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Approved Programme Budget for the Biennium 2000-2001

**This Programme Budget was approved on 24 and 25 June 1999
by the Twenty-second Joint Coordinating Board**

**UNDP/World Bank/WHO
Special Programme for Research
and Training in Tropical Diseases
(TDR)**



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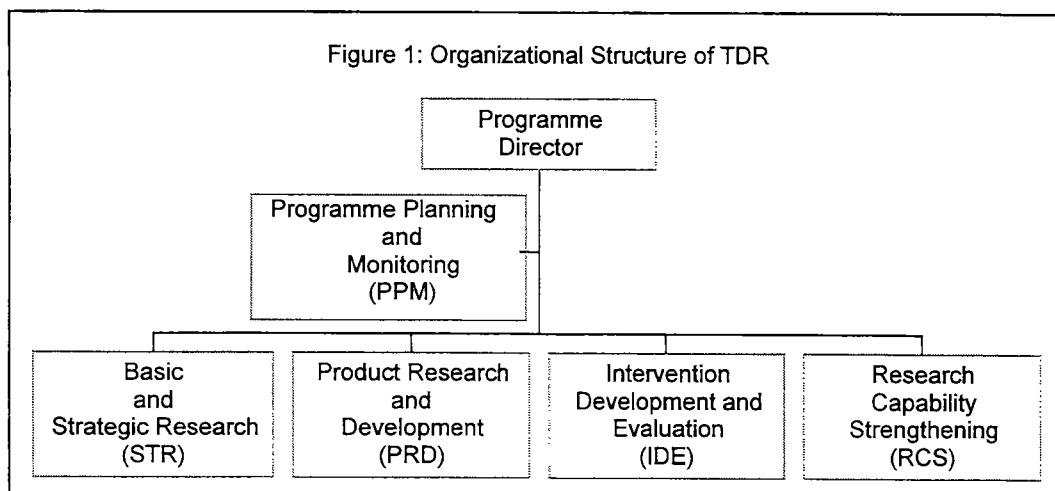


PROGRAMME OVERVIEW

The Special Programme for Research and Training in Tropical Diseases is a co-sponsored programme of the United Nations Development Programme (UNDP), the World Bank and the World Health Organization (WHO). It was established in 1975 with two interdependent objectives:

- To develop new methods of preventing, diagnosing and treating selected tropical diseases - methods which are applicable, acceptable and affordable by developing endemic countries, which require minimal skills and supervision, and which can be readily integrated into the health services of these countries.
- To strengthen the capability of developing endemic countries to undertake the research required to develop these new disease control strategies, through training in biomedical and social sciences and through support to institutions.

TDR is governed by: the Joint Coordinating Board (JCB) composed of donor countries, representatives of developing disease endemic countries, and others; the Scientific and Technical Advisory Committee (STAC) comprising renowned international scientists independent of TDR; and the Standing Committee which consists of representatives of the three co-sponsoring partners. WHO is TDR's executing agency.



TDR is housed in the Communicable Diseases cluster of WHO, and is organized on a trans-disease basis reflecting the scientific, technical and operational problems presented by tropical diseases. An integrated strategy is taken to research and development activities, which fall under three main areas:

- Basic and Strategic Research (earlier known as Strategic Research and re-named by STAC-21), reflected in Programme Area III.
- Product Research and Development, reflected in Programme Area IV.
- Intervention Development and Evaluation (earlier known as Applied Field Research and re-named by STAC-21), reflected in Programme Area V.

TDR supports training for individual scientists and institutions to strengthen research capacity in disease endemic countries. These activities, undertaken by the Research Capability Strengthening unit, are incorporated throughout the other three Programme Areas in TDR, and are described in this report under Programme Area VI.

Scientists acting as independent advisors to the Programme carry out peer review of project proposals - Steering Committees, Task Forces and the Research Strengthening Group are the mechanisms that bring groups of scientists together for this purpose. New Steering Committees and Task Forces are established, and existing ones phased out, as opportunities and priorities change.

INTRODUCTION

As TDR enters its 25th year, it is faced with new challenges and opportunities. The 1998-1999 biennium has been one of continuous change both within TDR and in the larger WHO context. In July 1998, WHO welcomed its new Director General, Dr Gro Harlem Brundtland, and TDR welcomed its new Director, Dr Carlos Morel. The incoming WHO administration launched a whirlwind of organizational change that has drawn TDR closer to other programmes. The creation of a Communicable Diseases Cluster (CDS) under one Executive Director, and the appointment of Department Directors, one of which is Director TDR, has facilitated collaboration between TDR and other CDS programmes. *Roll Back Malaria* (RBM), a new Cabinet Project housed in the CDS cluster, draws directly upon the research strengths of TDR, and TDR staff participate in the planning and execution of many RBM activities. In addition, a CDS cluster-wide project, the *Stop TB* initiative, acknowledges TDR's comparative advantage with respect to catalysing the development and testing of new diagnostics, drugs and vaccines in TB prevention and control. TDR further participates in the organization-wide Partnership for Health Sector Development (PHD) by promoting and funding research in the basic social and economic field.

As a new century approaches, and WHO marshals global attention to health, there is renewed urgency to address communicable diseases. But the challenges which face us are enormous; they stem from the complexity of the microorganisms, the changing environment, and the political, socioeconomic and behavioural context of tropical diseases. TDR's strong scientific reputation, its ability to draw upon a network of leaders in biomedical and social sciences in both industrialized and disease endemic countries, and its growing linkages with private sector partners, in particular, those in the pharmaceutical world, mean that the Programme is in a vitally important position to "make a difference" in generating new knowledge and tools to prevent and control tropical diseases and relieve the suffering of those affected by them.

