, focusing on public health needs and impact on the disease burden, taking into account the cultural sensitivity and operational feasibility. In the case of VL, TDR supported the development of miltefosine as the first oral drug and it also supported clinical development of Ambisome and Paromomycin. TDR has evaluated and validated rK39 rapid diagnostics for VL use in the Indian subcontinent and is currently evaluating an innovative diagnostic under development by an Indian - based academic / company collaboration. The research emphasis in this business line is on down stream implementation research activities to advise on elimination strategy and policy. TDR has significant experience in this area as evidenced by its research and capacity strengthening support that has fed into WHO supported elimination strategies for four other tropical diseases. To achieve this TDR always maintained consistent engagement with disease endemic country scientists and control programmes in a dynamic interaction process continuously looking for better solutions for disease control.

BUSINESS LINE 11: INTEGRATED COMMUNITY-BASED INTERVENTIONS

Needs and Opportunities

Several effective and simple interventions are available to prevent or treat infectious diseases of poverty such as malaria and neglected tropical diseases (NTDs). However these interventions often do not reach the affected populations that need them most, in particular, the poor and rural populations in Africa. Innovative ways of getting effective interventions to affected poor people are urgently needed. Community-based delivery strategies have been developed for different diseases, but vary in terms of community involvement, effectiveness and sustainability. Different control programmes implement their community-based strategies independently, resulting in inefficiencies and conflicting practices at the community level. There is an urgent need for effective strategies for co-implementation of community based interventions that build on effective models such as home management of malaria and community-directed treatment of onchocerciasis in which communities are empowered to manage the process themselves. Recent studies have indicated that co-implementation using the community directed model can greatly increase access to health interventions among poor populations, in line with WHO goals to promote integrated approaches that strengthen health systems.

Overall Objective

To develop innovative and efficient strategies for providing community based interventions to poor populations.

Specific Objectives

- To determine how to scale up the Community Directed Intervention (CDI) strategy and how to efficiently introduce it into new areas.
- To develop and test other community-level intervention strategies, especially for urban and post-conflict areas, for nomadic populations and through collaboration with other sectors such as in school health programmes.
- To determine the costs, benefits and limits of co-implementation of community-based health interventions, and how co-implementation can be simplified.
- To develop innovative solutions to the problem of conflicting incentive policies for community volunteers, and to develop mechanisms through which communities can enforce their demand for intervention supplies.

Activities

The business line will undertake large multi-disciplinary multi-country studies to explore and test new delivery strategies. The studies will be undertaken in close collaboration with national, regional and global disease control programmes, including APOC and the NTD and malaria programmes of WHO. As much as possible, the intervention strategies to be tested will be implemented through the regular health system. The preparation of the studies will involve extensive consultation with disease control programmes and ministries of health to carefully define the research needs and research questions, and exploratory studies to identify potential solutions that take into account critical social factors such as gender and economic status. The

focus of the business line will be on Africa and the research will use the extensive network of African public health and social science researchers that has been established in the context of previous research by TDR.

End-Products

- Strategy for upscaling CDI for co-implementation of interventions against NTDs and Malaria in areas where community directed treatment is already established for onchocerciasis control (2010).
- Strategy for CDI in areas where there is no onchocerciasis (2010).
- Delivery strategies for community based interventions in urban and post-conflict areas, and strategy for upscaling deworming through School Health Programmes (2011).
- Framework for co-implementation, including evidence on the costs and benefits of different co-implementation strategies, and on the type of interventions that are appropriate for co-implementation (2009-2011).
- Impact of conflicting policies for incentives to community volunteers documented and innovative solutions developed and tested (2011)
- Mechanisms to strengthen communities' influence on implementation strategy and help them reinforce their demands for support and supplies for interventions (2010).

Comparative Advantage

TDR has over the years acquired unique experience in the design and implementation of multi-country studies on innovative community-based interventions against infectious diseases in neglected populations. It has developed community based treatment strategies e.g. the Community Directed treatment with ivermectin and Home Management of Malaria, and the CDI strategy as an effective model for co-implementation of interventions. TDR has supported the training of a large network of scientists and researchers across a range of disciplines (including epidemiology, social sciences, economic research amongst others) thereby creating a unique network of researchers with expertise in the areas of community-based intervention approaches. TDR is a leading agency in the application of advanced social sciences in the design and evaluation of health intervention strategies. TDR has experience with involving disease control programmes and national health systems in the design and implementation of these studies, and in facilitating the effective transfer of research findings into policy and practice. As a WHO programme, TDR has close links with the relevant technical programmes of WHO, such as the African Programme for Onchocerciasis Control, Neglected Tropical Diseases and Global Malaria Programme, and effective access to ministries of health through the regional and country offices of the organization.

5. TDR IMPACT MONITORING AND MEASUREMENT

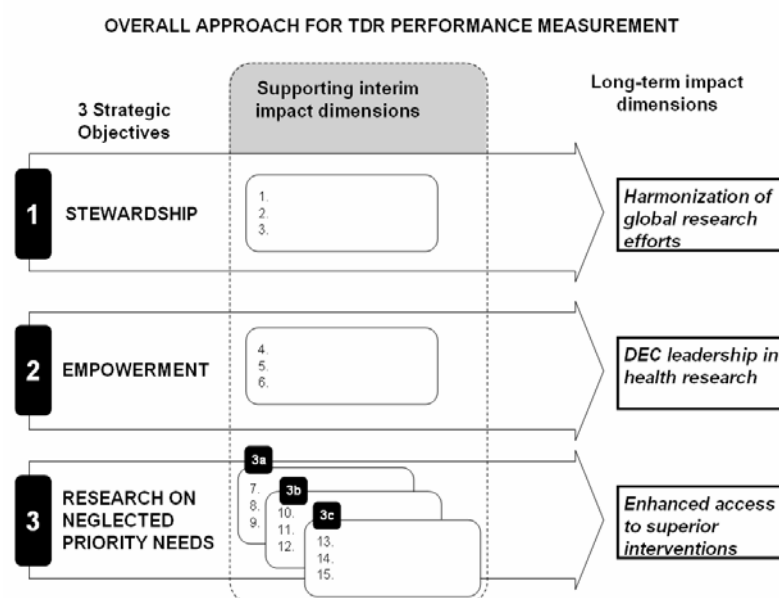
OVERALL APPROACH

A central problem with many monitoring methodologies is that the objectives of the organization are lost as one descends to specific metrics and milestone measurements of individual activities. The process proposed in this section avoids this by (i) Ensuring emphasis on the three strategic objectives - (1) Stewardship, (2) Empowerment and (3) Research on Neglected Priorities; (ii) Focusing on measurement of overall long term impact achieved against these objectives; (iii) Measuring interim progress towards achieving the overall long term impact through interim monitoring metrics; (iv) Cascading TDR level interim monitoring metrics to individual business lines.

In five years time (2012), TDR should be evaluated on the overall long term impact it has created on three specific dimensions that relate directly to its three strategic functions (described in greater detail below). Given

the nature of the strategic functions and their impact, the evaluation process, by definition, would need to be qualitative as well as quantitative in nature. The qualitative component would involve a detailed and rigorous survey of all of TDR's key stakeholders (e.g. control programmes, ministries of health, public private partnerships, lead investigators from developing and developed

countries, etc...) and the quantitative aspect would be based on a comprehensive review of all research outputs produced by TDR. This evaluation should be perceived not only as a formal review but also a check-point for course-correction for TDR as it develops its business plans for the subsequent six years. In the interim, TDR should be evaluated on fifteen supporting interim impact dimensions that relate to the targeted overall impact and provide a more immediate assessment of specific deliverables to help measure TDR's progress towards achieving that overall impact. These supporting impact dimensions would be tracked annually using a set of fifteen quantitative monitoring metrics that are tangible, feasible to measure, simple to understand and actionable. These metrics will cascade to the eleven business lines to ensure alignment of business line objectives with TDR strategy and monitor progress of the business lines.



TDR LONG TERM IMPACT MEASUREMENT

In five years time (2012), the three long-term overall impact dimensions that TDR would be evaluated on are:

- Harmonization of global research efforts
- Disease endemic country leadership in health research
- Enhanced access to superior interventions.