The Third External Review (1998) concluded that "TDR emerges as an important funding body for tropical disease research and its influence in the field as a whole can be considered significant. Through the generation of scientific knowledge it has, in a highly significant manner, contributed to progress and innovation in the field of tropical diseases".

The budget presented in this document is based on recommendations by the Scientific and Technical Advisory Committee (STAC) to implement the following major changes to the Programme:

- Add two more diseases - tuberculosis and dengue - to TDR's disease portfolio across all Programme Areas.
- Strengthen the basic social, economic and behavioural research aspects previously addressed in Applied Field Research and shift them to the (re-named) Basic and Strategic Research unit.
- Include diagnostics as an additional component under Product Research and Development.

STAC underlined that the new diseases should be included only if additional resources could be mobilized – their inclusion should not mean phasing out or reducing ongoing work. Therefore in this document, the budget is presented both with and without the extra resources required for the two diseases, the difference being clearly stated.

The budget and the recommendations by the STAC were endorsed by the Joint Coordinating Board (JCB) during its twenty-second meeting in June 1999.

During 1999 and the first half of 2000, TDR will develop a strategic plan which will incorporate the new diseases as well as the new functional areas of Diagnostics and Social, Economic and Behavioural Research into the work of the Programme. Scientific working groups will look into research needs and priorities for all of the diseases in TDR's portfolio to identify the areas where TDR can contribute the most and to establish criteria for phasing in and phasing out of activities in each area of the Programme.

Table 1. Approved Programme Budget 2000-2001 (US\$'000)

	Budget 2000-2001					
	Revised Programme 1998-1999 Budget		Exclusive of TB Dengue		TB/Dengue	Grand Total
I. Technical and Administrative Bodies	668	1.1%	598	0.9%	0	598 0.8%
II. General Activities R&D						
<i>Director's Initiative Fund</i>	1,830	2.9%	1,465	2.2%	0	1,465 2.0%
<i>Leprosy</i>	1,255	2.0%	1,270	1.9%	0	1,270 1.7%
III. Basic and Strategic Research	6,580	10.5%	9,987	15.1%	800	10,787 14.6%
IV. Product Research and Development	15,378	24.6%	16,226	24.6%	4,317	20,543 27.8%
V. Intervention Development and Evaluation	12,370	19.8%	10,503	15.9%	1,453	11,956 16.2%
VI. Research Capability Strengthening	17,104	27.8%	19,165	29.0%	1,291	20,456 27.7%
VII. Programme Management	7,060	11.3%	6,838	10.4%	0	6,838 9.2%
Total	62,245	100.0%	66,052	100.0%	7,861	73,913 100.0%

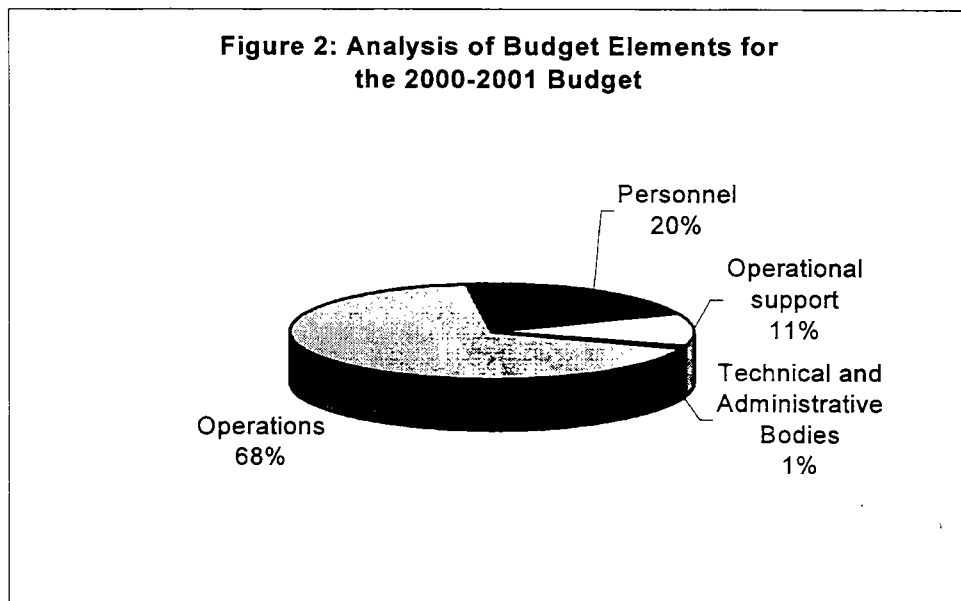
The Total Budget amount requested for the 2000-2001 biennium is US\$73,913,000, of which US\$7,861,000 is due to inclusion of TB and dengue in the TDR portfolio. TB and dengue aside, the budget has increased from US\$62,245,000 to US\$66,052,000 - an increase of 6.1%.

In addition to this core budget, WHO/TDR is seeking US\$6.5 million to establish a special fund for rectal artesunate, to channel support for its development, registration and clinical trial.

There are three main reasons for the 6.1% budget increase compared to the previous biennium. Firstly, following the Third External Review recommendation to strengthen the area of Strategic Research, the cost of 1.5 professional staff positions has been added to the budget, together with costs for the accompanying operations and operations support. As well, social, economic and behavioural research activities have been moved, together with a budget of US\$1 million and 2.5 professional staff posts, from Intervention Development and Evaluation (formerly Applied Field Research) to Basic and Strategic Research (formerly Strategic Research). This is also in line with JCB, which has often referred to the importance of Strategic Research - for instance, JCB-21 "Re-emphasized the importance of TDR's Strategic Research activities and warned against any further reductions in investment in this area".

The second reason for the budget increase relates to Product Research and Development and follows the STAC recommendation to include diagnostics as a new component. A budget of US\$600,000 has therefore been added. In addition, the staff positions in Product Research and Development that were approved, but not budgeted for, during the 1998-99 biennium, have now been filled. This is in line with the JCB-21 recommendation that, "subject to the availability of additional funding, TDR's Product Research and Development staff could be increased to enable TDR to play an important role in the Medicines for Malaria Venture (MMV)".

Thirdly, in the Programme Area on Research Capability Strengthening, the Third External Review recommended seeking a better balance between individual and institutional support and increasing the emphasis on epidemiology, entomology and social science. The budgets for these activities have therefore been adjusted upwards by approximately US\$300,000. In addition, the Multilateral Initiative on Malaria requires an additional US\$700,000 for the biennium – it is currently operating at an agreed level of US\$5 million with an approved budget of US\$4.3 million. Finally, and as for Product Research and Development, the staff positions approved in the 1998-99 biennium but not filled or budgeted for, have been included in the budget.



Regarding the financial implications of the restructuring of Intervention Development and Evaluation (IDE), according to recommendation by STAC, 2.5 staff members plus budget for Operations have been transferred from IDE to Basic and Strategic Research. With the inclusion of TB and dengue in TDR's portfolio, 1.5 new professional staff will be situated in IDE.

In the proposed budget for 2000-2001, 68% of the total has been allocated to Operations. In comparison, in the Approved Budget for the two preceding biennia, 67.7% and 67.1% were allocated to Operations. With the inclusion of TB and dengue, the proportion allocated for Operations will reach 70%.

One and a half staff positions will be freed up following the streamlining of management functions combined with economies of scale in the area of resource mobilization and IT services, as these functions will be devolved to the CDS Management Support Unit.

The number of General Service staff posts is increased in order to normalize some of the long-standing, "short-term", general service staff.

The total additional staff requirements for inclusion of TB and dengue are set to be 3 Professional and 2.5 General Service staff.

Table 2 below shows the staffing for 2000-2001 as compared to the current biennium. It should be noted that the approved budget for 1998-1999 was based on man-years while the budget for 2000-2001 is based on posts, allowing a more comprehensible and accurate picture of the situation.

Approved 1998-1999		Programme Area	Approved 2000-2001					
P	G		Exclusive of TB & Dengue		Inclusive of TB & Dengue Total		Increase	
P	G		P	G	P	G	P	G
0	0	I. Technical and Administrative Bodies	0	0	0	0	0	0
0.5	2.5	II. General Activities - R & D	0.5	0.5	0.5	0.5	0	0
1.5	1.5	III. Basic & Strategic Research	5.5	4.5	5.5	4.5	0	0
6.25	5	IV. Product Research & Development	6	5	7	6.5	1	1.5
6.25	5	V. Intervention Development & Evaluation	4.5	5	5.5	5	1	0
5	5	VI. Research Capability Strengthening	5	5	6	6	1	1
7.5	7.5	VII. Programme Planning & Management <i>Within TDR</i>	4.5	8	4.5	8	0	0
0	6	<i>Adm. Support Service, incl. MSU</i>	1	6	1	6	0	0
27	32.5	Total Posts	27	34	30	36.5	3	2.5

Operational workplans

TDR will be using the WHO-wide Activity Management System (AMS) to develop and monitor its operational workplans. Considerable effort will have to go into harmonizing workplans across WHO and ensuring that, for example, the composite workplans of Roll Back Malaria (RBM) and Stop TB (STB) capture, in a meaningful way, all the related activities of WHO, including those of TDR. Complete and comprehensive operational workplans for all of TDR's activities for year 2000 will be ready for Director TDR's approval at the beginning of December 1999.

Financing the Programme Budget

At the time of preparation of the Programme Budget for 2000-2001, the implementation rate for 1998-1999 indicated that the revised budget for the biennium would be fully implemented. The budget for the 1998-1999 biennium of US\$62,245,000 is slightly less than the total estimated resources available (US\$62.9 million), thus additional contributions are required to meet the recommended carry-over of US\$3,000,000. Apart from financing the carry-over, the budget for 2000-2001, without the inclusion of TB and dengue, will require additional contributions of approximately US\$8 million as compared with 1998-1999; while with the inclusion of TB and dengue, a further US\$7.8 million will be required.

This budget document is divided into seven Programme Areas:

- I:** Technical and Administrative Bodies
- II:** General Activities – Research and Project Development, including Leprosy
- III:** Basic and Strategic Research (STR)
- IV:** Product Research and Development (PRD)
- V:** Intervention Development and Evaluation (IDE)
- VI:** Research Capacity Strengthening (RCS)
- VII:** Programme Planning and Monitoring (PPM)

PROGRAMME AREA I: TECHNICAL AND ADMINISTRATIVE BODIES

Programme Area I includes aspects related to the costs of meetings for TDR's governing bodies, i.e., JCB, STAC and the Standing Committee; support for formal reporting to contributing partners and interested parties; and support for continued mobilization of resources for the Programme's activities.

Since the Third External Review was completed in 1998, and no such activity will be undertaken in 2000-2001, the costs for this budget item are reduced. The biennial Programme Report was produced in two versions: one to be accessed on the Web, consisting of about 150 pages and organized by disease, and a printed report of about 60 pages organized according to TDR's four functional units. It is foreseen that in the coming years there will be increasing transition to the Web for writing and distribution of this Report, as more of TDR's audiences gain Internet access. However, care will be taken to ensure that people without access to the Internet continue to have access to printed TDR documentation.