These three impact dimensions map directly to TDR's strategic functions of (1) Stewardship, (2) Empowerment and (3) Research on Neglected Priorities. Examples of some of the questions that would be reviewed through the proposed survey to provide a qualitative assessment by key stakeholders might include:

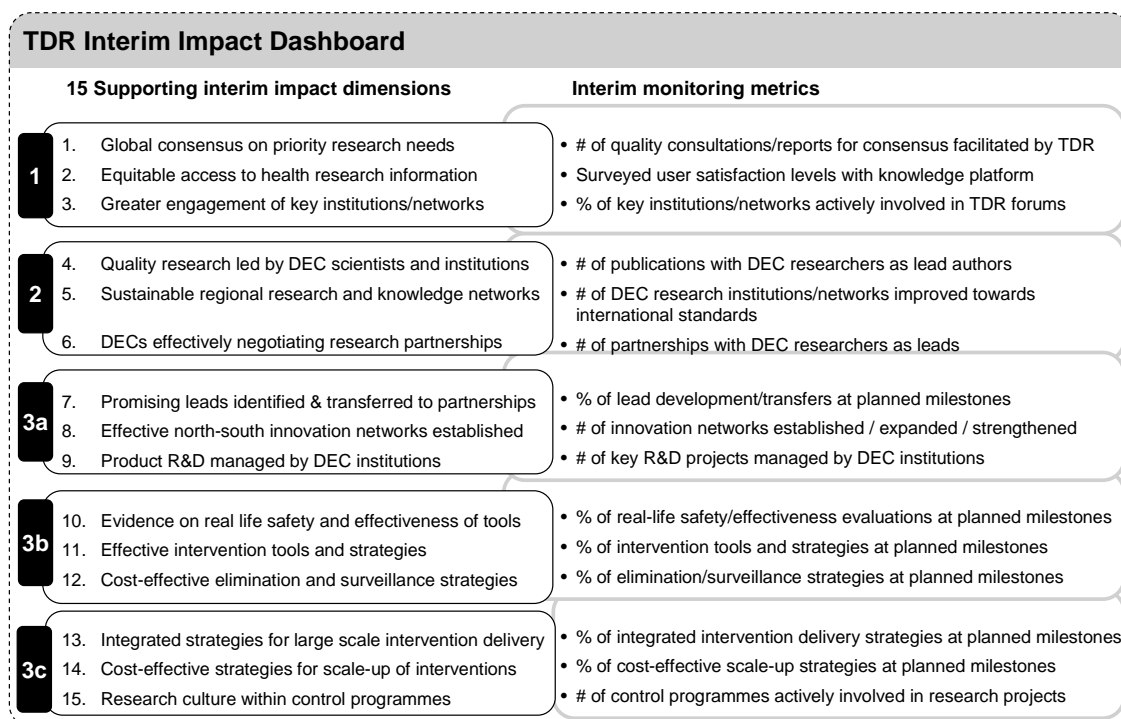
- Has TDR helped ensure a more coherent research approach?
- Is there greater engagement and leadership by disease endemic countries due to initiatives undertaken by TDR?
- Has research on neglected priorities, supported by TDR resulted in enhanced access to improved interventions?

The quantitative component of the overall long-term impact evaluation would include a comprehensive review of the output from the three strategic functions over the five years, in line with the fifteen monitoring metrics outlined in the next section.

TDR INTERIM IMPACT MEASUREMENT

The interim impact created by TDR will be measured annually using fifteen quantitative monitoring metrics. There are three monitoring metrics for each of the strategic functions of Stewardship (1) and Empowerment (2), plus nine for the strategic function of Research on Neglected Priorities (3) - three for each of the sub-functions of: foster innovation for product discovery and development (3a), foster research on development and evaluation of interventions in real life settings (3b), and foster implementation research for access to interventions (3c). The proposed metrics for monitoring these supporting impact dimensions are outlined as a "dashboard of indicators" illustrated below.

SUPPORTING INTERIM IMPACT DIMENSION MEASUREMENT

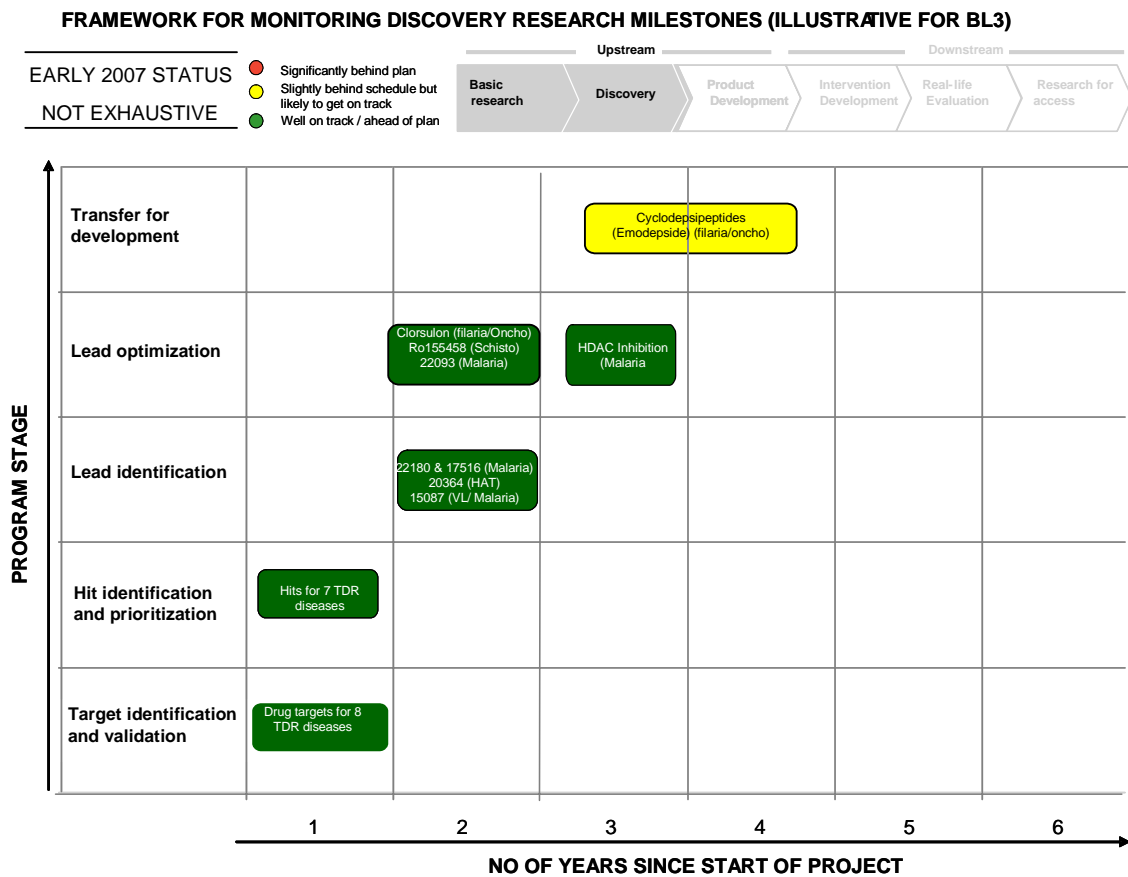


For the strategic function of Research on Neglected Priorities (3), given that multiple research initiatives would be undertaken within TDR across the different business lines, the metric reported at the TDR level would be the aggregate status across all those projects. The following chart gives examples of each of these research types (the list is illustrative and non-exhaustive).

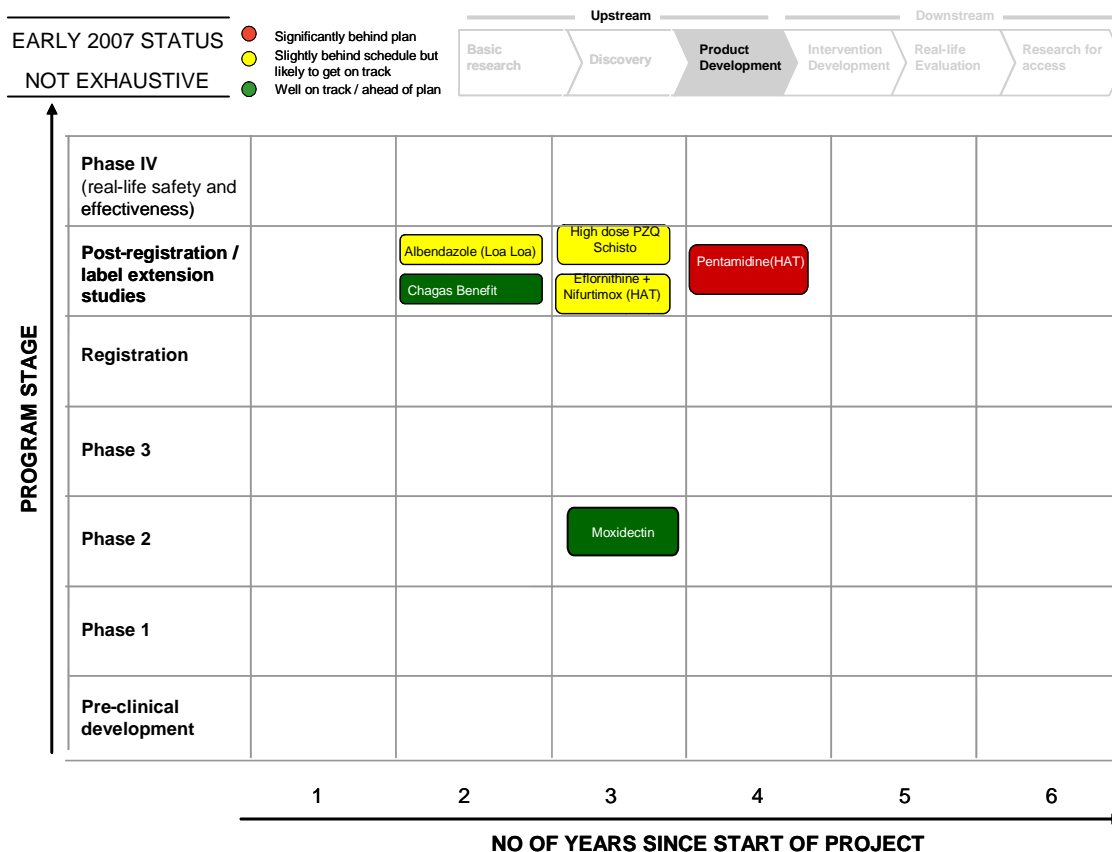
EXAMPLES OF RESEARCH RELATED TO STRATEGIC FUNCTION # 3

	Research type	Illustrative example	BL #
3a Innovation for product discovery and development	• Lead development	• Lead identification for helminths	• 3
	• Product development in DECs	• Genomic approaches to HAT vector control	• 5
		• Lead identified and development initiated by DEC institution-led project	• 4
3b Development and evaluation of interventions in real life settings	• Real-life evaluation of safety and/or effectiveness	• Point-of-care diagnostics for malaria	• 7
	• Intervention tool development	• Development and evaluation of moxidectin for onchocerciasis elimination	• 6
	• Intervention strategy development	• Strategies for use of ARV therapy in TB control settings in high HIV burden countries	• 8
	• Elimination/surveillance strategy	• Optimal combination of case-management and vector control for VL elimination	• 10
3c Implementation research for access to interventions	• Integrated intervention delivery	• Integrated community-directed delivery of interventions against NTDs and malaria	• 11
	• Scale-up strategy	• Strategies for national scale up of home management of malaria in African countries	• 9

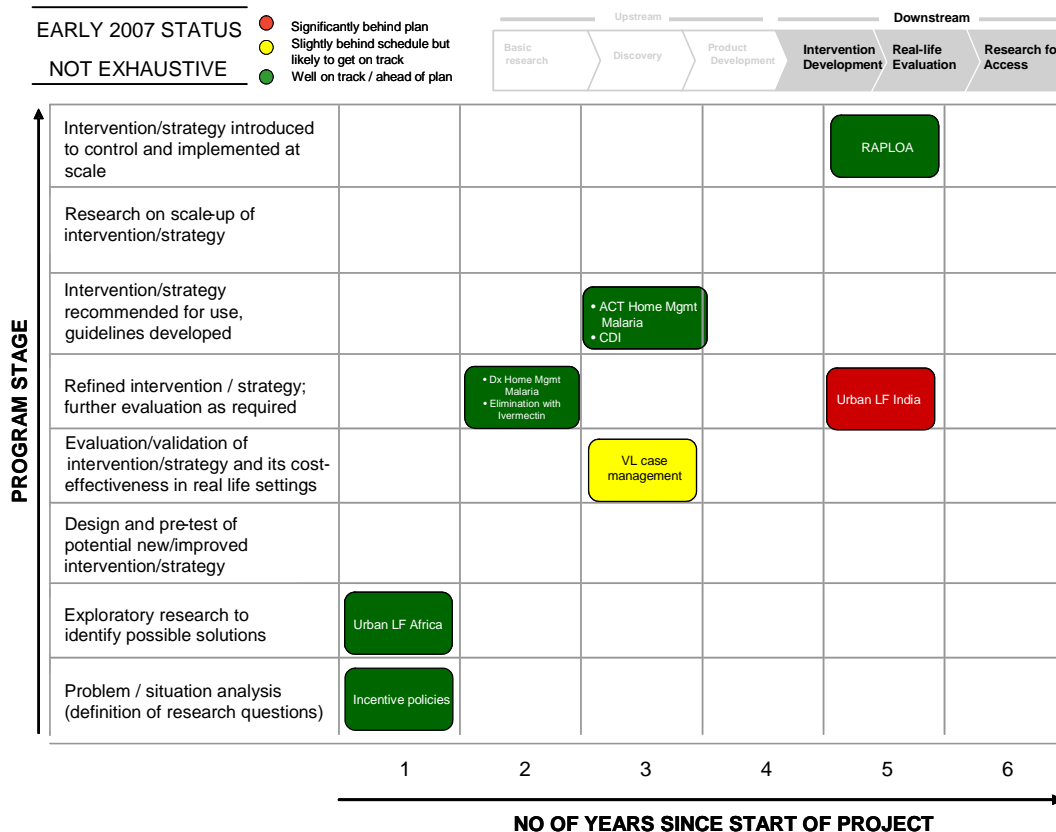
Since each project is likely to be at a different stage of progress, the framework proposed by TDR’s Scientific and Technical Advisory Committee would be used to monitor specific milestones for both upstream (discovery and product development) and downstream projects being undertaken by the individual business lines. This would then be aggregated to the TDR level. The y axis of the framework refers to the typical stages a research project goes through and the x axis refers to the years since the initiation of the project. Using this framework, status of projects could be monitored with colour codes indicating if they are well-on-track/or ahead (green), slightly behind, but likely to get back on track (yellow) or significantly behind plan (red). The frameworks for discovery, product development and downstream projects is illustrated below with examples of current status of projects that would fall under the purview of business line 3 (for discovery projects), business line 6 (for product development) and business lines 9, 10 and 11 (for downstream intervention and implementation research projects).



FRAMEWORK FOR MONITORING PRODUCT DEVELOPMENT MILESTONES (ILLUSTRATIVE FOR BL6)

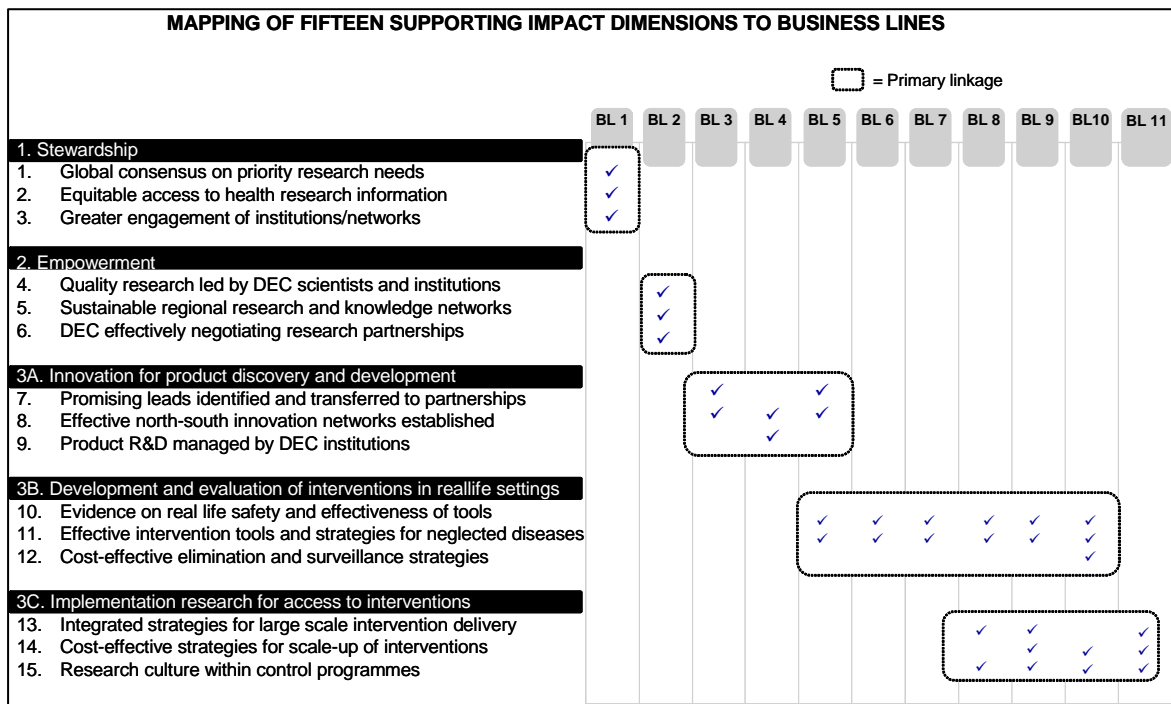


FRAMEWORK FOR MONITORING MILESTONES OF DOWNSTREAM RESEARCH (ILLUSTRATIVE FOR BL9,10,11)

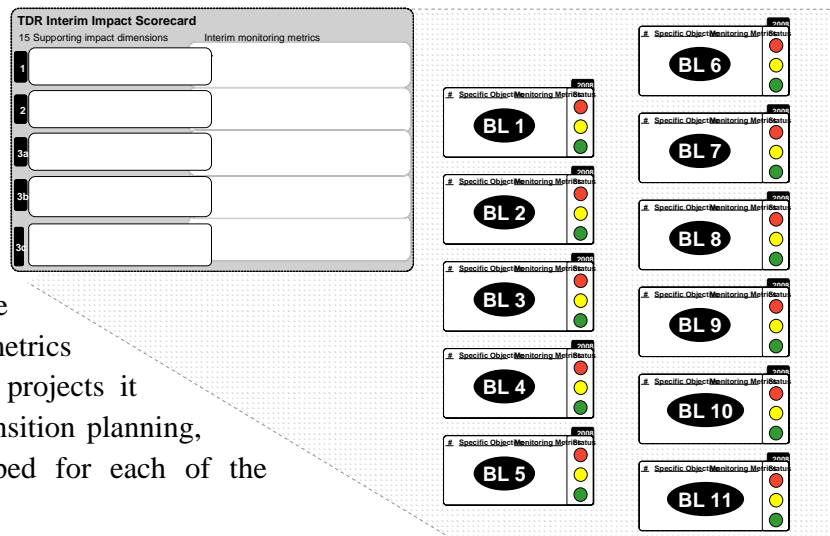


BUSINESS LINE MONITORING

The TDR interim supporting impact dimensions have also been mapped to the eleven business lines to indicate which business line is primarily responsible for ensuring TDR delivers on its targeted impact (note this mapping indicates *only primary* responsibility since each of the business lines has responsibilities related to stewardship and empowerment and similarly the business lines on stewardship and empowerment will directly contribute to the other business lines achieving their objectives). This mapping of the business lines is illustrated below.