Table 3: Technical and Administrative Bodies

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
Joint Coordinating Board	148	148	0
Standing Committee	60	60	0
STAC	160	160	0
Scientific and Technical Reviews	140	70	-70
Programme Report	100	100	0
Fundraising	60	60	0
Total	668	598	-70

PROGRAMME AREA II: GENERAL ACTIVITIES – RESEARCH AND PROJECT DEVELOPMENT

Director's Initiative Fund

Budgetary provisions under General Activities cover those activities - in research and project development and operations support - not assigned to a particular TDR Programme Area, which involve several of the TDR functional areas, or which require action in between SC/TF/RSG meetings.

The major budget item is the Director's Initiative Fund (DIF) which enables TDR to respond quickly and flexibly to innovative or promising research opportunities with limited amounts of seed funding. Support under the DIF is limited to US\$15,000 per project and is not renewable. If additional funds are required, requests are channelled to the relevant Steering Committee. The DIF is also used to fund Project Development Grants (PDG) limited to US\$10,000 per project. These grants provide assistance to researchers in developing countries in the preparation of proposals for submission to TDR. Approximately half of DIF funds are channelled to such support; the remainder are available for allocation to specific TDR components during the biennium. The DIF is a critical mechanism in the case of financial gaps during the biennium as it can protect, at least in the short term, specific areas of operation. The personnel services previously included under this Programme Area are, in the 2000-2001 Budget, covered under Programme Planning and Monitoring.

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000	2000-2001 US\$000	(Col 2-1) US\$000
	(1)	(2)	(3)
Director's Initiative Fund	1,005	1,000	-5
Personnel Services	355	0	-355
Temporary Assistance	200	200	0
Operations Support	150	150	0
Publications	100	100	0
Shipping/Insurance Adjustment	20	15	-5
Total	1,830	1,465	-365

Operations support under General Activities covers meetings, temporary advisors, consultants and duty travel when such activities cut across several Programme Areas or when they cannot be assigned to a particular Area. In addition, this item is used to supplement other operations support areas within TDR as required during the biennium.

Leprosy

The World Health Assembly Resolution WHA44.9 set a prevalence target of less than one case per 10,000 population for the global elimination of leprosy as a public health problem by the year 2000. The resolution has helped stimulate significant progress throughout the world - increased programme coverage and implementation of multidrug therapy has resulted in a

dramatic 76% reduction in global prevalence since 1990, with equally dramatic reductions in incidence. While the temptation might be to phase leprosy out of the TDR portfolio, it is recognized that the hardest-to-reach constitute the challenge for elimination. TDR is committed to ensure that it supports, as best it can, every effort to achieve global elimination, and is reviewing its research agenda to address remaining problems and challenges relevant to disease elimination. To accomplish this, TDR will interact closely with the Control, Prevention and Eradication Department of the CDS-Cluster.

Focus for 2000-2001

Immunology of leprosy (IMMYC)

A better understanding of leprosy transmission is important for monitoring the effect of multidrug therapy (MDT) in disease control programmes and for evaluating the feasibility of leprosy eradication. An improved skin test for specific detection of infection with *M. leprae* would be of considerable practical benefit in this context and TDR is currently evaluating (*in vitro* and in animal models) peptides based on *M. leprae*-specific gene sequences as novel skin test reagents. As planned, immune reactive peptides were identified in the 1998/1999 biennium, but re-screening of the sequences of those peptides against the now completed *M. tuberculosis* genome sequence indicated that a majority of the peptides recognized in leprosy patients were not specific for leprosy. The subsequent identification of new peptide sequences based on the completed genome sequences of *M. leprae* and *M. tuberculosis* delayed the initiation of Phase I clinical trials - originally planned for early 1999 - by one year. Given satisfactory outcome of the safety testing, clinical Phase II trials in endemic areas are envisaged for the end of 2000 or early 2001.

Table 5 Leprosy

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
Operations			
Immunology	650	650	0
Chemotherapy	300	300	0
Personnel Services	165	180	15
Operations Support	140	140	0
Total	1,255	1,270	15

Inflammatory reactional states and polyneuropathies (damage to peripheral nerves) are manifestations of leprosy which are often not prevented by anti-leprosy MDT. Their disabling sequels in particular make these phenomena the number one priority in leprosy research. Reactions and nerve damage appear to be due to immune hyperstimulation and TDR-sponsored studies have indicated that they are accompanied or preceded by measurable over-production of immune mediators, such as tumour necrosis factor alpha. Therefore, TDR Basic and Strategic Research is attempting to establish conclusively, by type of reaction (type I/II), a correlation between the levels of these immune system products and the development of reaction on the one

hand, and between reaction and development of disability on the other. Although success in basic research is difficult to forecast, the target for the 2000-2001 biennium is to develop a lead for an inexpensive and simple tool to predict reactions and/or nerve damage.

Chemotherapy of leprosy (THEMYC)

The search for better drugs for treatment of leprosy will continue and, in this connection, a new study has been initiated to compare the activities of HMR 3647, clarithromycin, moxifloxacin, ofloxacin, rifapentine and rifampin against *M. leprae* in the mouse footpad system. The major activity for the biennium, however, will be follow-up of patients recruited in the multicentre field trial of ofloxacin-containing multidrug regimens, being carried out at 15 centres in 8 countries. After reviewing the potential of the new regimens, the next step will be to ensure their application in the field.

PROGRAMME AREA III: BASIC AND STRATEGIC RESEARCH

Objective

- To promote basic research in the biomedical, behavioural, political, economic and social sciences and in so doing, encourage the pursuit of unexpected leads that can take research questions beyond those formulated by existing paradigms so as to gain new knowledge about fundamental processes related to tropical diseases.

Focus in 2000-2001

The Third External Review strongly supported TDR's investments in Strategic Research, pointing out that often such investments must be sustained over the long term prior to use of the knowledge in products (tools) for disease control. It called upon TDR to maintain a broad spectrum of Strategic Research so as to deal with future uncertainties and possible breakthroughs in Product Research and Development. As mentioned above, this functional area has been re-named, more comprehensibly, Basic and Strategic Research (STR).