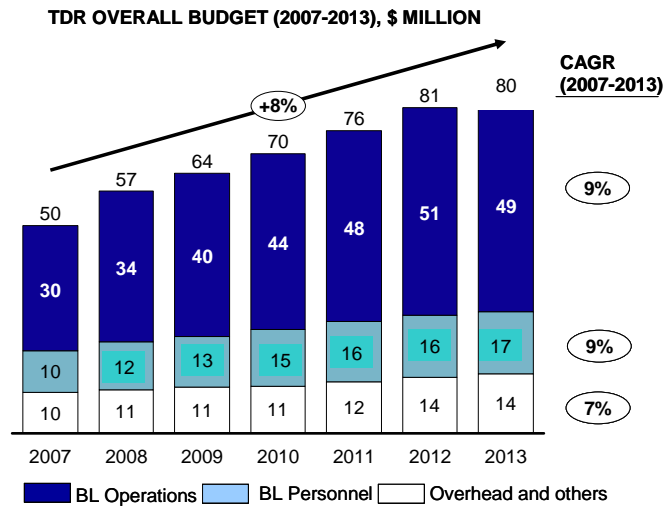
This mapping will allow for the interim monitoring metrics for TDR to be cascaded down to an individual business line level "dashboard of indicators" (as illustrated below) and **always ensure linkages of business line objectives to TDR's overall strategic goals.** Additionally, each business line is likely to have incremental monitoring metrics specific to the nature of the projects it undertakes. As part of the transition planning, 'dashboards' will be developed for each of the eleven business lines.



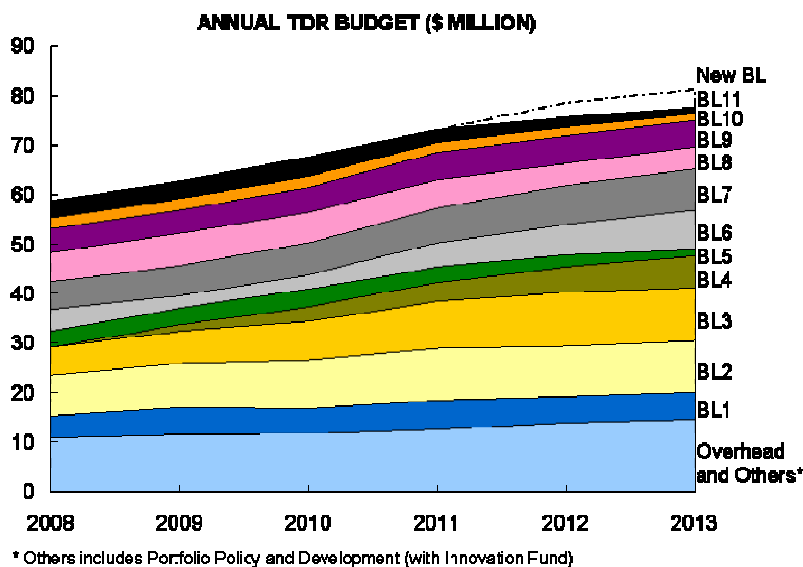
6. FUNDING

RESOURCE REQUIREMENTS

TDR currently has an annual budget of US\$ 50 M as reflected in its biennial budget for 2006-2007 of US\$ 100M. Over the next six years as the strategy becomes fully operational, TDR anticipates an increase of ~8% annualized growth rate resulting in a 2013 budget of US\$ 80 million (implying a US\$ 162 million budget for the biennium 2012-2013). Maintaining a portfolio of activities that creates leadership in stewardship and empowerment and also has a significant number of business lines to address neglected research priorities will require an increase of this magnitude. The annual growth in the budget is driven primarily by the operational and personnel expenses of the stewardship, empowerment and research on neglected priority business lines (~9%) and to a lesser extent by overheads (if the US\$ 1-2 million innovation fund considered in ‘overhead and others’ in the graph above is excluded, growth in overheads is ~6%).



TDR plans to proactively manage its portfolio of business lines both by phasing in and out business lines, and by ramping up and down key projects within business lines to ensure optimal utilization of resources. Resource requirements for business lines are indicated in the illustration



(left) and table (below). Much of the early increase in budget from 2007 to 2008-2009 occurs as a result of the rapid scale-up for the stewardship function (BL 1). Thereafter the increase between 2008-2013 occurs as a result of a steady increase in the empowerment function (BL 2), the planned introduction of business line 4 (product development in DEC) in

2009, the introduction of a further business line in 2011, which will be based in large part on information received through the stewardship function, and an additional increase due to several other business lines under the research on neglected priorities function. As discussed in section 4 under management of business lines (pages 15 and 16) the timing of exit from business lines is

especially difficult to predict. None of the business lines are currently envisaged to exit within 6 years, but several may do so within the subsequent four years. Business lines typically require a budget of US\$ 2-6 million per year, rising to as high as US\$ 10 million per year in some cases when fully operational. If budgets of business lines exceed this they are probably reaching a level of operation that would justify a spin-off of some or all of their activities to another organization/PPP (e.g. business line 3: lead discovery for drugs approaches that level). In other business lines a decline in resource requirements towards the end of 2013 is anticipated indicating that these business lines may be completed soon thereafter and replaced by new business lines (e.g. business line 10: elimination of visceral leishmaniasis; business line 5: innovative vector control interventions; business line 11: integrated community-based interventions).

Budget figures 2008-2013

<i>Budget in US\$M</i>							
BL	Business Line (BL) Name	2008	2009	2010	2011	2012	2013
1	Stewardship	4.6	5.8	5.1	5.8	5.3	5.5
2	Empowerment	8.1	8.7	10.1	10.7	10.9	10.9
3	Lead discovery for drugs	5.7	6.5	7.9	10.2	10.9	10.9
4	Innovation for product development in DECs	0.0	1.4	3.0	3.8	5.3	6.6
5	Innovative vector control interventions	3.4	3.5	3.5	3.3	2.4	1.3
6	Drug development & evaluation for helminths and other neglected tropical diseases	2.4	3.0	4.4	6.3	7.9	5.9
7	Accessible quality assured diagnostics	5.6	6.0	6.7	7.4	7.8	8.3
8	Evidence for treatment policy of HIV and TB co-infection	6.0	6.8	6.2	5.6	4.6	4.5
9	Evidence for antimalarial policy and access	4.8	4.8	5.0	5.6	5.6	5.6
10	Visceral leishmaniasis elimination	2.4	2.3	2.4	2.1	2.0	1.4
11	Integrated community-based interventions	3.4	3.7	4.0	2.9	2.1	1.3
	New BL					3.0	3.8
	BL 3-11 Coordination*	0.4	0.4	0.4	0.4	0.4	0.4
	Total BL Budget	46.7	52.9	58.6	63.9	68.0	66.1
	Other Activities**	2.0	2.2	1.8	2.3	2.8	2.8
	Overhead	8.4	8.8	9.5	10.0	10.6	11.4
	Total Annual Budget	57.1	63.9	69.8	76.1	81.4	80.2

* Personnel expenses only

**Includes portfolio policy & development, innovation fund and ongoing projects.

This growth rate in the targeted budget is modest, but necessary. The budget can be managed through judicious and prioritized selection of business lines that can grow in early years and then be supplemented with and / or replaced by additional business lines thereafter. In case the available financial resources are not sufficient to fund all business lines, the proposed business lines and/or key activities within business lines will be ranked, using the entry criteria, on disease endemic country need, research neglect, expected impact, added value, leverage, DEC leadership, resource availability and a strong action plan. This ranking will provide an objective basis for

prioritization of potential business lines and for decision making on which business lines to start and which to delay or cancel. For major decisions concerning budget, as outlined in the section on management of business lines, proposals by the TDR secretariat are reviewed by STAC for decision by JCB. An example of such prioritization in the current business plan is the conscious decision to delay the start of business line 4 (innovation for product development in disease endemic countries) to the year 2009 given the need for more preparatory work. Additionally, within each business line TDR has carried out a further prioritization of specific objectives, should it not be possible to obtain the budget increase required for full implementation of the business plan. This of course would result in certain objectives not being met.