The orientation of Strategic Research in TDR up to now has been on research that develops new product development opportunities. In keeping with this focus, TDR has centred its Strategic Research agenda on three areas: parasite genome, molecular entomology and pathogenesis. According to the Third External Review, the functional, rather than disease, organization of TDR has allowed full advantage to be taken of new developments in molecular biology and biotechnology. It has helped to create new international networks in parasite genome and molecular entomology with participation of top scientists.

Table 6 Basic and Strategic Research

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
<i>Exclusive of TB and Dengue</i>			
Operations	5,525	7,025	1,500
Personnel Service	770	2,512	1,742
Operations Support	285	450	165
<i>TB and Dengue</i>			
Operations		650	650
Personnel Service		0	0
Operations Support		150	150
Total	6,580	10,787	4,207

The orientation of Strategic Research in TDR has been critical to advancing knowledge on biological mechanisms through which disease operates. However, there is a need to broaden this vision to include examination of the social, economic and behavioural conditions that explain why a disease occurs in the first place and why it is so difficult to effectively combat.

There is increasing recognition, within TDR and elsewhere, that horizons must be widened to include the contextual setting in which people lead their daily lives, as individuals and population groups, and how these settings influence the emergence and maintenance of tropical diseases.

For this reason, STAC recommended that the area of Basic and Strategic Research be expanded to include research on socioeconomic and behavioural aspects of infectious diseases, with an emphasis on the diseases within the TDR portfolio, now proposed to include TB and dengue. Examples of research issues that might be explored include studies on demographic and socioeconomic transformations and their links to disease emergence and maintenance, and comparative studies of social and economic policies and their respective impacts on disease prevention and control programmes.

The proposed work will be guided by a Steering Committee that draws upon experts of multiple disciplines including, crucially, epidemiologists, political and health economists, health educators, public health professionals, and other behavioural and social scientists. Grants will be accorded on a competitive basis. Priority will be research that appears more likely to lead to breakthroughs in thinking about interrelated aspects of human systems and disease systems. Similar types of research were earlier undertaken in Task Forces, such as those on gender, health sector reform, health care financing, and environment.

While the importance of expanding the mandate of Basic and Strategic Research to include human systems components is recognized, there is also a need to modify the focus of the work carried out to date. Dramatic advances in genomics necessitate that TDR moves into a post-genome agenda to seek opportunities for the development of new tools, particularly by stimulating the area of bio-informatics. The area of molecular entomology has so far focused only on transgenic mosquitos and malaria, and this too must be broadened, particularly if TB and dengue are to be included in the TDR disease portfolio. Included must be other aspects of vector biology and vector interaction with viral, in addition to parasitic, pathogens. If basic research in TB and dengue is to be pursued aggressively, the areas of pathogenesis and functional genomics must also receive new resources.

PROGRAMME AREA IV: PRODUCT RESEARCH AND DEVELOPMENT

Objectives

- To promote and, where necessary, action the discovery and development to registration of affordable new drugs, diagnostics, and vaccines for selected tropical diseases, and their out-licensing.
- To extend the range of indications for existing products to tropical diseases, assess the potential of combinations of existing products, and transfer product research and development technology to disease-endemic countries.

Focus in 2000-2001

The Third External Review emphasized the importance of fostering partnerships with pharmaceutical companies as critical links for bringing products from development to registration. TDR can act as a centre for interested stakeholders to converge around mutual and complementary interests. While TDR is not a pharmaceutical company, it needs to have at its disposal a critical mass of expertise for drug and vaccine development, as signified by the Review.

Mindful that TDR cannot replicate industry, the 2000-2001 budget ensures that TDR can count on inside expertise that mirrors, on a much smaller scale, the different components of the product research and development cycle. Such internal strengthening is critical for the development of strong partnerships with private pharmaceutical companies; it ensures that dialogue is among equals.

In addition to the current four components of Product Research and Development, STAC recommended the inclusion of diagnostics as a fifth component.

New technology that permits the production of rapid and simple diagnostic assays could transform global surveillance and monitoring and make pathogen-specific medical care possible in the developing world. The relative ease of applying any number of different capture probes or antibodies in a given format has led to a situation in which diagnostic manufacturers have outpaced strategic thinking of public health experts. There are more tests potentially available than there are clear rationales for their use. Furthermore, the proper role and potential impact of such assays in communicable disease control is essentially unexplored.

TDR and WHO have an important role to play in the development of improved diagnostics applicable in low-income countries. This includes:

- Prioritization of needs for diagnostics.
- Elaboration of disease-specific test performance specifications.
- Development of global specimen, reagent or gene banks when necessary.
- Stimulation of industry to include TDR and WHO priority diseases and use simple formats.
- Establishment of networks for laboratory and field assessment of new diagnostics.

- Use of surveillance data, and regional information on health systems and availability of public funds, to form a clear market picture for attracting industry collaboration.
- Direct funding of proposals covering work which industry cannot be stimulated to undertake.

WHO currently houses a number of diagnostics initiatives for different communicable diseases, including tuberculosis (TBDI). Each initiative has its own Steering Committee and industry partners. The consolidation of diagnostics activities offers the opportunity of coordinating the activities of the smaller diagnostics research programmes, and expanding them as needed. The most pressing rationale for this is that strategic thinking is needed for WHO to focus its activities and develop priorities in this area. Other arguments for the development of such an operation include:

- A focused contact point for industry.
- Knowledge of formats and advances with cross-disease potential applicability.
- Savings in personnel needs.
- Consolidation of Steering Committees.
- Possibility of enhancing prioritization among multiple diseases.
- Improved strategic planning.