RESOURCE MOBILIZATION

TDR's vision and strategy identifies a series of focused activities that will, if properly undertaken, have a major health impact. In moving forward as a facilitator of innovative and needed health research, as well as a fund provider, TDR will place emphasis on leveraging resources in cash and in kind for its partners' activities as well as its own activities. However, this section will restrict itself to the funds required to flow through TDR to allow the Programme to meet its vision and fully implement its strategy.

With support from WHO and other co-sponsoring agencies and stakeholders, funding will be sought at two major levels. The first level will be undesignated and will support the Programme in its entirety. The second level of funding will be at the level of the business line. We believe that the business line concept leads to straightforward communication about the value of the research activities involved and business lines will be empowered to proactively raise funds.

Three major sources of funds have been identified: governmental and international public sector; philanthropy / NGO sector and private sector.

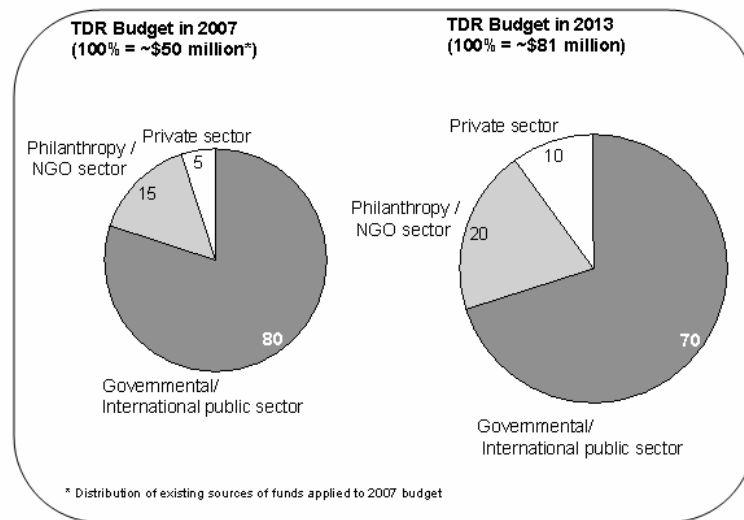
As a public sector based programme, with a strategy that is primarily directed at public sector goals, governmental and intergovernmental agency contributions remain at the core of TDR's resource base and TDR envisages retaining a high dependence on this sector and obtaining a support level of 70% from this sector.

The significance and importance of the philanthropy / NGO sector, both as stakeholders in the broadest sense, as cooperating parties able to attend Joint Coordinating Board sessions and as resource contributors and / or providers of technical and / or scientific support to the Special Programme, are greatly appreciated and recognized. They may frequently also be partners in research activities and may co-fund those activities with TDR. Recognizing that most contributions from this sector are likely to be designated contributions, attempts will be made to secure funds at the business line level. A target for 20% of funding from this sector will be set.

TDR continues to benefit from good interactions with industry and the private sector and will seek to enhance this through continued private sector funding, subject to WHO guidelines. We also see an opportunity to obtain funds from private individuals as well as from corporations. A target of 10% of funding will be set for this sector.

This targeted resource mobilization plan implies that while TDR will attempt to proactively seek a greater percentage of funding from the private and the philanthropy/NGO sector sources (as

shown in the graph below on estimated relative proportion of sources of funds in 2007 and 2013), it will still need to get significant additional resources from governmental and international public sector sources. Given the significance of the public sector funding sources, TDR plans to re-engage past contributors (in addition to maintaining current contributors in this category) and recruit new contributors, including from disease endemic countries. Lastly, TDR plans to actively monitor its efficiency in fund-raising through targeted metrics like % renewal rate of funding sources to ensure adhere to the resource mobilization plan.



RESOURCE JUSTIFICATION

The budget growth envisaged is essential if TDR is to effectively implement its new strategy, achieve its expected impact on the global research effort, promote DEC research leadership and deliver critical research outputs of value for infectious disease control in poor populations, as defined in its new vision statement.

TDR has been requested to take on a major new role of stewardship for research on infectious diseases of poverty with the aim to help develop a global consensus on research priorities, facilitate harmonization of research activities between partners and enhance the exchange and utilization of research information. Stewardship will be very labour intensive and require extensive outreach, knowledge management activities and consultative meetings for needs analysis, priority setting and harmonization that go far beyond the scope of activities currently funded by TDR. The expectations among partners in disease endemic countries and in the north about TDR's new stewardship role are very high, and significant additional work and funding are needed to meet those expectations. Because this is a priority area, a rapid scale up of resources is anticipated even within the first years of the plan and represents over 50% of the funding increase requested for the 2008-2009 biennium and 20% of the increase over six years.

The evolution of research capacity building to empowerment, and the corresponding shift from traditional research training to capacity building for research leadership by scientists from disease

endemic countries, also involves new activities such as support for research excellence, best practices and leadership in priority setting. Research capacity building has always been an important and successful TDR activity that has received a substantial share of the TDR budget. The budget for empowerment in 2008 corresponds approximately to the budget planned for research capacity strengthening in 2007. However, we seek to increase this area by 30% by 2013.

As in the past, the main share of the budget will go to support for specific research projects. Under the new strategy these will be undertaken through a limited number of focused business lines on research priorities that address critical gaps in the global research effort on infectious diseases. These research gaps need to be filled if the collective global research effort is to have the intended impact on infectious diseases of poverty.

Through analysis and consultations and technical review by STAC, eight critical research areas were identified for business line initiation by 2008. These are areas in which TDR has a strong comparative advantage and which build on TDR's existing portfolio. They range from drug discovery to feed the drug development pipelines of various organizations, to research on strategies for improved access to interventions by poor populations. An additional business line (BL 4) focused on promoting innovation for product development in DEC's is anticipated to start in 2009 and a further business line, based on analysis and output from the stewardship function plus discussion and endorsement by STAC and JCB, to start in 2011. These two additional business lines will account for 37% of the increase in budget by 2013. TDR believes this level of activity is needed if it is to remain a leading influence in global research and significantly contribute to the vision agreed by its stakeholders.

In summary, of the approximately \$30M budget increase envisaged between 2007 and 2013, discounting overhead costs, approximately 20% is due to stewardship, 10% due to empowerment, 37% due to bringing in two additional business lines and 33% due to increased resources to collectively manage and scale up the eight initial research business lines, which represent a prioritized and focused set of activities.

The research business lines will be managed professionally and in a businesslike manner. For each business line there is a detailed business plan that clearly defines deliverables and timelines, and the human and financial resources required. This approach of defining upfront all resources required to bring a major research undertaking to a successful and timely conclusion is a key element of TDR's new business model. It recognizes that attempting to carry on too many activities with limited resources delays research progress across the entire portfolio. It also has knock-on opportunity costs and increased overhead requirements as multiple smaller projects have to be managed, each yielding an increasingly limited impact. The new business model avoids under budgeting, and this explains, as indicated above, some of the additional budget growth.

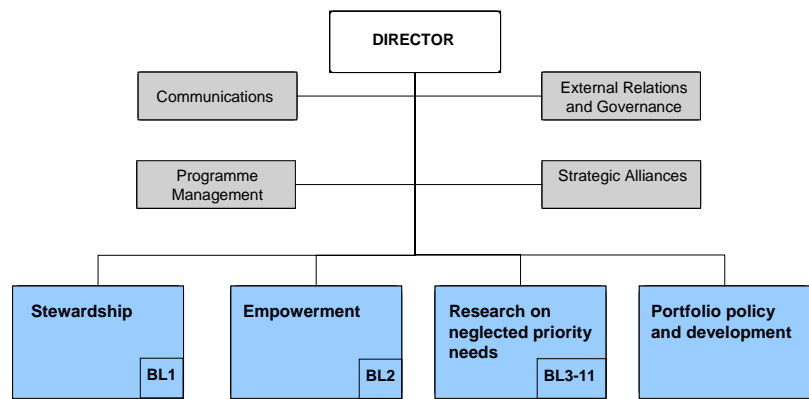
The new approach also implies that if it appears unlikely that the necessary resources will be available, TDR will delay or cancel a business line rather than try to work with an inadequate budget that fails to ensure delivery within an appropriate timeframe. This of course would result in certain objectives not being met.

7. OPERATING MODEL

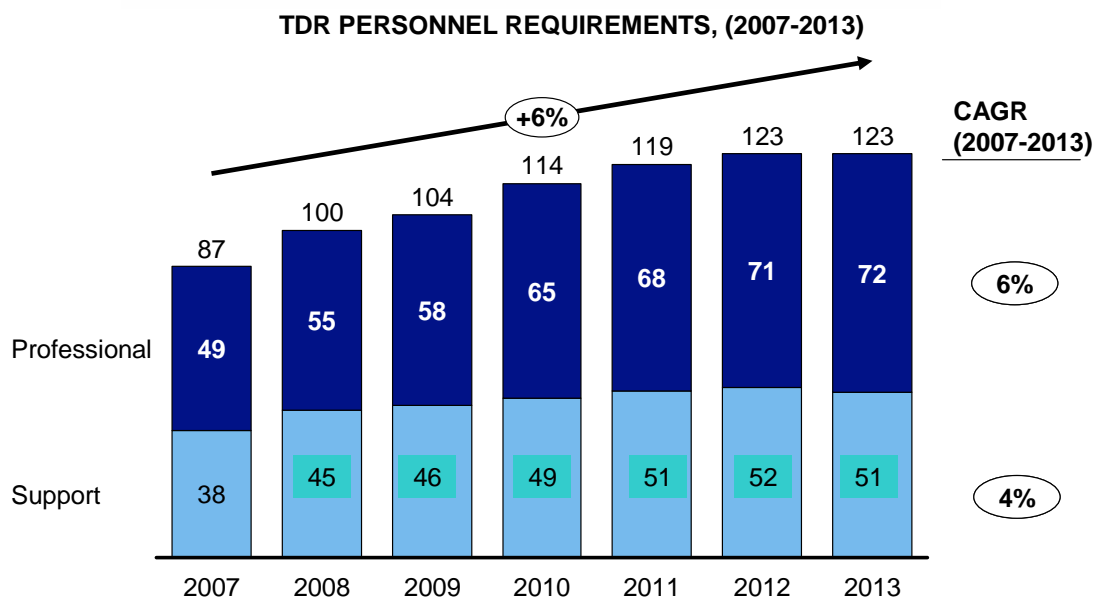
ORGANIZATION STRUCTURE

To implement the new strategy, TDR proposes to restructure its operating model and align its organization structure and supporting processes to match its three strategic objectives. Under the revised organization structure, four functional areas report to the director's office including: (i) Stewardship (BL1), (ii) Empowerment (BL2), (iii) Research on Neglected Priority Needs (BLs 3 to 11) plus, as, an integral part of the organization (iv) a small Portfolio Policy and Development team which will

be responsible for metric monitoring and management of the 'innovation fund'. The director's office would be supported by the traditional service functions of Communication, External Relations and Governance, Programme Management and Strategic Alliances. The



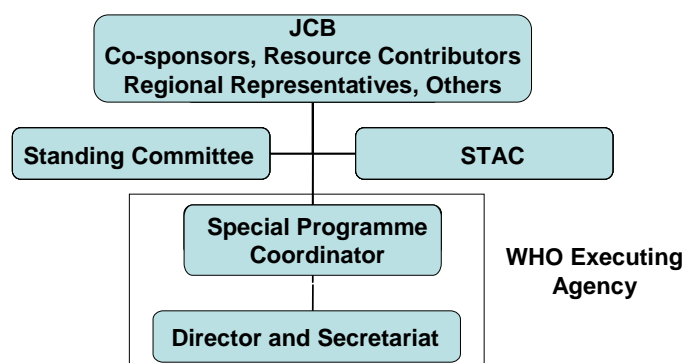
The proposed organization structure will establish clear responsibilities and accountabilities and also foster a sense of entrepreneurship. Each business line will have clearly dedicated resources thereby enabling better focus on stated objectives and targeted activities. As part of the revised organization structure TDR will have to grow its staffing levels at an annual rate of ~6% from current levels of ~85 to ~120 by 2013.



GOVERNANCE STRUCTURE

STAC, JCB and Standing Committee

In 1978 TDR was established as a co-sponsored Special Programme to be governed through a Joint Coordinating Board (JCB). The Board consists of: (i) 12 disease endemic countries elected through the six WHO regional committees and primarily represented through ministries of health; (ii) 12 resource contributor countries primarily represented by development agencies; (iii) 6 other co-operating parties⁷ and (iv) the 4 co-sponsoring agencies. Additional countries which contribute to or support the Programme or are directly affected by the diseases dealt with by TDR, as well as intergovernmental and other non-profit making organizations which provide financial, technical and/or scientific support to TDR may attend the JCB sessions as observers, thereby keeping the operations of the JCB open and transparent.



The JCB is supported by a Scientific and Technical Advisory Committee (STAC) comprised of globally recognized experts, for example heads of institutes or research councils, who are regularly advising their governments and other agencies on research and health issues. This committee undertakes an annual scientific review of the Programme and advises on strategy.

A Standing Committee consisting of the four co-sponsoring agencies, namely UNICEF, UNDP, the World Bank and WHO reviews the overall management of the Programme. Recently the different arms of governance have been further linked by inviting both the chair and vice-chair of the JCB and the chair of STAC to attend the meetings of the Standing Committee on an ex officio basis to facilitate communication and dialogue among the various governing bodies of TDR. This has led to enhanced communication and dialogue, including with WHO, and has facilitated governance and management of the programme. The possibility of inviting other members of the JCB to regularly attend these meetings on the same basis is now being assessed.

⁷ Co-operating parties are: a) governments contributing resources, governments contributing technical and / or scientific support, or governments whose countries are directly affected by the diseases dealt with by TDR; b) intergovernmental and other non-profit making organizations contributing resources or providing technical and / or scientific support to TDR.

Steps to further enhance the efficiency of the governance structure and to strengthen disease endemic country engagement and representation are under development.

This model has provided TDR with convening power, legitimacy and access to global expertise and knowledge from multiple disciplines and sectors over the last 30 years. While the fundamental structure of the model should remain equally relevant within the context of the revised strategy, TDR is currently in the process of determining how interactions with STAC and JCB could be further enhanced.

Strategic links with WHO and other co-sponsoring agencies

TDR is co-sponsored by UNICEF, UNDP, the World Bank and WHO, and stronger links with all of them will be developed. Of these agencies the closest and most prominent link is with WHO. TDR is administered and implemented by WHO, which acts as its Executing Agency.

WHO

TDR enjoys significant benefit by being associated with WHO. WHO disease control expertise helps define research priorities and translate research findings into policy. TDR staff has access to WHO regional and country offices and support structures, and through these structures to Ministries of Health. WHO benefits from TDR's research expertise and TDR-partnered accomplishments that have provided evidence for the development of intervention tools and strategies for several infectious disease control programmes. TDR's operationalization of research through discrete business lines will facilitate future interactions with WHO's disease control departments at both global and regional level. Documents defining common objectives and cooperating mechanism are being developed between TDR and WHO's disease control departments.

Specifically TDR plans to ensure greater regional influence on its policy and strategy through the following:

- Participation in TDR's governing body, the Joint Coordinating Board (JCB), by JCB members selected by the WHO regional committees will be more strongly supported to represent the regional interests and the regional committee meetings will be formally utilized to provide annual feedback on TDR's activities to the regional committees.
- TDR strategic linkages with WHO regional offices and regional linkages with the Programme's co-sponsors and development agency contacts will be strengthened.
- There will be an interface between TDR's Scientific and Technical Advisory Committee, which annually reviews the Programme and provides strategic advice and the WHO regional advisory committees on health research. These committees consist of prominent scientists who can assist in assessing research needs and opportunities in the different regions.

WHO is in the process of developing a research strategy that will facilitate better coordination of research activities within the Organization and TDR is playing a lead role in this discussion. WHO has recently placed more emphasis on research and in its Eleventh General Programme of Work (2006-15) WHO highlights itself as an organization that seeks to "utilize the fruits of science and technology" and defines one of its six core functions as "shaping the research agenda

and stimulating the generation, translation and dissemination of valuable knowledge." This fits with TDR's new strategy and its emphasis on stewardship. It is envisaged that the activities associated with stewardship and empowerment will become increasingly fundamental to WHO's role in research and that there should be little difficulty in effectively linking TDR activities to the future WHO strategy.

Other co-sponsoring agencies

There will be increased co-sponsor support for, and use of, TDR and a reinforcement of messages of common significance and value to TDR and the agencies. In particular there will be increased coordination and action on global advocacy for research on infectious diseases of poverty and for TDR as a Special Programme. This will be extended to further enhance support for fundraising where the reach of the World Bank to financial institutions and UNICEF's power of advocacy will be critically important. The co-sponsors will further elaborate their role in supporting TDR and make appropriate commitments.