A diagnostics activity will be a sister operation to the current drug and vaccine discovery research work of TDR. It will feed off the same genome and post-genome agenda. It will funnel candidate diagnostics into TDR's Product Research and Development unit pipeline and will thus be monitored and reviewed by its Research and Development Committee.

Components

The main components of TDR Product Research and Development are:

- Drug Discovery Research.
- Vaccine Discovery Research.
- Diagnostics Research.
- Product Development – to regulatory approval.
- Core Activities – to facilitate all of the above.

The specific activities of each of these areas supported by the budget are:

Drug Discovery Research

- Effective network into academic and pharma biologists and chemists.
- Functional interface with the Basic and Strategic Research unit of TDR.
- Portfolio of identified and validated biological targets.
- Series of lead chemicals for optimization.
- Portfolio of predevelopment drug candidates.
- Series of development proposals submitted to R&D committee, which are accepted.
- Contribution towards new technology transfer programme.

Vaccine Discovery Research

- Effective network into academic and pharma biologists and immunologists.
- Functional interface with Basic and Strategic Research in TDR.
- Watching brief of possible novel adjuvants for vaccine formulation.
- Portfolio of candidate vaccine antigens.
- Portfolio of predevelopment vaccine candidates.
- Series of product development proposals approved by the R&D committee.
- Contribution towards new technology transfer programme.

Diagnostics Research

- Effective network into academic and pharma biologists and chemists.
- Functional interface with Basic and Strategic Research in TDR.
- Portfolio of pertinent research activities.
- Specimen banks and identified field sites for assessment and validation of potential products.
- Portfolio of predevelopment candidates.
- Series of development proposals submitted to R&D committee, which are accepted.
- Contribution towards new technology transfer programme.

Product Development

- Portfolio of candidate drugs in development.
- Portfolio of candidate diagnostics and vaccines in development.
- Planning activities as an integrated process of product research and development.
- System for coordination and quality control of preclinical work (GMP/GLP).
- System for coordination, quality assurance and quality control of clinical work (GCP/GLP).
- Series of regulatory submissions submitted which are accepted.
- Contribution toward new technology transfer programme.

Core Activities

- Effective line management and financial/administrative/planning structure for TDP.
- Effective R&D committee for scientific and technical review and for monitoring of technology transfer.
- Improved interactions with private sector, including actioned MMV.

Table 7 Product Research and Development

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
<i>Exclusive of TB and Dengue</i>			
Operations	12,000	10,990	-1,010
Personnel Service	2,448	2,758	310
Operations Support	930	1,876	946
<i>Diagnostics</i>			
Operations	0	408	408
Personnel Service	0	0	0
Operations Support	0	194	194
<i>TB and Dengue</i>			
Operations	0	3,052	3,052
Personnel Service	0	585	585
Operations Support	0	680	680
Total	15,378	20,543	5,165

* The budget does not include the Medicines for Malaria Venture (MMV)

The increase in budget for operational support relative to operations projected for 2000/01 is principally a reflection of the need to enhance the quality of the various development activities financed by PRD to bring them closer to international standards of good practice. The recruitment of a preclinical and a clinical coordinator in 1998 means that it is now opportune to action this need with appropriate training courses for preclinical and clinical monitors as well as for the PIs themselves. PRD is working very closely with RCS in the planning and implementation of these activities.

PROGRAMME AREA V: INTERVENTION DEVELOPMENT AND EVALUATION

Objectives

- To develop interventions and provide solid, large-scale evidence of efficacy and effectiveness of products,* interventions,** and instruments of policy in reducing the burden of the tropical (and other) diseases in the TDR portfolio.
- To identify solutions to circumvent and combat anticipated or emerging problems that disrupt efficacy of public health applications.
- To provide evidence on efficacy, cost-effectiveness, acceptability and sustainability of interventions to support rational public health policies.

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
<i>Exclusive of TB and Dengue</i>			
Operations	8,575	7,600	-975
Personnel Service	2,785	2,303	-482
Operations Support	1,010	600	-410
<i>TB and Dengue</i>			
Operations	0	1,000	1,000
Personnel Service	0	303	303
Operations Support	0	150	150
Total	12,370	11,956	-414

Focus in 2000-2001

As the Strategy Group has yet to set priorities for the IDE unit, described below are ongoing initiatives and current plans, which are expected to continue during the biennium.

Restructuring of the unit

IDE will undergo fundamental restructuring in line with the recommendations of the External Review, but also taking into consideration the broader changes that have occurred within WHO as well as the expansion of the TDR disease portfolio. This should enable TDR to better fulfil its planned mission.

* Products include drugs, vaccines, equipment and tools for public health, prostheses, and diagnostics.

** Interventions - public and personal - include combinations of products, algorithms, information or policies that reduce the risk, duration or severity of an adverse health condition.

The proposal approved by STAC in March 1999 included:

- Transformation of the Applied Field Research unit into an Intervention Development and Evaluation unit (IDE) with better articulation of its mandate.
- Configuration of a priority-setting Strategy Group comprised of research and control experts, to consider the distribution of funds according to priority public health needs in tropical and other infectious diseases in line with the TDR disease portfolio.
- A transition period where Task Forces will continue to oversee the implementation of these priorities to ensure sound research in priority areas.
- A role for IDE as catalyser and coordinator of national and international (organizations/institutions) partnerships and technical input, based on consideration of the notorious cost of large-scale trials.
- Development of a management system that will sustain department-driven initiatives but also allow for investigator-initiated research, and expansion into additional disease areas.
- The devolving of future research in gender, health sector reform, health care financing and environment to Basic and Strategic Research.

Assessments of efficacy of new/improved public health strategies

Ongoing are:

- Large, randomized trials to quantify the survival benefit of early treatment of severe malaria with rectal artesunate (see Table 9). These trials will assess the role, and quantify any survival benefit, of a single rectal dose of artesunate given early to children with severe malaria in areas where no effective alternative treatment exists for patients who cannot take drugs by mouth and who are referred to hospital for injectable treatment.
- Large, community, randomized trials to measure the impact on burden of disease of improving the home management of uncomplicated malaria. Pilot studies are under way to test the acceptability and validity of different strategies for improving home management of febrile illnesses in children. Results are expected in mid-2000 in preparation for large studies, which will examine the impact on mortality and morbidity.
- Large-scale trials of strategies to prevent severe anaemia in children. Studies in Africa in areas of high and intense malaria transmission will establish which of the two alternatives - iron supplementation or intermittent treatment - is more effective in protecting infants at risk from severe anaemia during the first year of life.

Public health applications: combatting problems

Action to combat rapidly emerging resistance to antimalarial drugs involves:

- Identifying the most useful markers of resistance, and generating protocols, standardizing techniques, and carrying out training and capacity building.
- Validating the use of identified markers in early detection of resistance.
- Mapping the location of resistance.

- Optimizing drug combination regimes using chloroquine, or sulfadoxine/pyrimethamine or amodiaquine, in combination with artesunate;* results from the trials will then be applied to other artemisinin derivatives.
- Safety and efficacy studies of combination versus single agent treatment regimens, which may lead to studies on drug presentation and packaging, and then to registration and marketing of fixed drug combinations.

Ways of circumventing poor access to health services include:

- Strategies to improve home use of antimalarials for uncomplicated malaria - innovative strategies being explored include unit dose pre-packaging of antimalarials, strengthening community drug distribution channels, developing household skills, reorienting health services and intensifying IEC.
- Strategies for timely referral of severely ill children for appropriate treatment. Studies will involve traditional healers in interventions to promote early referral for appropriate treatment of severely ill children.
- Community Directed Treatment of lymphatic filariasis & onchocerciasis. A variety of activities is in progress on public health impact, advocacy, rapid mapping, evaluating and improving Community Directed Treatment, and assessing the impact of mass treatment.

Intervention implementation and evaluation: developing guidance

- To maximize the impact and sustainability of impregnated bednets: research to select and evaluate strategies of product development, intervention implementation, and promotion.
- To improve vector control in Chagas disease: studies on vectors (house infestation, population dynamics) and control methods (cost-effectiveness, impact).
- To assess the epidemiological impact of control strategies for African Trypanosomiasis: cohort studies of treatment of seropositive but apparently aparasitaemic patients in different environments; evaluation of the specificity of the Card Indirect Agglutination Test for Trypanosomiasis (CIATT).

Special Fund for Rectal Artesunate

Objective

- To create a special fund to channel support for the development, registration and execution of clinical trials of rectal artesunate to quantify the role and benefit of its early administration in inhibiting the evolution of malaria to severe and fatal outcomes.

WHO Director General's initiative to *Roll Back Malaria* has heightened the urgency to demonstrate that malaria morbidity and mortality can be decreased. The Task Force on Severe Malaria has concentrated efforts on the potential of artesunate in suppository form to significantly reduce mortality of acute *non per os Plasmodium falciparum* malaria patients. Children and infants are the main beneficiaries, and it is this age group that is also at greatest risk of early death from malaria. A plan for the development and registration of rectal artesunate has

* Artesunate is an artemisinin compound which is rapidly and highly effective against drug-resistant *P. falciparum*.

been developed in collaboration with TDR's Product Research and Development unit, the project management of Roll Back Malaria, and WHO's Health Technology Development Cluster. This plan involves the execution of clinical trials to quantify the role and benefit of early administration of rectal artesunate in inhibiting the evolution of malaria to severe and fatal outcomes.

Because of the great promise of this product, TDR is seeking special funding to accelerate the process of registration and field testing of the suppositories. Thus, TDR, in collaboration with its partners within WHO, proposes that a special fund be set up through TDR to mobilize support for this particular work. US\$6.5 million is being sought in the next two years to expedite registration and field trials. The field trials will be carried out in six countries in Africa and south-east Asia.

Budget Item	Revised Budget 1998-1999 US\$000 (1)	Approved Budget 2000-2001 US\$000 (2)	Decrease/Increase (Col 2-1) US\$000 (3)
Operations	-		
Post-registration		1,210	1,210
Field Trials		4,000	4,000
Personnel Service	-		
Operations Support	-	0	0
Pre-registration		1,290	1,290
Total		6,500	6,500

PROGRAMME AREA VI: RESEARCH CAPABILITY STRENGTHENING

Objective

- To strengthen, through support to institutions and through training, the capabilities of developing disease endemic countries to carry out control related research and to participate in the global effort to develop new methods of prevention, diagnosis, control, and treatment of the TDR diseases.

Focus in 2000-2001

The Third External Review recommended:

- Further creation of networks of centres of excellence to enhance South-South collaboration, with a focus on the needs of least developing countries.
- Strengthening the development of regional and/or national strategies, in close collaboration with national institutions, to ensure focus on national priorities and enhance sustainability.
- A balanced approach between the training of individuals and institutional strengthening, and between training in biomedical fields and social sciences.
- Building a comprehensive database on TDR trainees and grantees, recognizing achievements of these individuals and TDR-supported institutions.

These recommendations mirror those made by STAC and JCB. In addition, the Review recommended measuring the impact of RCS activities, an exercise which will be finalized in 2000. It will provide additional input for fine-tuning TDR strategies in capability strengthening.

The major areas of RCS focus in 2000-2001 are therefore on:

- Establishing strong research groups in disease endemic countries and stimulating creation of networks among them.
- Developing institutions of international reputation in countries of the South to enhance South-South collaboration.
- Transferring technology and know-how to developing countries, particularly skills needed to meet R&D needs.
- Countries with least developed research capacity.
- Promoting distance learning, including continued establishment of Internet connectivity.
- Celebrating TDR's 25th year in 2000 by highlighting the accomplishments of TDR-supported grantees and institutions and establishing a TDR alumni association for communication and advocacy.

In the 1998-1999 biennium, TDR responded to the creation of the Multilateral Initiative on Malaria (MIM) by establishing a Task Force to promote and coordinate research projects, and by assigning a newly recruited scientist to dedicate 50% of time to MIM, to ensure necessary impetus for the Initiative. While the Initiative has resulted in twenty partnership projects between African, North American and European scientists on malaria, other capacity strengthening activities have had to be reduced, in particular, the institution-building aspects for other diseases

in regions other than Africa. MIM activities related to monitoring and technical assistance provision to funded projects will continue to be needed in 2000-2001, particularly in view of TDR's catalytic role to *Roll Back Malaria* in Africa.

The increase in budget for personnel is due to one professional and one general service staff post, approved by JCB (21) but not filled or included in the 1998-99 budget, having now been included. A staff member whose costs used to be shared with another WHO programme has now been included as fully paid by RCS. Two staff, who in 1998-99 were partly funded from PRD, are included fully in the 2000-2001 budget for RCS.

In addition, human and financial resources are required to support capacity building in the areas of tuberculosis and dengue.

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
<i>Exclusive of TB and Dengue</i>			
Operations	10,994	11,324	330
MIM	4,300	5,000	700
Personnel Service	1,435	2,455	1,020
Operations Support	375	386	11
<i>TB and Dengue</i>			
Operations	0	800	800
Personnel Service	0	491	491
Operations Support	0	0	0
Total	17,104	20,456	3,352

PROGRAMME AREA VII: PROGRAMME PLANNING AND MONITORING

Objective

- To anticipate trends and needs that arise from the dynamic environment in which the Special Programme carries out its activities, and guide and implement effective and efficient procedures that facilitate the ongoing execution of the Programme's activities in the context of change.

Focus in 2000-2001

For some time, TDR has had its own administrative structure which has included professionals in the areas of management, finance and budget, personnel, communications, information systems and external relations. Having its administration de-centralized to the programme level has undoubtedly been beneficial to the Programme. TDR has been able to design special information systems tailored to its special needs, including mechanisms that facilitate careful monitoring of financial expenditures and budget reporting. These assets have enhanced TDR's credibility as a transparent, well-run programme that is a sound donor investment. Ongoing links with TDR's co-sponsors and other contributing partners have been possible with a full time External Relations Officer, and TDR's public profile has been well served by the communications/media team that it has at its disposal. As a Special Programme, TDR had circumvented many, but not all, of the bureaucratic stumbling blocks that WHO's other regular programmes encountered on a daily basis.

With the restructuring of WHO's divisions into clusters and the decentralization of its administrative structure into Management Support Units (MSUs), TDR has been able to devolve some of its administrative functions to the MSU - mainly personnel, and to some extent, budget and finance functions. The areas of Informatics and Resource Mobilization, which have been housed within the TDR Programme Planning and Monitoring unit, has also been absorbed into the Communicable Diseases Cluster, although TDR has maintained some support functions to these hubs. TDR's programme management continues to include a strong communications team which maintains ongoing contact with multiple audiences through continuous updating of its Web site as well as the traditional hard-copy *TDR news* (for audiences without access to the Internet).

Programme management in TDR will be adjusted as it becomes clear how much the MSUs will be able to maintain TDR's flexibility and close budget monitoring. For this reason, the budget for Programme Planning and Monitoring includes provision to maintain and further strengthen the Programme's planning, administrative, and monitoring functions. These functions will be carried out in close collaboration with the MSU.

In 2000-2001 TDR will support one full time equivalent (FTE) P-staff and 6 FTE General Service staff in the MSU - some administrative functions have devolved from TDR to the MSU and some have devolved from Central Administration to the MSU. It is envisaged that the staff posts previously supported in the Central Administration of WHO will be transferred to the MSU at the beginning of the 2000-2001 biennium.

Budget Item	Revised Budget	Approved Budget	Decrease/Increase
	1998-1999 US\$000 (1)	2000-2001 US\$000 (2)	(Col 2-1) US\$000 (3)
Operations			
Communication	125	200	75
Evaluation		60	60
Personnel Service			
Staff	3,325	2,867	-458
Temporary assistance	270	170	-100
Overtime	20	20	0
Staff training	35	40	5
Consultants	20	15	-5
Operations Support			
Information systems	310	360	50
Supplies and Equipment	40	50	10
Duty travel	100	100	0
Audit fees	75	75	0
Administrative support	1,290	1,431	141
Common services	290	290	0
Premises/rent	900	900	0
Postage/telephone, etc.	260	260	0
Total	7,060	6,838	-222

The Third External Review recommended development of a long-term vision and preparation of a strategic plan for TDR. This plan began to be developed during 1999 as a programme-wide priority with involvement of all staff and stakeholders; it will include criteria for evaluating different aspects of the Programme. Specific funds have been set aside in the 2000-2001 budget to carry out at least one ex-post or value-for-money evaluation each year. A performance framework will be established in the newly introduced WHO-wide Activity Management System (AMS) based on the strategic plan. Further development and strengthening of TDR's information systems began in 1999, hence the budget for information systems has been increased for year 2000.

The Third External Review further recommended establishing a formal communication strategy. Previously resources for communication activities were drawn from several parts of the budget; however, for 2000-2001, a budget has been specified for the overall TDR communication strategy, while each Steering Committee will allocate budget as appropriate.