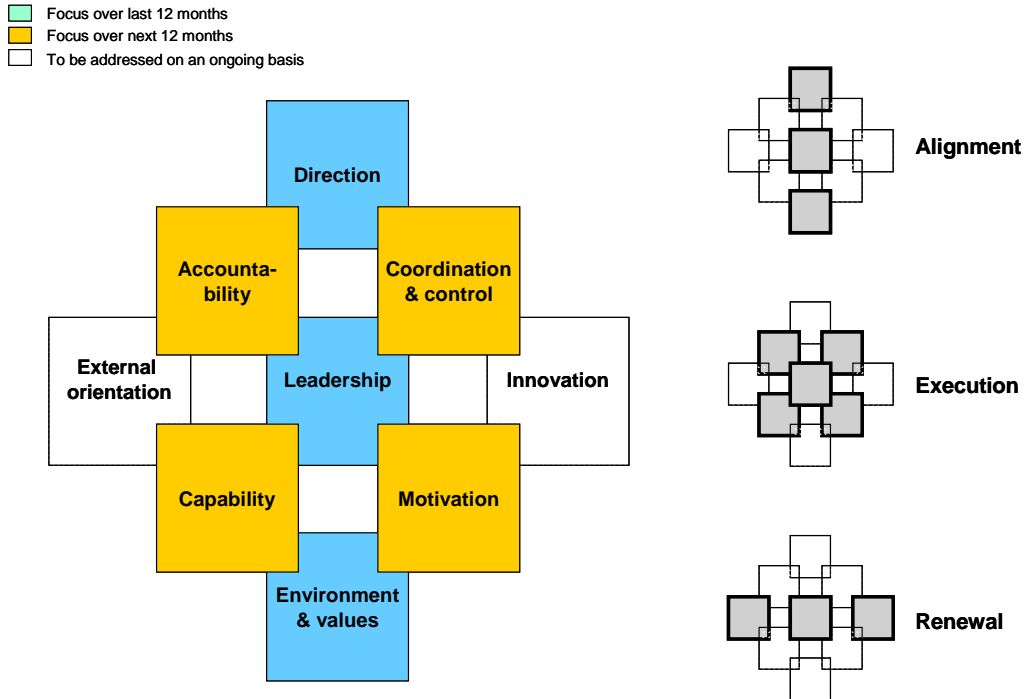
TDR will improve its operational links with research and strategically related activities within the co-sponsor organizations, exploring more visible research, stewardship and research empowerment roles for this unique network of international agencies. In this regard, documents defining common objectives and cooperating mechanism are being developed between TDR and the co-sponsoring agencies so that TDR can better dovetail its activities with their needs.

This will most notably manifest itself at regional level with direct and leveraged support for implementation and intervention research and appropriate research policy and capacity building. It is envisaged that such engagements will also benefit TDR activities by highlighting multisectoral issues, thus broadening the impact of research for health. Properly positioned, TDR could become the infectious disease research arm of WHO and its other co-sponsoring agencies.

CHANGE MANAGEMENT

As TDR transitions to this revised operating model which is better aligned with its strategic objectives, it will be critical to ensure adequate emphasis on change management. In general as organizations attempt to enhance their performance, there are typically nine dimensions of change that they need to prioritize from. These dimensions relate to (i) alignment, (ii) execution and (iii) renewal.

Over the last twelve months as part of the vision and strategy determination exercise, TDR has focussed on the alignment dimensions of organizational performance. It has provided new direction in the context of a changing external environment and installed new leadership positions to support this process. Going ahead over the next twelve months, TDR would need to emphasize on the execution aspects of change management: (i) installing processes for coordination and control, (ii) enhancing capability and skill levels, (iii) installing monitoring mechanisms to ensure accountability and (iv) motivating staff and scientific committees proactively.



Source : McKinsey & Company

Coordination and Control

The business line model will facilitate a uniform management structure for activities in TDR. Each business line will have an advisory committee and a TDR manager, with associated staff, fully responsible for scientifically and technically operationalizing the mandate of the business lines. The committees should advise on business line strategy, and review activities and research projects both strategically and technically. Their actions and outputs will in turn be reviewed annually by TDR's Scientific and Technical Advisory Committee.

The introduction of the business line model as the principal mode of operation for TDR will provide an important opportunity to redesign and simplify TDR's administrative procedures. Delegation of authority for routine decision making to the business line manager, corresponding optimization and simplification of administrative procedures and the aggressive use of information technology to automate processes, integrate administrative information and support online scientific review will significantly accelerate the processing of research proposals and contracts. The business line model could also bring greater clarity for, and ease of interaction with, external partners.

As part of the transition planning TDR will define the procedures, committees, meetings and approval processes to achieve the above stated outcomes. Specifically, defining primary and secondary responsibilities between business lines focused on specific research activities and the supporting business lines of Stewardship and Empowerment will be undertaken. The resulting clear understanding of responsibilities across business lines will ensure effective coordination and non-duplication of efforts.

Capability / skill levels

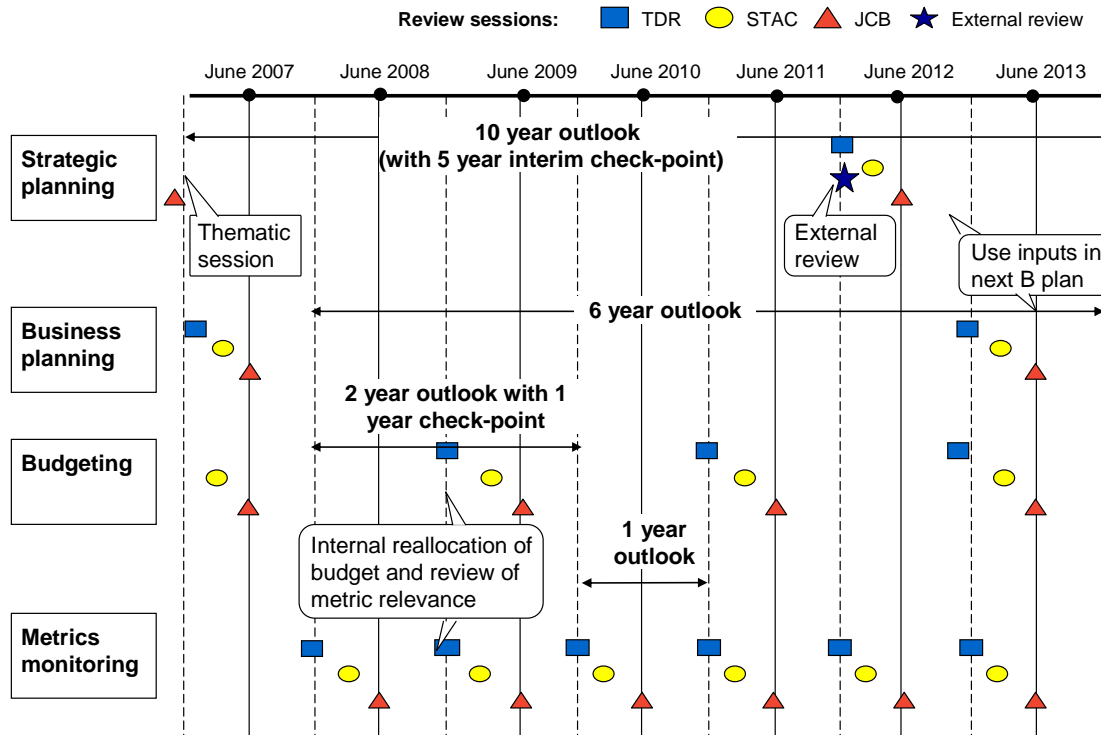
Adopting a more 'business-like' approach will require the development of new skills within TDR. Managing a business line requires strong elements of strategy, planning, coordination, negotiation skills, management of small teams and a capacity to link and integrate the business line into TDR's overall strategic plan and the bigger international environment. Additionally, given increased emphasis on downstream projects related to intervention and implementation research, TDR would need to enhance research skills in these areas as it broadens its focus from its historical upstream related research.

This will be taken into account in developing TDR's future human resource strategy and could involve a number of tactical choices like focusing on recruiting staff with adequate management experience, public health expertise, negotiating experience and using external experts as consultants where necessary.

Accountability

In order to ensure effective implementation of the strategy, it is important that metrics are monitored as an integral part of the overall strategic planning, business planning and budgeting processes. The strategy planning cycle is for a period of ten years with an interim check point in 5 years time (i.e. JCB 2012). As stated earlier, the overall impact indicators will be assessed at this time based on an external review (to report 6 months earlier in December 2011) that would involve a qualitative and quantitative assessment regarding TDR's ability to deliver the desired overall impact. This checkpoint of TDR's 10 year strategy is also expected to influence the next cycle of business planning, post 2013. The process would be repeated thereafter on a six year cycle. The budget would continue to be determined on a biennium basis in line with WHO budgeting cycle and would be presented to JCB six months prior to the beginning of the biennium. The interim metrics would be monitored more regularly, on an annual basis every year by STAC and JCB and even more frequently within TDR (review every six months). It is anticipated that this regular performance and portfolio review will also be the forum to consider continued relevance of the metrics and the allocation of budgets across business lines for the second half of every biennium. The portfolio policy and development function will be responsible for facilitating the entire process and ensuring that the relevant indicators and gender mainstreaming are monitored within each business line in a timely manner and that they stay aligned with TDR's overall strategic objectives.

KEY PLANNING PROCESSES AT TDR AND LINKAGES TO METRIC MONITORING



Motivation

It is expected that the increased stewardship nature of activities embedded in each business line, the entrepreneurial opportunity of managing business lines semi-autonomously and the enhancement in targeted budgets would provide enhanced motivation to TDR staff and scientific committees. On an ongoing basis business line teams will be constantly recognized through both formal and informal mechanisms for exceptional achievements as part of TDR’s Human Resource Strategy.

8. KEY RISKS AND MITIGATING MECHANISMS

Financial Risk

TDR has set itself a target of achieving a ~8% annualized growth in its budget by 2013 from its current level in 2007. However, over the last few bienniums TDR has not received funding in line with its strategic resource mobilization plans and would need additional funding to capture opportunities identified in TDR's strategy. Given the public sector nature of its programme, TDR would need to continue to rely on governmental and intergovernmental public sector contributions (70% of targeted funds) to achieve its resource mobilization goals. Lack of support on this front could greatly limit TDR's ability to achieve its targeted strategic objectives. It is believed that the clarity of this plan, based on a TDR stakeholder supported vision and strategy and its positioning of TDR within the global framework of activities, will in itself prove to be a positive factor in achieving funding goals. In order to further mitigate this risk, TDR would proactively seek funding opportunities from other avenues like private sector and philanthropic organizations to complement public sector funding.

Scientific Risk

A significant portion of TDR's research is dedicated to the development of innovative tools and strategies. For example new drug discovery and development has an inherent risk of not delivering the desired product (industry experience is that out of 10 drug candidates entering development only 1 reaches regulatory approval). Similarly, given the hypothesis driven nature of intervention and implementation research, there is a possibility of negative results (which in themselves can be beneficial in terms of impact since they can potentially save significant healthcare expenditure on misguided policies). Realizing this aspect of scientific risk inherent to the nature of its research, TDR will proactively take steps to monitor the progress of its projects to ensure that resources are dedicated to projects with most promise of delivering the intended impact and terminating others in a timely manner. By involving leading experts and extensive due diligence, TDR will enhance the likelihood of its scientific research achieving the desired impact.

Environmental Risk

As TDR attempts to broaden its role through stewardship and empowerment initiatives, some stakeholders may not accept that TDR (or any other single organization) takes the lead in facilitating research priority setting for infectious diseases. This would become an issue primarily if TDR, as a secretariat, is perceived as setting the priorities itself. It will be important, therefore, to clarify that TDR will only be facilitating an objective scientific process of analysing research needs and opportunities, and identifying evidence-based research priorities, and that all key partners will collaborate in this process. TDR will in effect be a vehicle for developing priorities. It will not be the sources of priorities.

Similarly, TDR's success in development of new intervention tools (especially drugs) would be dependent on its ability to attract industry and other academic and research institutions to collaborate as per required levels (e.g. supplying drug targets from academia, supplying free drugs and other intervention tools by industry). TDR plans to leverage its experience in building win-win partnerships to mitigate this risk.

Finally lack of adequate infrastructure in disease endemic countries could limit the true impact of intervention/implementation research being pursued by TDR. This issue exemplifies why capacity building and the concept of empowerment are central to TDR's vision and mission and why these elements are integrated into the business line activities. TDR also plans to leverage its strong linkages with control programmes, WHO regional presence and planned stewardship activities, involving ministries of health, to ensure due process is followed for evaluation and, where appropriate, successful implementation of the initiatives it supports.

Project Execution Risk

Given TDR's methodology of working in collaboration with multiple key stakeholders, TDR's control on project timelines is limited due to interlinkages with other partner commitments. Sometimes this also includes uncertainties associated with work in some countries (political and socioeconomic instability, disasters, and infrastructure related challenges). TDR plans to leverage its facilitation experience to mitigate this risk and deliver against planned milestones.

Human Resource Related Risk

The implementation of a business line based operating model would require significant enhancement of managerial and administrative capabilities to ensure smooth functioning. Going ahead, there is a greater emphasis required on strategic management that would involve managing partnerships and broader programmes (as opposed to just managing individual research activities). TDR plans to enhance the same by actively training and / or recruiting personnel with excellent track records in research plus project management experience, public health expertise and leveraging talent from partner organizations.

Secondly, as TDR undertakes the transition towards a greater emphasis on downstream projects related to intervention and implementation research, it recognizes the need to build associated capabilities. During the transition phase, TDR plans to leverage the use of specialized consultants in relevant areas and in the long term, TDR will proactively recruit talent according to its needs.

Transition Risk

As TDR implements the new business line based operating model, it would need to proactively mitigate the associated transition risk. Specifically, coordination of overlapping areas of work across multiple business lines would need to be ensured through appropriate managerial mechanisms. This will ensure that both internally and externally TDR business lines are synergistic and not duplicative. TDR has already initiated the process of planning for the transition period of 2007 and these are being shared and reviewed with its management and governance bodies.

9. CONCLUSION

Under the direction of its new strategy, TDR is attempting a bold transition to fill critical gaps in global research related to infectious diseases of poor populations. It is undertaking a new global **stewardship** effort to facilitate and manage knowledge required to support needs assessment, priority setting, and harmonizing of activities across multiple partners. It is also leading the change from traditional capacity building to **empowerment** of researchers, public health professionals and institutions in DEC's so that they can lead research activities and more effectively use results to inform national/regional policy and practice. Last but not least, TDR is selectively targeting **research on neglected priority needs** that it is well positioned to address. These priority needs span the entire spectrum of research - from discovery and product development, to intervention development and evaluation, to enhancing intervention access - but are focussed on areas which are of most importance to control programmes and ministries of health and are not adequately addressed by other partners.

By undertaking this effort, in 5 years time (2012), TDR plans to achieve (1) **Greater Harmonization of research efforts**; (2) **Stronger DEC leadership in health research**; (3) **Enhanced access to superior interventions**. TDR's ability to achieve this impact would be determined through a detailed and rigorous qualitative survey of TDR's key stakeholders (e.g. control programmes, ministries of health, PPPs, etc...) and also a comprehensive quantitative review of all outputs produced by TDR under each of the strategic functions in the interim period (as measured by the interim monitoring metrics on page 44). These include

1) Stewardship

- Number of quality consultations/reports for consensus facilitated by TDR
- Surveyed user satisfaction levels with knowledge platform
- Percentage of key institutions/networks actively involved in TDR forums

2) Empowerment

- Number of TDR supported publications with DEC researchers as lead authors
- Number of DEC research institutions / networks operating at international standards
- Number of TDR derived partnerships with DEC researchers as leads

3) Research on Neglected Priorities

- Number of new leads developed and transferred
- Number of innovation networks established/expanded/strengthened
- Number of key TDR derived R&D projects managed by DEC institutions
- Number of real-life evaluations on safety/effectiveness which have influenced policies
- Number of developed intervention tools/strategies adopted
- Number of developed integrated intervention delivery strategies adopted
- Number of cost-effective scale-up strategies adopted

- Number of developed elimination/surveillance strategies adopted
- Number of control programmes actively involved in research projects

To operationalize this strategy, TDR will initially introduce eleven distinct business lines each supported by a robust business plan that details deliverables, timelines and partnerships. Two business lines will relate directly to the strategic functions of stewardship and empowerment respectively and are viewed as constant elements of the 10 year strategy. The others relate to the strategic function of Research on Neglected Priorities and may be more time limited dependent on achievements and changing needs. The introduction of business lines and restructuring of TDR's organization to better support these business lines will provide the necessary focus required to implement TDR's strategy and also ensure the desired accountability. There is an emphasis on defining and capturing the best science and realizing the opportunities resulting from that science, supported by clear objectives, tangible end-products, detailed resource requirements and interim milestones. These make each business line plan an attractive cost-effective proposition for research-driven public health impact and one that compares favourably with, and complements, other internationally directed research efforts.

Despite the significant magnitude of the targeted impact, TDR envisages its funding requirements to increase by a modest but necessary annual growth rate of ~8%, resulting in a 2013 budget of US\$ 80 million (compared to 2007 budget levels of US\$ 50 million). By adopting a strategic management approach that would involve managing partnerships and leveraging broader programmes (as opposed to just conducting individual research), TDR plans to limit the increase in its personnel requirements to only 6% annualized growth over the next six years and focus the majority of the budget increase primarily on business line related operational activities (9% annualized growth). To effectively capture the opportunities identified in its strategy and deliver on the impact stated above, TDR would need enhanced support from funding sources. While TDR will attempt to proactively seek greater funding from the private sector (10% of targeted funds) and the philanthropy/NGO sector sources (20% of targeted funds), it is planned that the governmental and international public sector will still provide majority of resources (70% of targeted funds). Due to the clear linkages between resource requirements and end-products from each business line, donors are expected to have excellent visibility and transparency of outcomes achieved from funding.

The scope of the targeted public health impact and the critical gaps in global research that TDR plans to address are significant. The declared vision of 'an effective global research effort on infectious diseases of poverty, in which disease endemic countries play a pivotal role' deserves to be realized. TDR believes that this business plan (and that of each contributing business line) addresses the challenges of fostering the vision and represents a compelling opportunity for investment in research on infectious diseases of poverty.

**Special Programme for Research & Training
in Tropical Diseases (TDR) sponsored by**
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The Special Programme for Research and Training in Tropical Diseases (TDR) is a global programme of scientific collaboration established in 1975. Its focus is research into neglected diseases of the poor, with the goal of improving existing approaches and developing new ways to prevent, diagnose, treat and control these diseases. TDR is sponsored by the following organizations:

