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UNDP/WORLD BANK/WHO
Special Programme for Research and Training in Tropical Diseases
(TDR)

Proposed Programme Budget
for the 1990-91 Biennium and
Estimates for 1992-93

ABBREVIATIONS AND ACRONYMS

BCV	Biological Control of Vectors Component
CHEMAL	Chemotherapy of Malaria Component
DIF	Director's Initiative Fund
FIELDMAL	Applied Field Research in Malaria Component
GS	General Service Staff
IMMLEP	Immunology of Leprosy Component
IMMAL	Immunology of Malaria Component
JCB	Joint Coordinating Board
M	Million
MISTR	Management Information System of TDR
OCT	Onchocerciasis Chemotherapy Project
P	Professional Staff
RSG	Research Strengthening Group
SER	Social and Economic Research Component
SFR	Swiss Franc
STAC	Scientific and Technical Advisory Committee
STRC	Scientific and Technical Review Committee
SWG	Scientific Working Group
TDR	Special Programme for Research and Training in Tropical Diseases
THELEP	Chemotherapy of Leprosy Component
UNDP	United Nations Development Programme
WHO	World Health Organization

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EXECUTIVE SUMMARY

The UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) was established in 1975 to undertake research and development for new and improved tools to control six major groups of tropical diseases and to strengthen the research capabilities of tropical countries in which these diseases are endemic. TDR's technical and administrative bodies both review scientific and technical activities and provide guidance and support for the Programme's administrative and financial requirements (sections 1.1, 1.2 and 1.3).

Major programme thrusts and priorities for 1990-91 reflect the recommendations of the Second External Review Committee, as well as other policy decisions of the Joint Coordinating Board. Research capability strengthening, which will receive US\$ 18.9 million or 25.9 per cent of the Proposed Budget, continues to be a major priority. Among the TDR target diseases, malaria is the most important, with budget allocations of US\$ 15.1 million, followed by leprosy with US\$ 6.6 million and filariasis with US\$ 4.8 million. Other priority areas, as identified by the ERC, are field research, rational drug development and social and economic research (section 1.4).

The Programme Budget proposed for the 1990-91 biennium amounts to US\$ 72 940 200, an increase of 15.0 per cent over the 1988-89 Revised Budget of US\$ 63 421 300. The level of the Proposed Budget is in line with the ERC recommendation that TDR will require an increase in funding of at least 25 to 30 per cent in real terms over the next five years. TDR depends on voluntary contributions for most of its income and contributions required to finance the Proposed Budget are about US\$ 66 million, an increase of US\$ 8 million over anticipated contributions of US\$ 58 million in 1988-89. Other sources of income, including the carry-over from the current biennium, bring total estimated funds available to US\$ 76 million. Most of the budget increase will be allotted to Programme Operations, which will increase from 72.1 per cent of the Revised Budget for 1988-89 to 73.2 per cent in 1990-91, while all other Budget Elements, notably Personnel Services and Operational Support, decrease (section 2).

Separate texts for each of the 12 research and development components in Programme Area II present the objectives, current highlights, planned activities and financial requirements of each component. The General Activities Component includes the Director's Initiative Fund, with a proposed allocation of US\$ 1 500 000. It is proposed that the purpose of this Fund be expanded to permit the Director to increase the Operations budgets of research and development components to meet new or increased requirements during the biennium. An amount of US\$ 750 000 is allocated for Operational Support under General Activities; most of this amount would be re-allocated to other components as required during the biennium (section 4).

In Research Capability Strengthening (Programme Area III), emphasis will be placed on consolidating new initiatives undertaken in 1988-89, such as programme-based grants and the joint TDR-Rockefeller Foundation programme. The results of a study on TDR research training activities will be available during the biennium. A new component on Epidemiology and Field Research Support is being created within Area III. Its broad objective is to promote field research within TDR, particularly related to field trials of new intervention tools. It will establish and support networks of field researchers in developing countries, assist in the design, preparation and implementation of field research projects, and support training in relevant disciplines (section 5).

Programme Management (Programme Area IV) provides direction, guidance and supervision for all Programme activities, support for technical and administrative bodies and for scientific operations and activities. In addition, Programme Management is responsible for financial management, information systems and office automation, communications and publications and personnel and procurement services. Major thrusts in 1990-91 will be the consolidation and effective use of microcomputer technology to improve management and information at all levels and improved public information activities (section 6).

The Programme Budget for 1990-91 contains a total of 162 proposed staff years, an increase of 6 staff years over the approved staff years for 1988-89. Two additional General Service posts are proposed for Research Capability Strengthening, whose existing staff can no longer cope with the demands of expanded activities (section 7).

TABLE 1 Budget Summary (US\$000 and Per Cent)

PROGRAMME AREA/COMPONENT	1988-1989		1990-1991		1992-93	
	(1) APPROVED BUDGET	(2) REVISED BUDGET	(3) PROPOSED BUDGET	(4) INCREASE/(DECREASE) (3)-(2)	(5) PER CENT	(6) ESTIMATED
I Technical and Administrative Bodies	645.0	645.0	645.0	0.0	0.0	700.0
--Per cent of Total	1.1	1.0	0.9	0.0		0.8
II Research and Development						
General Activities	1 873.0	827.1	1 342.5	515.4	62.3	1 500.0
Director's Initiative Fund	525.0	665.0	1 500.0	835.0	125.6	1 700.0
Chemotherapy of Malaria	4 734.0	5 105.0	6 025.5	920.5	18.0	6 900.0
Immunology of Malaria	4 487.0	4 887.0	5 575.0	688.0	14.1	6 400.0
Applied Field Research in Malaria	1 887.0	3 125.0	3 500.0	375.0	12.0	4 000.0
Schistosomiasis	2 387.0	2 592.0	3 000.0	408.0	15.7	3 400.0
Filariasis	3 787.0	4 472.0	4 775.0	303.0	6.8	5 400.0
African Trypanosomiasis	2 937.0	3 256.0	3 300.0	44.0	1.4	3 800.0
Chagas Disease	2 137.0	2 283.0	2 600.0	317.0	13.9	3 000.0
Leishmaniases	2 287.0	2 614.0	3 000.0	386.0	14.8	3 400.0
Immunology of Leprosy	3 337.0	3 405.0	3 800.0	395.0	11.6	4 300.0
Chemotherapy of Leprosy	1 887.0	2 281.0	2 800.0	519.0	22.8	3 200.0
Biological Control of Vectors	2 274.0	2 281.0	2 300.0	19.0	0.8	2 600.0
Epidemiology	800.0	525.0	0.0	(525.0)	(100.0)	0.0
Social and Economic Research	2 037.0	2 113.3	2 525.5	412.2	19.5	2 900.0
Subtotal-Programme Area II	37 376.0	40 431.4	46 043.5	5 612.1	13.9	52 500.0
--Per cent of Total	63.0	63.8	63.1	59.0		63.3
III Research Capability Strengthening						
General Activities	1 557.0	1 849.4	2 255.2	405.8	21.9	2 500.0
Institution Strengthening	5 850.0	7 300.0	8 300.0	1 000.0	13.7	9 500.0
Training	6 700.0	5 700.0	5 700.0	0.0	0.0	6 500.0
Epidemiology and Field Research	734.0	816.1	2 650.0	1 833.9	224.7	3 000.0
Subtotal-Programme Area III	14 841.0	15 665.5	18 905.2	3 239.7	20.7	21 500.0
--Per cent of Total	25.0	24.7	25.9	34.0		25.9
IV Programme Management						
Personnel	3 035.0	3 177.4	3 456.2	278.8	8.8	3 900.0
Operational Support	650.0	700.0	700.0	0.0	0.0	800.0
General Support	1 849.0	1 849.0	2 138.0	289.0	15.6	2 400.0
Regional Offices	953.0	953.0	1 052.3	99.3	10.4	1 200.0
Subtotal-Programme Area IV	6 487.0	6 679.4	7 346.5	667.1	10.0	8 300.0
--Per cent of Total	10.9	10.5	10.1	7.0		10.0
GRAND TOTAL	59 349.0	63 421.3	72 940.2	9 518.9	15.0	83 000.0

1. PROGRAMME OVERVIEW

1.1 Objectives

The Special Programme for Research and Training in Tropical Diseases (TDR) was established in 1975 with two interdependent objectives:

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

TDR's activities are targeted towards six disease groups: malaria, schistosomiasis, filariasis (including onchocerciasis or river blindness), the trypanosomiasis (both African sleeping sickness and the American form, Chagas disease), the leishmaniases and leprosy.

1.2 Structure

The Special Programme is co-sponsored by the United Nations Development Programme (UNDP), the World Bank, and the World Health Organization (WHO), with WHO as the Executing Agency. TDR's structure includes the following scientific and administrative bodies (see also Figure 1):

Joint Coordinating Board (JCB) - The JCB, TDR's senior management body, meets annually to review TDR activities, consider long-term plans, determine the budget and evaluate progress. The 30 members of the JCB include representatives of 12 governments selected by financial contributors to the Programme, 12 governments of countries affected by TDR's target diseases, three governments or agencies selected by the JCB itself and the three co-sponsoring agencies.

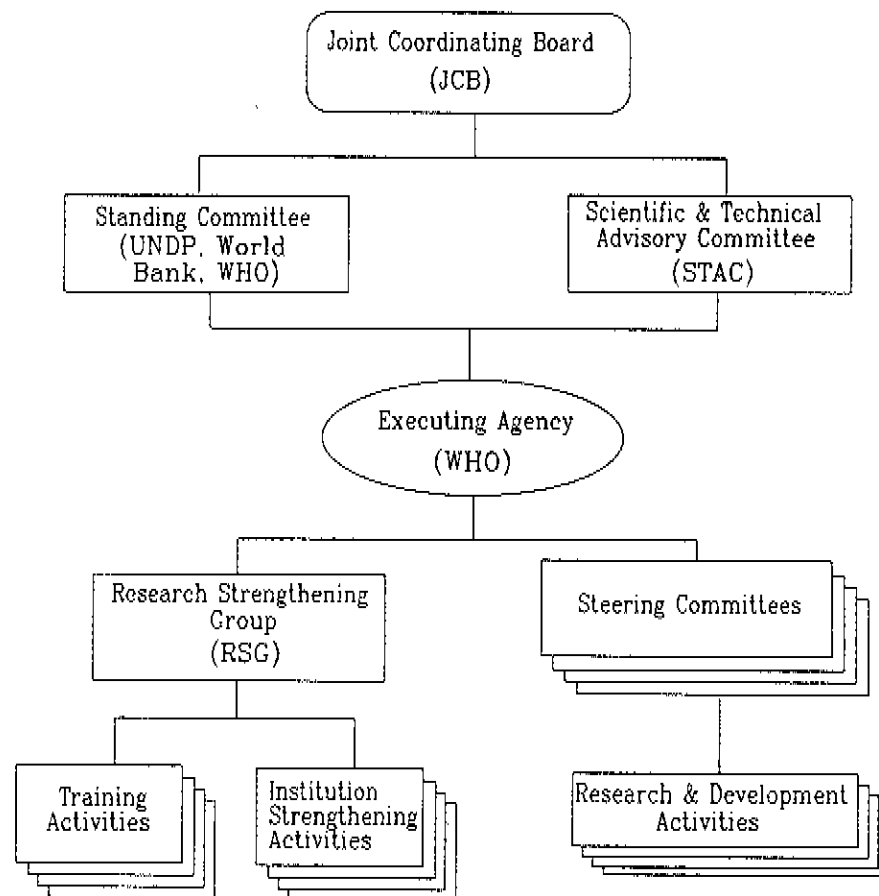
Scientific and Technical Advisory Committee (STAC) - STAC, composed of 15 to 18 experts from a wide range of scientific disciplines, acts as technical advisor to both the JCB and the Programme secretariat. It reviews the Programme's scientific activities and reports its findings to the JCB. Detailed evaluations of TDR components and of trans-disease aspects of the Programme are carried out by scientific and technical reviews including STAC members and other experts.

Standing Committee - Representatives of the three co-sponsors meet at least twice a year as the Standing Committee to oversee the overall management and financing of the Programme.

Steering Committees and Scientific Working Groups (SWGs) - TDR's research and development activities are organized on the basis of Components which are established by STAC for each of TDR's target diseases. Trans-disease Components for social and economic research, and biological control of vectors deal with disciplines important to several diseases. Research and development activities are managed through *Steering Committees*, which meet at least once a year to prepare research plans, assess research proposals and review scientific progress. *Scientific Working Groups* bring together scientists involved in TDR activities to make periodic state-of-the-art reviews and elaborate new strategies in specific areas.

Research Strengthening Group (RSG) - Major responsibility for implementing TDR's efforts to strengthen the research capabilities of tropical countries rests with the RSG. Its 12 to 15 members, selected for their experience in research management and training in developing countries, prepare overall plans, review proposals for research strengthening and evaluate progress. Key members of the TDR Secretariat constitute the *Secretariat Committee for Research Training* which meets several times a year to consider applications for research training.

FIGURE 1 TDR's Technical and Administrative Bodies



Coordination of TDR's activities with other WHO programmes responsible for assisting Member States to improve their disease control activities is reinforced through a matrix organization approach. The Secretaries of the TDR Steering Committees are co-located with the relevant WHO disease control programmes: Malaria (MAP), Parasitic Diseases (PDP), Leprosy (LEP) and Vector Biology and Control (VBC), while WHO Unit Chiefs serve as Secretaries of TDR Scientific Working Groups.

Regular communication and cooperative efforts link TDR's research and development and research capability strengthening and training activities to WHO's other special and global programmes, especially the Human Reproduction Programme (HRP), the Diarrhoeal Diseases Control Programme (CDD), the Expanded Programme of Immunization (EPI), and the Global Programme on AIDS (GPA).

1.3 Targets

TDR's general targets for the period 1990-95 are as follows:

- (1) Goal-oriented research and development, aiming to achieve:
 - field application or advanced clinical trials of improved or new chemotherapeutic agents for at least three of the six diseases;
 - field applications or assessment of large-scale trials of a candidate leprosy vaccine, advanced trials of one or more possible malaria vaccines, and field application or advanced trials of one or more vaccines against cutaneous leishmaniasis;
 - field application or advanced trials of new simple tests and micro-techniques for diagnosing disease and for monitoring drug susceptibility;
 - field application or advanced trials of two or more new biological agents for the control of disease vectors; and
 - establishment of the epidemiological, social and economic bases for the development of more effective national strategies for the integrated control of six diseases.
- (2) Through the strengthening of national institutions of the tropical countries affected by the diseases, the Programme will assist in developing:
 - a network of 80 to 100 self-reliant national research and training centres, and technical collaboration among developing countries; and
 - through training, a base of 300 to 400 scientists from tropical countries for research careers in their home countries.

(Eighth General Programme of Work 1990-95, WHO, 1987.)

1.4 Major Programme Thrusts and Priorities 1990-91

Major programme thrusts and priorities are reflected in proposed budget allocations for the various components, as contained in the relevant sections on the research and development and research capability strengthening activities. Several dimensions are of particular importance. It has long been TDR policy, most recently re-affirmed in the decisions of the Joint Coordinating Board on the recommendation of the Second External Review Committee, that approximately 25 per cent of the total Programme Budget should be devoted to Research Capability Strengthening, Programme Area III. The Programme Budget approved by the JCB in June 1987 for the 1988-89 biennium provided 25.0 per cent for Programme Area III, while the most recent revised budget, including the budget revisions approved by the Board in June 1988, decreased the per cent slightly, to 24.7. The Proposed Programme Budget for 1990-91 allocates 25.9 per cent of the total budget to Programme Area III, which includes the newly-created Epidemiology and Field Research Support Component (Tables 1 and 2.3).

Research capability strengthening is a priority area identified by the Programme Director in his report to JCB(11) in June 1988. Several initiatives were undertaken in 1987 and 1988 to re-orient the Programme's research capability strengthening activities and to broaden the scope of assistance available to developing country institutions and scientists. These initiatives are described in section 5, Research Capability Strengthening.

One important consequence of the significant increase in research capability strengthening activities in 1988-89 has been the emergence of severe strain on the ability of the current staff resources to administer the rapidly-growing activities. This constraint is most serious in terms of support personnel (General Service) and for this reason, it is proposed to increase the secretarial/clerical staff of Programme Area III by two new posts (see section 7).

In terms of diseases, malaria continues to receive the highest proportion of funds. The three malaria components together are allocated US\$ 15.1 million (32.8%) out of the proposed budget of US\$ 46.0 million for Research and Development, Programme Area II. The two components focused on leprosy receive about US\$ 6.6 million or 14.3 per cent of the Programme Area II budget, followed by filariasis at US\$ 4.8 million or 10.4 per cent. The remaining diseases - African trypanosomiasis, schistosomiasis, leishmaniasis and Chagas disease - are allocated between 5.6 and 7.1 per cent of the budget. The trans-disease components, Biological Control of Vectors and Social and Economic Research, receive 5.0 and 5.5 per cent of the budget respectively.

In 1987 and 1988 there was a noted increase in the quality, number and value of research and development and institution strengthening and training proposals received by TDR. The number of proposals increased from 432 in 1986 to 531 in 1987 and 669 in 1988, while the average budget of TDR-funded projects rose by about one-third during the same period. It is anticipated that the number of proposals submitted to TDR will continue to increase, as a result of scientific advances in the understanding of tropical diseases and the development of new control tools, and greater awareness of TDR among scientists in both developing and developed countries.

The Second External Review Committee identified three main areas for the evolution of the Programme's activities in the coming period:

- field studies, especially relating to the testing of new disease control products developed with TDR support;
- rational drug development, based on improved knowledge of the life cycles of the disease pathogens; and
- social and economic research, especially on the economic burden and development policy aspects of tropical diseases.

Field research is defined as research which involves the collection of primary data from individuals, their communities and/or their environments in tropical disease-endemic countries. The definition also includes research on disease vectors and field trials of new disease control products. Field research thus encompasses a very wide range of disciplines and includes research supported under the various disease-oriented Steering Committees, as well as under trans-disease research components of Biological Control of Vectors and Social and Economic Research. TDR support for epidemiology and field research projects has increased substantially in recent years, from about US\$ 4.5 million in 1985-86 to US\$ 7.9 million in 1987-88 - 27 per cent of total project funding for research and development. It is anticipated that funding for epidemiology and field research projects will continue at a high level, as new disease control products developed with TDR support reach the stage of field testing.

In response to changing programme requirements, especially the need for improved capabilities in developing endemic countries to undertake field trials of products resulting from TDR-supported research, it has been decided to establish a new component within Programme Area III on Epidemiology and Field Research Support. The broad objective of this component is to promote, develop and support multidisciplinary field research leading to improved strategies for the control of tropical diseases. Personnel resources for the component are drawn from existing resources of the Epidemiology Component (which is disestablished) and from the Biological Control of Vectors Component.

A key activity of the Epidemiology and Field Research Support Component will be to support the establishment and consolidation of multidisciplinary field research networks to assist field-based investigators. The new component will also support training activities in such disciplines as epidemiology and entomology, and will work in close consultation with Research Capability Strengthening and with Social and Economic Research. Disease-specific research projects will continue to be supported through the relevant disease-oriented Steering Committees, while the Epidemiology and Field Research Support Component will have a budget of US\$ 2.65 million in 1990-91, including US\$ 1.5 million for operations. Further information on the Epidemiology and Field Research Support Component is contained in section 5.1.

Drug development is a major area of TDR activity. The External Review Committee emphasized *rational* drug development as an important future thrust. Rational drug development in this sense refers to the development of new drugs to control tropical diseases based on improved knowledge of parasite biology, including parasite structure, metabolism and mechanisms of penetration of human cells. TDR supports drug development for all the TDR target diseases, with major expenditures for malaria, filariasis, African trypanosomiases, and leprosy. It is estimated that project expenditures for drug development and testing are currently in the order of US\$ 7-8 million per biennium. During 1989 the Scientific and Technical Advisory Committee is conducting a perspective thematic review on the directions and organization of TDR's research and development related to drugs. This review will assess TDR's drug development activities and make recommendations on priorities for TDR drug development activities. Information on current activities and future plans is contained in the relevant sections for each component.

In keeping with the recommendations of the External Review Committee and the decisions of the Joint Coordinating Board, increased emphasis is being placed on the integration of social and economic research activities supported by the Programme with the development and application of new disease control products. Projects involving both disease-specific and the Social and Economic Research Components have been developed in Chagas disease, leprosy and African trypanosomiasis. The budget of the SER Component in the 1988-89 biennium is US\$ 2.1 million; the proposed budget amount for the 1990-91 biennium is US\$ 2.5 million.

2. PROGRAMME BUDGET AND FINANCING

2.1 Budget Level

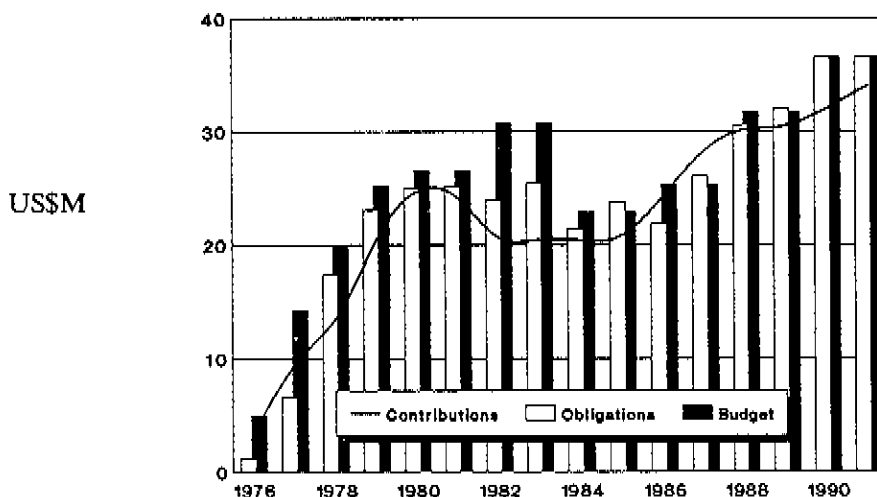
The Programme Budget proposed for the 1990-91 biennium is US\$ 72 940 200. This represents a 22.9 per cent increase over the amount of US\$ 59 349 000 approved by the JCB in June 1987 for the 1988-89 biennium and a 15.0 per cent increase over the 1988-89 Revised Budget of US\$ 63 421 300 approved in June 1988. The Proposed Budget reflects an assessment of Programme requirements balanced against estimates of the financial resources likely to be available to TDR during the biennium. Figure 2 shows the evolution of TDR contributions, obligations and budget from 1976 to 1988, with projections for 1989 and 1990 (biennial budgets have been divided into two equal annual amounts).

The Proposed Budget also takes into account the conclusions of the Second External Review Committee of TDR. Reviewing the Programme's financial situation, the Committee expressed concern with the apparent levelling off of contributions to TDR at US\$ 20 to 25 million shortly after the establishment of the Programme. In the light of additional resources required for areas identified for future expansion, the Committee concluded that in the next five years there will be a need for funding at least 25 to 30 per cent in real terms above the present budgeted levels (*Report of the Second External Review Committee, TDR, 1988, p.71*).

In its discussion of the Report and recommendations of the ERC, the Eleventh Session of the Joint Coordinating Board in June 1988 recognized that the areas for future evolution of the Programme's activities, as identified by the ERC and the Programme Director, would require funding increases over current budget levels. The Board decided that it would consider the magnitude of these increases in the light of specific plans in areas of future evolution to be developed by the Programme Director and reviewed by the STAC. These plans would be incorporated into the Proposed Programme Budget for the 1990-91 Biennium and Estimates for the 1992-93 Biennium, together with any other documentation which may be useful in this respect.

The Proposed Programme Budget of US\$ 72 940 200 is within the range required for the TDR budget to reach the level recommended by the External Review Committee by the 1992-93 biennium. This level is reflected in the Estimated amount for 1992-93 contained in Table 1 (Executive Summary), which forecasts a budget level of US\$ 83 000 000 for 1992-93. In addition to the increase in real terms suggested by the ERC, the forecast budget figures for 1990-91 and 1992-93 contain an allowance of about 3 per cent per year for inflation.

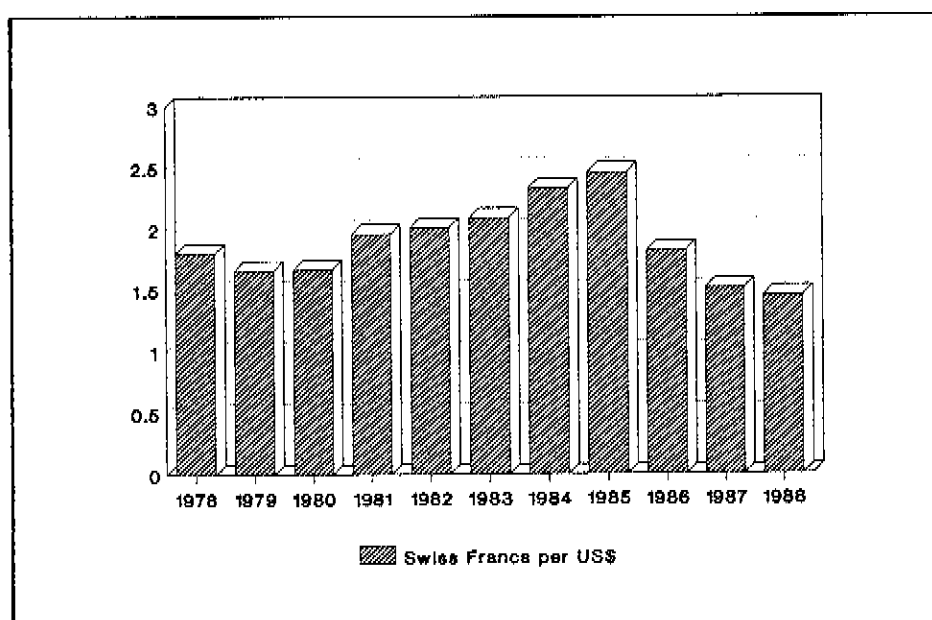
FIGURE 2 TDR Contributions, Obligations and Budget 1976-91 (US\$M)



1976-88 Actual figures
1989-91 Estimates/Requirements

TDR finances, both contributions and obligations, are strongly affected by two major international financial influences, currency fluctuations and inflation. In recent years, currency fluctuations, especially the value of the US dollar against other major currencies, have been the predominant influence on TDR. For TDR financial purposes, the value of the US dollar in terms of Swiss francs is the most relevant exchange rate; Figure 3 illustrates the fluctuation in the official UN exchange rate for the Swiss franc between 1975 and 1988. After a steady increase in value between 1981 and 1985, the dollar fell sharply in 1986 and 1987 and continued to decline in 1988, despite a short-term increase in mid-year. In the first four months of 1989, the US dollar increased considerably in value against most other major currencies.

FIGURE 3 Swiss Franc/US Dollar Average Annual Exchange Rates 1975 - 1988



The decline in value of the US dollar relative to other major currencies has two principal effects on TDR's finances. On the one hand, the US dollar value of contributions to TDR in other major currencies increases as the dollar declines. An analysis of contributions to TDR from 16 major contributors during 1986, 1987 and 1988 indicated that about 63 per cent of the increase in contributions (expressed in US dollars) over 1985 was the result of exchange rate gains as a consequence of the decline of the US dollar relative to other major currencies (see Financial Report for 1988 and Revised Programme Budget for 1988-89, document TDR/JCB(12)89.7). On the other hand, the decline in value of the US dollar increases certain TDR costs, especially all Geneva-based expenditures, including salaries and allowances, communications, supplies and premises. The impact of currency fluctuations on the costs of TDR operations (research and development, and research capability strengthening) is difficult to assess with any degree of precision, but the decline in the value of the US dollar in the period 1985-88 is undoubtedly a major factor in the rapid increase in the average cost or funding level of TDR-supported research and development projects in recent years. Average annual TDR funding of research and development projects increased from US\$ 24 250 during the period 1982 to 1986 to US\$ 29 220 in 1987 and US\$ 32 860 in 1988.

For budget purposes the WHO budget exchange rate used for the 1990-91 WHO budget, Sfr 1.65 to the US dollar, has been used to establish Geneva-based costs, especially personnel. This is the same rate used for the 1988-89 budget.

TDR is also affected by international inflation. After relatively high rates of inflation in the late 1970's and early 1980's, inflation in industrialized countries decreased considerably in recent years (Table 2.1). Nevertheless, the previous high inflation combined with stagnant contributions and declines in obligations during the period 1981 to 1986, strongly eroded the constant value of contributions to TDR and TDR obligations, to the point that only now is the real value of contributions to TDR returning to the peak level achieved in 1980. Increases in inflation rates beginning in 1988 will once again threaten the real value of TDR's financial resources and expenditures for research and research capability strengthening.

TABLE 2.1 Approximate Inflation Rates - Industrialized Countries, 1979-87 (Per Cent)

1979	1980	1981	1982	1983	1984	1985	1986	1987
8.3	10.4	8.9	5.8	3.6	6.0	4.1	3.3	2.8

Source: IMF, *International Financial Statistics Yearbook 1988*, GDP Deflators.

2.2 Financing the Programme Budget

TDR depends on voluntary contributions from governments, international institutions, foundations and nongovernmental organizations for most of its income. Funds undisbursed at the end of each biennium become available in the subsequent biennium. Both the World Bank and WHO maintain undisbursed funds in interest-earning accounts that provide further sources of income.

Contributions required to finance the Proposed Budget for the 1990-91 Biennium are about US\$ 66 million. This represents an increase of US\$ 8 million or 13.8 per cent over anticipated contributions of US\$ 58 million for the 1988-89 biennium. The carry-over of undisbursed funds from 1988-89 is projected to be US\$ 7 million. Interest and other income during 1990-91 is forecast to total US\$ 3 million. Total funds expected to be available to TDR during the 1990-91 biennium are estimated at US\$ 76 million. Based on obligations of US\$ 72.9 million projected in this Proposed Programme Budget, there is an estimated closing balance of US\$ 3.1 million at the end of 1990-91 biennium (see Table 2.2).

TABLE 2.2 Estimated Financial Status 1990-91

	US\$ M
Estimated opening balance, 1 January 1990	7.0*
Income:	
Contributions required	66.0
Interest	2.0
Other income**	1.0
Total income	69.0
Estimated funds available	76.0
Estimated obligations (Proposed Budget)	72.9
Estimated closing balance, 31 December 1991	3.1

* Includes a contribution of US\$ 1.8 million received in 1987 from the MacArthur Foundation for the years 1990, 1991 and 1992.

** Primary savings on unliquidated obligations.

2.3 Proposed Budget Allocations

TDR's budget may be classified in two dimensions: Programme Area/Component and Budget Element. The *Programme Areas* (PA) are:

- | | |
|--------|---|
| PA I | <i>Technical and Administrative Bodies</i> includes the JCB, STAC, the Standing Committee and related items; |
| PA II | <i>Research and Development</i> covers budget provisions for the disease and trans-disease components; |
| PA III | <i>Research Capability Strengthening</i> includes the Epidemiology and Field Research Support Component; and |
| PA IV | <i>Programme Management</i> covers the Office of the Programme Director, programme management, information, communications, premises and other common services, as well as the costs of TDR-funded personnel in WHO Regional Offices. |

Budget Elements, which provide a functional breakdown of the budget, are:

- | | |
|--|---|
| <i>Operations</i> | - expenditures for research and development projects, institution strengthening activities and training grants; |
| <i>Personnel Services</i> | - salaries and related costs for TDR staff, including temporary and Regional Office personnel paid by TDR, and administrative support at WHO headquarters; |
| <i>Operational Support</i> | - meetings, consultants, temporary advisers and duty travel; |
| <i>Technical and Administrative Bodies</i> | - corresponds to Programme Area I; |
| <i>Other</i> | - expenditures for information services, public information and publications, office supplies, common services, premises and other items not included in other Budget Elements. |

Tables 2.3 and 2.4 present proposed budget allocations by Programme Area and by Budget Element, with corresponding data for the budget initially approved by the JCB and the most recent Revised Budget for the 1988-89 biennium. In terms of Programme Areas, the per cent allocated to Research Capability Strengthening (Programme Area III) increases from 24.7 per cent in the Revised Budget for 1988-89 to 25.9 per cent in the Proposed Budget for 1990-91, with a decrease from 63.8 per cent to 63.1 per cent in Research and Development (Programme Area II). This shift is caused primarily by the creation of the Epidemiology and Field Support Component within Programme Area III. This new Component has a proposed budget of US\$ 2.65 million out of the total budget of US\$ 18.9 million for Programme Area III (see Table 5). The additional responsibilities have increased the proportion of the budget allocated to Programme Area III slightly beyond the traditional target figure of 25 per cent of the total budget.

Within TDR Budget Elements, there are increases in the proportion of the budget devoted to Operations, from 72.1 per cent in 1988-89 to 73.2 per cent in 1990-91 and decreases in Personnel, Operational Support and Technical and Administrative Bodies. Although two new posts are proposed in the Budget, the overall increase in the Personnel Budget Element is considerably less than the rate of increase of the budget as a whole. A very high proportion - 80.1 per cent - of the budget increase is devoted to Operations, with 11.5 per cent of the increase for Personnel and 5.6 per cent for Operational Support.

TABLE 2.3 Budget Summary by Programme Area (US\$000 and Per Cent)

Programme Area	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3) - (2)
I Technical and Administrative Bodies	645.0	645.0	645.0	0.0
- Per Cent of Total	1.1	1.0	0.9	0.0
II Research and Development	37 376.0	40 431.4	46 043.5	5 612.1
- Per Cent of Total	63.0	63.8	63.1	59.0
III Research Capability Strengthening	14 841.0	15 665.5	18 905.2	3 239.7
- Per Cent of Total	25.0	24.7	25.9	34.0
IV Programme Management	6 487.0	6 679.4	7 346.5	667.1
- Per Cent of Total	10.9	10.5	10.1	7.0
TOTAL	59 349.0	63 421.3	72 940.2	9 518.9

TABLE 2.4 Budget Summary by Budget Element (US\$000 and Per Cent)

<i>Budget Element</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	43 045.0	45 745.0	53 370.0	7 625.0
- <i>Per Cent of Total</i>	72.5	72.1	73.2	80.1
Personnel Services	10 389.0	10 861.3	11 955.2	1 093.9
- <i>Per Cent of Total</i>	17.5	17.1	16.4	11.5
Operational Support	3 320.0	4 170.0	4 700.0	530.0
- <i>Per Cent of Total</i>	5.6	6.6	6.4	5.6
Technical and Administrative Bodies	645.0	645.0	645.0	0.0
- <i>Per Cent of Total</i>	1.1	1.0	0.9	0.0
Other	1 950.0	2 000.0	2 270.0	270.0
- <i>Per Cent of Total</i>	3.3	3.2	3.1	2.8
TOTAL	59 349.0	63 421.3	72 940.2	9 518.9

3. PROGRAMME AREA I: TECHNICAL AND ADMINISTRATIVE BODIES

The budget allocation to this Programme Area covers the cost of meetings of the Joint Coordinating Board (JCB), the Standing Committee and the Scientific and Technical Advisory Committee (STAC). The amounts provide for one annual meeting each of the JCB and STAC and for three meetings of the Standing Committee per year. Provision is also made for scientific and technical reviews, including Prospective Thematic Reviews, carried out by STAC.

The biennial Programme Report is a formal report to the JCB and is an important source document for other interested individuals and institutions on the progress made by TDR-supported activities towards achieving the Programme's objectives. The provision covers the direct costs associated with the Programme Report, primarily editing, artwork, printing and translation.

Fundraising activities include visits to present and potential contributors for the purpose of increasing awareness of TDR and financial support for the Programme.

The External Review Committee completed its activities with the presentation of its report and recommendations to JCB(11) in June 1988 and a budget provision is no longer required.

TABLE 3 Programme Area I: Technical and Administrative Bodies (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Joint Coordinating Board (JCB)	140.0	140.0	140.0	0.0
Standing Committee	30.0	30.0	35.0	5.0
Scientific & Technical Advisory Committee	160.0	160.0	160.0	0.0
Scientific & Technical Reviews	100.0	100.0	100.0	0.0
Programme Report	150.0	150.0	160.0	10.0
Fundraising Activities	50.0	50.0	50.0	0.0
External Review Committee	15.0	15.0	0.0	(15.0)
TOTAL	645.0	645.0	645.0	0.0

4. PROGRAMME AREA II: RESEARCH AND DEVELOPMENT

4.1 General Activities

Budget provisions under General Activities cover research and development and operational support activities not assigned to a particular disease or trans-disease component or which involve several components.

The major budget item is the Director's Initiative Fund (DIF), which enables TDR to respond rapidly to innovative or promising research opportunities with limited amounts of "seed" funding. Support under the DIF is normally limited to US\$ 15 000 per project and is not renewable. If additional funds are required, requests are channelled to the relevant Steering Committee for consideration in the normal fashion. The DIF is also utilized to fund Project Development Grants, which provide assistance to researchers in developing countries to prepare proposals for submission to TDR Steering Committees.

At its sessions in 1987 and 1988, the Joint Coordinating Board discussed proposals for providing increased flexibility with respect to Operations within the Programme Budget. The External Review Committee recommended that the DIF should, in addition to its existing purposes, be used to increase the budgets of components, and that the budget level should be US\$ 1 million per year (US\$ 2 million per biennium). In its discussion of this recommendation, the Board agreed that the Director should present to the JCB proposals for expanding the purpose and level of the DIF, with the budget amount proposed for 1990-91 not to exceed US\$ 1.5 million.

The Revised Budget for 1988-89 contains an amount of US\$ 665 000 for the DIF and a reasonable estimate of requirements for the DIF's existing purposes is US\$ 750 000 for 1990-91. It is proposed that the objectives of the DIF be extended along the lines suggested by the ERC, that is, to include the possibility that the Director could increase the Operations budgets of research and development components to meet increased or new requirements during the biennium. The budget allocation proposed is US\$ 1.5 million. Since about US\$ 750 000 would be required for small grants under the DIF, in practice only about the same amount, US\$ 750 000, would be available for eventual reallocation to the Operations budgets of components. This would provide a modest but welcome element of flexibility within the overall Programme Budget - about 1.0 per cent of the overall budget and 1.4 per cent of total Operations budgets. Requirements for additional amounts which cannot be met from this mechanism would continue to be considered within the framework of the Procedures for Budget Revision approved by the JCB in June 1987.

No budget provision is proposed under the budget item Field Research Fund. The amount of US\$ 1 million, which the JCB had set aside in approving the Programme Budget in June 1987, was reserved for new field research activities by decision of the JCB in June 1988, on the recommendation of the Scientific and Technical Advisory Committee and the Programme Director. Subsequently, the entire amount was allocated to Applied Field Research in Malaria. Continuing increased requirements in this component are contained in the proposed budget for 1990-91 (see section 4.4) and other requirements for field research are reflected in the Epidemiology and Field Research Support Component (see section 5.1). The budget item for Field Research Fund is not required in 1990-91.

Because of the difficulty of forecasting accurately requirements for Operational Support of the various components, an amount of US\$ 750 000 is proposed for Operational Support under General Activities. Funds would be re-allocated from this budget item during the biennium to supplement the Operational Support budgets of other research and development components as required.

TABLE 4.1 General Activities (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Director's Initiative Fund	525.0	665.0	1 500.0	835.0
Field Research Fund	1 000.0	0.0	0.0	0.0
Personnel Services	203.0	203.0	222.5	19.5
Temporary Assistance	50.0	95.1	100.0	4.9
Operational Support	400.0	309.0	750.0	441.0
Publications	200.0	200.0	250.0	50.0
Shipping & Insurance Adjustments	20.0	20.0	20.0	0.0
Total	2 398.0	1 492.1	2 842.5	1 350.4

4.2 CHEMOTHERAPY OF MALARIA

Objectives

- Develop new drugs for the treatment and prevention of malaria
- Improve the use of drugs which are already available
- Promote basic research aimed at identifying new approaches to malaria chemotherapy

Current Highlights

A formulation has been developed and toxicity testing is nearly complete leading to clinical trials of arteether, the ethyl ether derivative, of the Chinese antimalarial qinghaosu. Chinese registration data for artemether (the methyl ether injectable derivative) are also being reviewed for possible expansion of clinical experience with this derivative as well.

TDR supported synthesis of new molecules related to the active moiety of qinghaosu. These "trioxanes" show activity *in vitro* and *in vivo* against malaria and other parasites. Research is directed to defining the toxicity of these compounds, and to development of a watersoluble derivative of the most active compound of the series.

Mefloquine has now been registered in several countries, both for the treatment and prevention of drug-resistant falciparum malaria. Halofantrine, potentially useful in treating mefloquine-resistant cases, is now registered in France and is undergoing further dose-finding studies to optimize treatment schedules.

A new approach to chloroquine resistance has been developed using verapamil, a calcium channel blocker used in the treatment of cardiovascular disorders. Verapamil, like other calcium antagonists, appears to "reverse" chloroquine resistance *in vitro*.

A DNA probe for the diagnosis of *Plasmodium falciparum* malaria has been developed and field tested. Sensitivity is approximately as good as operational microscopy, and specificity is better. The major limiting factor is the need for a radioactive marker, which implies that the test must be performed in a central laboratory, not at the field level.

Planned Activities, 1990-91

The major thrust of the Chemotherapy of Malaria Component will be the clinical testing and registration of arteether, the qinghaosu derivative of current interest. Testing will be carried out initially in asymptomatic or mildly ill patients, and will quickly proceed to treatment of severely ill cases.

A DNA probe based on the *mdr* gene is under development for detection of drug resistant *P. falciparum*. Further work is required before this is a field test, but it has the potential for replacing the cumbersome *in vitro* test based on parasite cultivation currently in use.

The approach to "reversal" of chloroquine resistance through the concomitant use of calcium channel blockers will be followed up, with the intention of identifying an agent of this class which is less cardioactive than verapamil but equally effective in association with chloroquine against resistant *P. falciparum*.

Increasing attention will be devoted to research on parasite physiology and biochemistry with the objective of identifying exploitable targets for novel chemotherapeutic agents.

TABLE 4.2 Chemotherapy of Malaria (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	4 000.0	4 300.0	5 200.0	900.0
Personnel Services	484.0	484.0	500.5	16.5
Operational Support	250.0	321.0	325.0	4.0
Total	4 734.0	5 105.0	6 025.5	920.5

4.3 IMMUNOLOGY OF MALARIA

Objectives

- ° Develop malaria vaccines
- ° Improve diagnostic tests for malaria

Current Highlights

The Programme is pursuing vaccines based on pure parasite antigens that specifically stimulate protective immune responses. Following initial clinical trials with prototype *P. falciparum* sporozoite vaccines, in which partial immunity to challenge infection was achieved, other vaccine constructs are being prepared for evaluation in human volunteers. Anti-*P. vivax* sporozoite vaccines are also being developed for clinical trial. A highly immunogenic stage-specific antigen of *P. falciparum* liver schizonts has been identified and cloned; its potential as a vaccine target is being evaluated.

Many of the *P. falciparum* genes encoding asexual blood stage vaccine candidate molecules have now been cloned. Encouraging immunization studies in monkeys have been carried out, and in a human volunteer study immunization with a synthetic hybrid polymer based on several merozoite proteins resulted in delayed or suppressed parasitaemia following challenge infection. Studies on the asexual blood stage antigens of *P. vivax* are in progress and the gene encoding a major schizont/merozoite surface protein has been isolated.

An important advance has been the cloning of sexual stage antigens of *P. falciparum* and *P. vivax* which mediate transmission-blocking immunity. As a result, the production and evaluation of these molecules as vaccine candidates now becomes feasible.

Planned Activities, 1990-91

Several malaria vaccine candidates will reach the stage of clinical evaluation in human volunteers within the next funding period. TDR is likely to be involved to differing degrees according to the source and type of vaccine involved. In the case of transmission-blocking vaccines, TDR funds all of the laboratories concerned and will have to retain a major responsibility for the developmental phases since vaccines of this type will only be used in developing endemic countries and industrial interest may be limited. Increased funds will be needed to meet the cost of preclinical and clinical evaluation of transmission-blocking vaccines.

TDR will continue both to fund vaccine research and to coordinate the development of candidate vaccines, focusing particularly on:

laboratory-based research on malaria vaccines against sporozoites, liver stages and asexual blood-stage and sexual-stage parasites;

further analysis of immune responses and immunopathological complications of malaria infections and following malaria vaccination;

better tests for detecting infection in both human and invertebrate hosts, and for measuring protective immune responses, which could be used to assess vaccine efficacy as well as in other epidemiological studies of malaria;

trials in non-human primates of prototype vaccines and trials in human volunteers of vaccine candidates.

TABLE 4.3 Immunology of Malaria (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	4 000.0	4 330.0	5 000.0	670.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	200.0	270.0	275.0	5.0
Total	4 487.0	4 887.0	5 575.0	688.0

4.4 APPLIED FIELD RESEARCH IN MALARIA

Objectives

- ° Improve malaria control through research related to planning, application and evaluation of control measures
- ° Validate and field test methods applicable to all steps of this process and to transfer the resulting techniques to areas where they are needed
- ° Improve vector control methods by elucidating vector bionomics and assessing methods for preventing man/mosquito contact

Current Highlights

Chloroquine resistance has spread to most African and Middle East countries where *P. falciparum* is endemic, whereas in some Asian countries chloroquine resistance seems to diminish due to the reduced drug pressure. Sensitivity to sulphadoxine plus pyrimethamine remains satisfactory in most of Africa, but sensitivity to quinine is diminishing. Chemoprophylaxis in African children reduces mortality and morbidity and it does not seem to impair immunity. New cytogenetic, enzymatic and immunological tools have shown epidemiologically important genetic heterogeneity in vectors and have allowed the vectorial role to be clarified for several situations. Amongst the control methods, insecticide-impregnated bednets seem especially promising.

Immunological studies have shown that naturally acquired immunity to sporozoites requires long and repeated exposure. Several asexual blood stages of parasites revealed antigenic variability important for the selection of vaccine candidate substances.

Trends in research applications have shown a marked increase in the quantity, quality and cost of projects, and as a result the originally approved Fieldmal budget for the 1988-89 biennium had to be supplemented by US\$ 1 200 000.

Planned Activities, 1990-91

Future emphasis is required in four main areas:

- 1) The development and evaluation of malaria control strategies with particular attention to operational problems, such as the use of alternative drugs, the prevention of malaria in pregnancy and the possibility of slowing down the development of drug resistance. Further efforts are needed in the development and use of new diagnostic methods.
- 2) Improvement of vector control through a better knowledge of the behaviour and the vectorial role of several anopheles species in specific ecotopes; the adaptation of classical control tools and trial of newer tools.
- 3) Determination of epidemiological factors relevant for the development of malaria vaccines through studies on the patterns of inoculation and the development of natural immunity, the antigenic diversity and the protection associated with immune reaction to specific antigenic epitopes, candidates for vaccine studies.
- 4) Understanding the interaction between malaria and HIV infections.

TABLE 4.4 Applied Field Research in Malaria (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 450.0	2 650.0	3 000.0	350.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	188.0	200.0	12.0
Total	1 887.0	3 125.0	3 500.0	375.0

4.5 SCHISTOSOMIASIS

Objectives

- ° Develop safe and reliable antischistosomal drugs, simple field diagnostic methods and preventive measures
- ° Develop a schistosomiasis vaccine capable of providing long-term protection
- Identify and strengthen neglected areas of research

Current Highlights

The number of field research projects has started to increase, including a study of urban schistosomiasis in a focus in Brazil, testing a diagnostic antigen in Sudan, assessment of schistosomiasis morbidity in an endemic area in China, and investigation of protective immune responses (particularly cell-mediated immunity) which is carried out in the Gambia and Zimbabwe. Identification of a snail inhibitory compound is being supported as well as research on the role of ecdysteroids in miracidial-snail interactions. Control strategies in Côte d'Ivoire will provide baseline data to assist creation of a national action plan.

Chemotherapy studies are clarifying the mode of action of praziquantel and oxamniquine, helped by studies of the anatomy and function of the adult schistosome membrane, and by identification of genetic changes in schistosomes associated with drug resistance. The goal is to develop probes for detecting drug resistant parasites in field populations.

A collaborative study involving six Chinese institutions engaged in the evaluation of schistosome infection by serological tests has started. Work towards a prototype vaccine has identified major protective antigens, which have now been cloned. *S. haematobium* antigens for research are now available.

Planned Activities, 1990-91

Applied field research remains the highest priority. A meeting on field research held in 1988 is expected to result in the funding of six new proposals under the Schistosomiasis Component at an estimated cost of \$1,000,000 over the years 1989-91. These proposals include two projects in China and one in Malawi on schistosomiasis control, evaluation of the Schistosomiasis Control Programme in Brazil, the role of snail control in conjunction with chemotherapy and characterization of morbidity by ultrasound measurements in schistosomiasis mansoni.

Work on the mode of action of schistosomicidal compounds will continue to be encouraged and basic research on a vaccine against schistosomiasis will be a priority. Research towards production of monoclonal antibodies and identification of candidate vaccine antigens, using molecular biology techniques, goes hand in hand with the design of new diagnostic test systems geared to detecting circulating or excreted antigens. Further work on species other than *S. mansoni* will be promoted. Field trials of serological assays will be stimulated, and an SWG meeting on the role of diagnostic approaches in schistosomiasis control is planned for early 1990.

TABLE 4.5 Schistosomiasis (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 950.0	2 150.0	2 500.0	350.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	155.0	200.0	45.0
Total	2 387.0	2 592.0	3 000.0	408.0

4.6 FILARIASIS

Objectives

- Obtain and develop better drugs and drug regimens
- Develop better immunodiagnostic tests and possible vaccines
- Reduce inflammatory reactions to dead worms
- Improve the scope and efficacy of methods of filarial disease control

Current Highlights

Community-based trials of ivermectin, an effective, single-dose microfilaricide for onchocerciasis, are being carried out in Africa and Central America. Dosage schedules of diethylcarbamazine (DEC) continued to be tested to improve its use in lymphatic filariasis.

Two macrofilaricides from Ciba-Geigy S.A. continue to be tested in humans. Pharmacokinetic studies of one of these compounds are also underway using the leaf monkey animal model.

The search continues for better antigens and improved diagnostic tests using hybridoma and recombinant DNA technology, including specific antibody probe development, antigen purification and in vitro production, as well as epitope identification and molecular biological production of most promising antigenic leads with diagnostic potential. Research includes animal model systems that reliably reproduce major clinical features of human disease, together with studies on identification of specific vectors of onchocerciasis and lymphatic filariasis and determination of their epidemiological roles.

Planned Activities, 1990-91

New filaricides, especially macrofilaricides, will continue to be the highest priority. The search for a single-dose, non-toxic macrofilaricide (especially for onchocerciasis) in collaboration with the Onchocerciasis Chemotherapy Project (OCT), will continue through biochemical studies, screening and synthesis. A special TDR/OCT Preclinical Drug Development Team has been formed to address the issues of antifilarial drug discovery and more effective monitoring of results. Further development of new drugs currently in clinical trials--ivermectin and the two Ciba-Geigy compounds will continue. Studies will examine the impact on adult worms of five successive doses of ivermectin given at six monthly intervals, in order to elucidate the effect of the drug on the reproductive capacity of female worms. Since use of this drug could lead to far better compliance in mass therapy, extensive clinical trials in endemic areas against lymphatic filariasis are planned.

Immunological research will continue the search for a sensitive and specific diagnostic test for prepatent, patent and occult infection with emphasis on detection of non-immunogenic circulatory parasite products. Further work to clarify the role of host protective responses in filarial infections will also help to assess the prospects for immunoprophylaxis. Identification of immunogens involved in host protective mechanisms, and development of methods for their characterization, production and administration in immunoprophylactic regimens need to be carried out. Studies on pathogenesis will continue using newly developed animal models.

TABLE 4.6 Filariasis (US\$000)

<i>Budget Items</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	3 300.0	3 900.0	4 200.0	300.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	200.0	285.0	275.0	(10.0)
Total	3 787.0	4 472.0	4 775.0	303.0

4.7 AFRICAN TRYPANOSOMIASSES

Objectives

- Strengthen disease control through a better understanding of the epidemiology of the disease
- Develop new and effective drugs and improve the use of existing drugs
- Improve patient management through better knowledge of the disease's immunology and pathology

Current Highlights

A double antibody sandwich ELISA has been developed for the detection of antigens present in sera of infected animals. Evaluation of the method in experimental *T. b. rhodesiense* infections in monkeys and against 39 documented sera from sleeping sickness patients showed it is promising for immunodiagnosis.

Results from clinical trials with eflornithine (DFMO), involving 282 patients with *gambiense* sleeping sickness (of whom 206 were refractory to melarsoprol have shown that 270 are cured, establishing eflornithine as an effective therapy for *T. g. gambiense* infection. The refractoriness of *T. b. rhodesiense* to eflornithine in a limited number of patients in East Africa points to the need for alternative therapy or treatment regimen.

Crystals of triosephosphate isomerase (TIM) and glyceraldehyde phosphate dehydrogenase (GADPH) have been obtained and their structure determined. Using computer graphics, preliminary attempts have been made to design compounds which specifically inhibit these glycosomal enzymes.

Studies on receptors for LDL (low density lipoprotein) and transferrin in bloodstream forms of *T. b. brucei*, suggested that the trypanosome LDL receptor is different from that of the host and that interference with the functioning of the receptor significantly inhibits trypanosome growth.

Lectins secreted by tsetse flies have a critical function in relation to the completion of the trypanosome life cycle in tsetse. Establishment and maturation of the parasite in the tsetse midgut have been shown to be lectin-mediated.

Planned Activities, 1990-91

Evaluation and further development of the antigen detection enzyme immunoassay will be carried out in a multicentre trial, and the ELISA will be adapted for evaluation in the field.

Clinical trials with eflornithine will continue in *T. b. gambiense* areas to determine the minimum effective dosage and the optimum treatment regimens. Trials have been planned in *T. b. rhodesiense* areas involving the administration of eflornithine in combination with suramin. A clinical trial with nifurtimox has been planned to determine the potential of this drug in the treatment of *T. b. gambiense* infection.

Large scale evaluation of traps and screens for tsetse control will be continued in Cote d'Ivoire and Uganda, with the possibility of initiating similar projects in other endemic countries.

TABLE 4.7 African Trypanosomiases (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	2 500.0	2 750.0	2 800.0	50.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	219.0	200.0	(19.0)
Total	2 937.0	3 256.0	3 300.0	44.0

4.8 CHAGAS DISEASE

Objectives

- Develop and evaluate vector control methods
- Increase knowledge of parasite molecular biology to promote vaccine development
- Improve treatment through a better understanding of the immunopathogenesis of chronic lesions

Current Highlights

Insecticidal paints have proven effective for the control of domestic triatomine vectors. The paints retain their insecticidal activity for 18 months after application, which compares very favourably with residual insecticide spraying. An insecticidal fumigant canister has been tested in a rural endemic area in Santiago del Estero, Argentina, in a primary health care programme and was found useful as a complementary measure for triatomine vector control between spraying cycles.

Field testing of the insecticidal paints and the fumigant canister in Brazil and Argentina were carried out in collaboration with the respective government Chagas Disease control programmes. The above new vector control methods are being commercially produced by local manufacturers in Brazil and Argentina.

Important advances towards development of a vaccine include cloning of *T. cruzi* genes that encode for immunoprotective antigens, which are now being produced by chemical synthesis or recombinant DNA technology, in laboratories in Argentina, Brazil, Venezuela and the USA. These will be initially tested as diagnostic reagents.

Drug screening is being pursued and negotiations with the pharmaceutical industry have been initiated to develop further one promising compound.

Planned Activities, 1990-91

The newly developed vector control tools will be tested in different ecological and epidemiological situations in Bolivia, Honduras, Paraguay, Uruguay and Venezuela.

Basic research on the molecular biology of *T. cruzi* aimed at vaccine development and identifying targets for chemotherapeutic attack will continue. Relevant defined antigens, produced by DNA recombinant technology or chemical synthesis, will be field tested for diagnosis purposes in the endemic areas. Improved diagnostic and blood screening methods using DNA probes will be evaluated in hospital settings.

Case-control epidemiological studies designed to assess possible associations between parasite subpopulations and clinical forms of the disease, will be initiated in central Brazil, Chile, Honduras and Venezuela.

TABLE 4.8 Chagas Disease (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 700.0	1 800.0	2 100.0	300.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	196.0	200.0	4.0
Total	2 137.0	2 283.0	2 600.0	317.0

4.9 LEISHMANIASES

Objectives

- Develop vaccines against cutaneous forms of the disease
- Use available drugs more efficiently
- Identify specific molecules as vaccines or drug targets or for immunodiagnostic tests
- Identify the protective immune responses in the human
- Develop tools for the control of reservoir hosts and vectors in different geographic areas

Current Activities

Combined chemotherapy (antimonials plus allopurinol) is starting as a multicentre trial in four Latin American centres; trials with antimonials plus gamma interferon will follow. A whole killed parasite vaccine is being prepared under appropriate conditions for human use.

This vaccine candidate is being tested against *L. major* infection in nonhuman primates and clinical trials in humans will follow. Several leishmanin preparations (skin test antigens, used as an aid for diagnosis and for epidemiological studies) are being prepared and will be field-tested in different foci for selection of a reference antigen(s). The direct agglutination test and a simplified dot-ELISA are being evaluated in the field.

Screening for new drugs against leishmaniasis is focused on compounds with known activity, and on drugs already in use in humans against other diseases. Topical treatment of cutaneous leishmaniasis using an ointment with paromomycin with or without methyl-benzothoniumchloride is being planned and should start soon. The vector-parasite relationship is also being studied with the aim of developing means of blocking vectorial function of sandflies e.g. with microorganisms. Several genes of *Leishmania* have been isolated and cloned for study of their roles as targets of drugs, antigens for diagnosis or vaccine candidates. Several nonhuman primate models are being developed for vaccine and drug studies. Candidate vaccines are being tested in primate models.

Planned Activities, 1990-91

The vaccine candidates selected on the basis of experimental studies will be pursued in clinical trials against cutaneous leishmaniasis. New diagnostic tests such as dot ELISA and hybridization techniques with DNA probes, will probably enter field trials, and training is envisaged during testing of these techniques and evaluating the new leishmanins. In addition, plans are being made to exchange monoclonal antibodies (produced with or without TDR support) amongst different laboratories before organizing a workshop in which those useful for diagnostic tests could be selected. Combined chemotherapy or special targeting of available drugs should reach phase II or phase III clinical trials -- especially for combinations of antimonials plus allopurinol or gamma interferon.

It is anticipated that large scale production of specific molecules will become necessary during 1990-1991, to be used as vaccines or for diagnostic tests. In addition, their evaluation in primate models and field trials will require further funds. The increase in budget is proposed to cover these activities.

TABLE 4.9 Leishmaniases (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 850.0	2 130.0	2 500.0	370.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	197.0	200.0	3.0
Total	2 287.0	2 614.0	3 000.0	386.0

4.10 IMMUNOLOGY OF LEPROSY

Objectives

- Development of vaccines and effective ways of using them
- Development of new tools for laboratory and field use in epidemiological studies
- Understand the immunopathology of the disease in order to control and prevent the reactions and nerve damage which lead to deformity

Current Activities

Two large-scale, long term immunoprophylaxis vaccine trials involving a total of approximately 150 000 study subjects are currently under way in Venezuela and Malawi. These trials will assess whether a combined vaccine consisting of BCG plus heat killed *M. leprae* gives greater antileprosy protection than BCG alone. Preliminary results from seroepidemiology studies on these two target populations are being analyzed, together with additional studies in other leprosy-endemic regions. The armadillo colonies which supply the *M. leprae* required for the production of this first generation vaccine are being maintained. The mycobacterial proteins defined by genes isolated from the WHO *M. leprae* and *M. tuberculosis* recombinant DNA expression libraries have been further characterized, including the determination of their complete sequence in many cases. These data should allow the elucidation of all the antibody-binding epitopes and T-cell stimulating determinants present in the various *M. leprae*-specific proteins under investigation, thus leading to the development of improved serological tools and skin test antigens.

The successful introduction of foreign DNA into cultivable mycobacteria has been obtained using a shuttle phasmid, representing the first step in the development of a second generation engineered vaccine. In addition, vaccinia virus recombinants expressing the genes for several *M. leprae* antigens have been produced as potential vaccine vehicles.

Planned Activities, 1990-91

The leprosy vaccine trials in Venezuela and Malawi will continue, and a third major trial in south India is contemplated in the near future. Epidemiological investigation in several endemic regions using currently available serological tests will be extended. Initial results of these investigations require further analysis and interpretation.

New immunodiagnostic tests based on synthetic peptides or recombinant proteins (to measure specific antibodies or specific skin test reactions) will be developed, in addition to DNA/RNA probes for the detection of *M. leprae* infection.

The development of a second generation of leprosy vaccines based on recombinant DNA technology will be continued; this requires further characterization of the *M. leprae* genes identified to date, their expression and scaled up production in appropriate vectors, including genetically engineered BCG, salmonella or vaccinia virus recombinants.

TABLE 4.10 Immunology of Leprosy (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	2 900.0	2 900.0	3 300.0	400.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	218.0	200.0	(18.0)
Total	3 337.0	3 405.0	3 800.0	395.0

4.11 CHEMOTHERAPY OF LEPROSY

Objectives

- ° Promote research leading to improved use of existing drugs
- ° Develop new drugs, new combinations of drugs and new approaches for monitoring chemotherapy

Current Highlights

Large-scale field trials of multidrug therapy (MDT), two each on multibacillary (MB) and paucibacillary (PB) leprosy, are under way; and three field trials of fixed duration (two year) MDT in previously untreated MB cases are being conducted. The epidemiological impact on transmission of *M. leprae* of implementation of MDT is being studied in one of the field trials.

Screening activities, especially on fluoroquinolones and other newer antibacterials are being continued. Studies on the physiology, chemical structure and metabolism of *M. leprae*, should contribute to improvements of in vitro drug screening systems, and cloning and expressing the dihydrofolate reductase (DHFR) and RNA polymerase genes of *M. leprae* in cultivable micro-organisms should improve our understanding of the target enzymes of anti-leprosy drugs.

Due to misuse, secondary resistance to rifampicin (the most important component of the current MDT regimens) has been reported and many of the strains were also resistant to dapsone. The gravity of the problem at the global level remains unclear. Surveys of secondary as well as primary rifampicin-resistant leprosy have been undertaken in selected areas. Level of primary dapsone-resistance are also being monitored in certain areas.

TDR has undertaken three "immunoreactivity" trials, designed to determine the acceptability to patients of repeated vaccinations, and to measure the efficacy of candidate vaccines, in terms of converting the skin-test response to a soluble *M. leprae* antigen. In addition, the therapeutic effects of gamma-interferon alone or in combination with chemotherapy are being evaluated in mice.

Planned Activities, 1990-91

Current activities relate particularly to the surveys of rifampicin resistance, long-term follow-up on the efficacy of MDT in MB and PB leprosy (including the evaluation of the impact of MDT on leprosy transmission) short-term clinical trials on the therapeutic effects of new combinations of drugs, drug screening and basic research on *M. leprae*, and the studies on the mechanisms of leprosy reactions and nerve damage.

New initiatives in the 1990-1991 biennium will include the use of nude mice for experimental chemotherapy and the neonatally thymectomized rat in controlled clinical trials to evaluate the possible additional therapeutic effects of adding ofloxacin to the MDT regimen for MB leprosy.

In order to obtain large amounts of *M. leprae*-derived gyrase to develop an *in vitro* system for screening new fluoroquinolones against *M. leprae*, the *M. leprae* gene encoding the gyrase will be cloned and expressed in cultivable micro-organisms. Research into the development of *in vitro* systems for viability testing, drug screening and drug susceptibility testing based on new biotechnology will be promoted. Operational research on implementation of WHO/MDT through primary health care is necessary.

TABLE 4.11 Chemotherapy of Leprosy (US\$000)

Budget Item	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 450.0	1 800.0	2 300.0	500.0
Personnel Services	287.0	287.0	300.0	13.0
Operational Support	150.0	194.0	200.0	6.0
Total	1 887.0	2 281.0	2 800.0	519.0

4.12 BIOLOGICAL CONTROL OF VECTORS

Objective

- Identify and develop natural biological regulators of vectors, such as pathogens and parasites, toxin-producing organisms, and vertebrate and invertebrate predators suitable for control of vectors of the six target disease groups

Current Highlights

Several biological agents with vector control potential are now used in disease control programmes: *Bacillus thuringiensis H-14*, *B. sphaericus* and different species of fish. *B. thuringiensis H-14* is now increasingly used against blackflies in West Africa, against

mosquito vectors in China, and USSR, and against nuisance mosquitos in the USA, Canada and some European countries. Testing of commercial samples of *B. sphaericus* has also shown good results against *Culex* and some *Anopheles* and *Mansonia* species. They are capable of recycling, even in heavily polluted water, to provide effective mosquito control to ten weeks under certain conditions. Large scale operational use of *B. sphaericus* has begun for controlling vectors of filariasis and malaria in Cameroon and Thailand.

Studies on toxin production, genetic coding and mode of toxin action confirmed the possibility of producing more potent larvicidal bacterial agents by genetic engineering methods. Insecticidal genes were transferred and expressed into blue-green algae which might be a food source for mosquito larvae. Ecological studies of fresh water habitats provide basic data for understanding the larval food sources leading to improved candidates formulations for vector control. In addition, some larval food sources may be candidates for genetic transformation to express insecticidal genes.

Methods of *B. thuringiensis H-14* fermentation, using media from locally available materials have been developed in tropical countries and their efficacy has been evaluated in several vector control programmes.

Planned Activities, 1990-91

Further research will be concerned with development and operational evaluation of promising control agents in large scale field trials. Biological agents accorded high priority for future development include asporogenic bacillus mutants, indigenous larvivoracious fish, nematodes and long-acting formulations of *B. thuringiensis H-14*, *B. sphaericus* and *Lagenidium giganteum*. Field trials of new agents will be conducted in different parts of the world in an attempt to study as many vector species in as wide a range of environmental conditions as possible.

New biotechnology methods will be used to improve the properties of existing biocontrol agents, to create new ones, as well as to increase toxin production and enhance the residual activity of larvicidal pathogens.

The search for new pathogens and parasites suitable for vector control will be intensified in tropical endemic countries through the network of collaborating laboratories. Biological control agents included in integrated disease control programmes will be evaluated from an epidemiological standpoint in collaborative research involving disease-specific TDR components. Additional funds are requested to cover activity on large scale operational use of *B. sphaericus* in endemic areas as well as an increase in research in the field of biotechnology and genetic engineering.

TABLE 4.12 Biological Control of Vectors (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 550.0	1 550.0	1 800.0	250.0
Personnel Services	574.0	574.0	300.0	(274.0)
Operational Support	150.0	157.0	200.0	43.0
Total	2 274.0	2 281.0	2 300.0	19.0

4.13 SOCIAL AND ECONOMIC RESEARCH

Objectives

- ° Increase the effectiveness of disease control programmes by integrating human behavioural factors into programme design and management
- ° Determine the impact of social, cultural, demographic and economic conditions on tropical disease transmission and control
- ° Promote the design and use of cost-effective, acceptable disease control measures and policies

Current Highlights

Projects focus on human behaviour in relation to the epidemiology of tropical diseases and their control; on the development of interdisciplinary approaches for the evaluation of biomedical and social interventions for disease control and on social and economic studies of alternative disease control measures and policies. Current research includes applied studies of the social and behavioural aspects of disease transmission and control, intervention research, studies of the economics of tropical disease control, methodological development and training. Social and economic issues and methods are also important components of TDR's field research networks and the development of social science methods for application to interdisciplinary studies is an increasingly urgent priority. Another current activity of the Component is the promotion of social and economic research on tropical diseases among scientists working on related problems. This is done through the dissemination of information through a Social Sciences and Tropical Disease Network in Latin America, as well as a new Social and Economic Research Project Reports series to disseminate the results of research projects.

Planned Activities, 1990-91

Further research will be concerned with social factors affecting patient compliance with respect to specific disease control measures; the reliability of community perceptions of disease prevalence for targeting control activities; intervention studies to evaluate the costs, effectiveness and acceptability of different tools for the control of selected diseases; research on resource allocation to tropical diseases and on the economic impact of development projects in relation to disease transmission and control; studies of health policies as applied to tropical diseases, in close collaboration with disease control programmes; the development and assessment of methodologies, particularly with respect to interdisciplinary research; and with the continued promotion of social and economic research on tropical diseases.

TABLE 4.13 Social and Economic Research (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
Operations	1 500.0	1 275.0	1 650.0	375.0
Personnel Services	287.0	384.3	500.5	116.2
Operational Support	250.0	454.0	375.0	(79.0)
Total	2 037.0	2 113.3	2 525.5	412.2

5. PROGRAMME AREA III: RESEARCH CAPABILITY STRENGTHENING

Objectives

- Strengthening institutions in endemic developing countries to carry out the necessary research and research training activities required to control and prevent the TDR target diseases

Current Activities

Institution Strengthening

Following the in-depth review of the Research Capability Strengthening (RCS) by the Scientific and Technical Advisory Committee during 1986-87 and the re-organization within the Programme during 1987, several new initiatives were introduced to accelerate scientific development of institutions and research workers in disease endemic countries.

Experience within the Programme has shown that linkages with research groups in the developed world have a salutary effect on the development of institutions in disease endemic countries. With this in view, a joint funding venture was initiated with the Rockefeller Foundation (RF), USA, aimed at promoting laboratory, clinical and field research on the six target diseases of TDR in countries where the diseases are endemic.

Partner institutions, at least one of which must be located in an endemic country, were invited to submit proposals to this venture. After a two-step selection process twelve partnerships have been funded: partner institutions in the disease endemic countries are funded by TDR and those in the developed countries by the Rockefeller Foundation. A meeting of all principal investigators is planned for December 1989. This occasion will be used to present the research and institution strengthening activities carried out by them, and to resolve any problems hindering the smooth operation of partnerships.

Up to the end of 1988, TDR had funded 143 institution strengthening grants including 18 grants to institutions involved in the joint TDR-RF venture. Of the 58 long-term grants awarded so far, 36 had completed their five year support by the end of 1988. The impact of these long-term grants on the building of research capacities in different institutions has been quite variable. Institutions with strong leadership and a core of well-trained research workers, and which were able to generate national support, generally benefitted most from these grants.

Some of the institutions which had received strengthening grants needed further support focused on clearly defined objectives in order to become competitive for securing research funds. With this in view a new type of programme-based grant has been established to assist institutions and research groups to carry out high quality research focused on small number of scientific problems relevant to the control of one or more TDR target diseases. Letters of intent were invited, reviewed in November 1988, and those selected were invited to submit detailed proposals for consideration by the Research Strengthening Group at its meeting in June 1989. It is planned to fund about 12-15 such grants during 1989-90.

In addition to the programme-based grant mechanism, two other new initiatives have been introduced during the biennium. These are the development of field research networks and TDR's initiative for biotechnology. Details of the field research networks are given below in the section on Epidemiology and Field Research; the initiative for biotechnology is designed

to effect a transfer of technology for producing biological reagents for disease diagnosis and for use in epidemiological studies related to disease transmission and vector control. Site visits have been carried out to a number of biotechnology oriented research centres in endemic countries, including those which have received TDR research strengthening grants, to assess their potential and interest in participating in this venture. A limited number of these institutions are being asked to submit detailed proposals, including links with a suitable institution in the developed world to facilitate transfer of required expertise and to provide opportunities for specialized training.

Research Training

Research training and visiting scientist grants, which were previously largely restricted to staff members of institutions receiving research strengthening grants, are now also available to scientists from other institutions involved in research on TDR target diseases. Provision for research training will increasingly be made with institution strengthening grants, particularly within programme-based and TDR-RF grants. Therefore the funds for this budget line have been kept at the same level in the coming biennium.

Up to December 1988, the Programme has sponsored 615 research training grants (RTGs), 57 visiting scientists grants (VSGs) and nearly 108 re-entry grants. By the end of the current biennium 60% of the TDR trainees will be back in their respective institutions on completion of their training. A study on the impact of the RTGs and the VSGs on research capacity building is planned for 1989.

During 1988, a detailed evaluation was carried out of seven TDR-supported master's degree (MSc) courses in medical entomology and four in epidemiology. This evaluation highlighted the difficulties in organizing such courses under the conditions prevailing in most endemic countries, and revealed the strengths and weaknesses of the individual courses. It was clear that these courses have helped meet an important need for training entomologists for research and disease control activities. Professionals with this expertise are in short supply in endemic countries. The evaluation found that MSc courses with the most successful outcomes were those with an on-going institutional field research project with participation by most of the faculty. For the future it has been decided that instead of supporting additional MSc courses directly, institution strengthening mechanisms will be used to develop basic capacities for research and training.

Planned Activities

During the coming biennium, emphasis will be placed on consolidating current activities such as the TDR-RF venture, programme-based grants and field research networks. Particular attention will be devoted to establishing pragmatic mechanisms for monitoring the various research strengthening grants and for ensuring the development of human resources within the context of these grants. It is anticipated that a second round of proposals will be invited and funded under the joint TDR-RF venture.

In disease endemic countries where one or more institutions have already been strengthened and a cadre of research workers trained with TDR support, efforts should be made to strengthen their links with research workers sponsored by other components of the Programme. Further efforts to promote and develop TDR collaborative activities will be focused in those endemic countries where there has been little or no TDR input so far. In this respect, TDR will adopt differentiated approaches which take into account the needs and capacities of countries. In those countries where there may not be a viable institutional structure for strengthening or realistic opportunities for sustainability, research capacity will be built up through training of potential research workers, initially within their countries through participation

in active research projects. The focus of research projects in these countries will be research directly related to disease control activities. TDR sponsored research and development projects involving endemic countries will be increasingly utilized for training young scientists from these countries. As research capacities improve, it is anticipated that opportunities for research training at an advanced level will also become available in some of these countries.

The information system for monitoring of RCS activities within TDR will be upgraded, as a result of new information requirements following increased involvement of disease-specific Steering Committees in RCS related activities and the establishment of the new initiatives mentioned above.

TABLE 5 Programme Area III: Research Capability Strengthening

<i>Component/Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
<i>General Activities</i>				
Personnel Services	1 037.0	1 134.3	1 435.2	300.9
Temporary Assistance	50.0	95.1	100.0	4.9
Operational Support	450.0	600.0	700.0	100.0
Publications	20.0	20.0	20.0	0.0
Subtotal	1 557.0	1 849.4	2 255.2	405.8
<i>Operations</i>				
Institution Strengthening	5 850.0	7 300.0	8 300.0	1 000.0
Training	6 700.0	5 700.0	5 700.0	0.0
Subtotal	12 550.0	13 000.0	14 000.0	1 000.0
<i>Epidemiology and Field Research Support (Table 5.1)</i>				
Subtotal	734.0	816.1	2 650.0	1 833.9
<i>Total</i>	14 841.0	15 665.5	18 905.2	3 239.7

5.1 EPIDEMIOLOGY AND FIELD RESEARCH SUPPORT

Objectives

- Promote field research within TDR, particularly related to field trials of new intervention tools
- Establish field research networks as mechanisms for training in project formulations and design, methodologies and techniques of field research, and as a means to encourage project-to-project linkages to reduce isolation of investigators
- Encourage and provide resources for training in epidemiology, entomology, economics and social sciences for individuals who will conduct field research on intervention strategies and implement control strategies

Current Highlights

The increasing need for field evaluation of new tools in a defined epidemiological context has resulted in an increase in the number and quality of field projects funded by the disease-specific components of TDR. Recognition of the importance of well-designed multi-disciplinary studies incorporating appropriate epidemiological, social science and, where applicable, entomological methods, has led to the creation of the Epidemiology and Field Research Support Component within the Research Capability Strengthening area. The new group is composed of the staff of the former Epidemiology Component, an entomologist and secretary from Biological Control of Vectors Component. The group works closely with the Social and Economic Research Component. The group has structured workshops organized under the auspices of disease-specific components to develop outline protocols for field studies to address high priority topics not currently being addressed by TDR-sponsored research. Multi-disease workshops are also being conducted in which training in planning and protocol development is provided for investigators who have indicated an interest in conducting multi-disciplinary studies.

Planned Activities, 1990-91

The major new initiative is to establish multi-disciplinary field research networks to provide support for field-based investigators. To highlight the objectives of this networking the programme will be called **Field Links for Intervention and Control Studies (FIELDLINCS)**. This programme will facilitate interchange among field researchers; strengthen their capacity for multi-disciplinary research; provide regular workshops on protocol development, project management, standardization issues, data analysis, and/or specific field research methods; support for short term training courses; serve as a focus for multi-centre trials; foster links between field researchers and national disease control programmes; and link those in endemic areas with their colleagues in technically advanced countries in order to contribute to the transfer of skills to endemic areas.

Operational support in the form of equipment or services will be provided to organizations or institutions selected on a competitive basis to serve as resource centres for regional or national networks. The development of an international data base of current field research projects funded by TDR and other donor organizations will complement the FIELDLINCS Programme.

The Epidemiology and Field Research Support Component, in close coordination with the SER Component, will continue to maintain a regular overview of field research throughout the Programme and will participate in the development and assessment of field research plans of other Components. It will also develop methods and specific protocols for epidemiological studies. A particularly important area will be operational research carried out by or with national disease control programmes in relation to the development of new intervention strategies.

TABLE 5.1 Epidemiology and Field Research Support (US\$000)

<i>Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (4)
Operations	0.0	0.0	1 500.0	1 500.0
Personnel Services	484.0	529.1	900.0	370.9
Operational Support	250.0	287.0	250.0	(37.0)
Total	734.0	816.1	2 650.4	1 833.9

6. PROGRAMME AREA IV: PROGRAMME MANAGEMENT

Objectives

- Provide direction, guidance and supervision of all Programme activities
- Support the TDR technical and administrative bodies (JCB, STAC and Standing Committee)
- Provide supporting facilities and services for Programme activities and operations carried out by Research and Development Components (Programme Area II) and Research Capability strengthening (Programme Area III)

Current Highlights

Responsibility for the overall direction, coordination and supervision of the Programme Secretariat rests with the Programme Director, assisted by a small support staff. Programme Management includes external relations, financial, personnel, procurement and administrative services and management information.

External relations activities are the meetings of TDR's technical and administrative bodies and relations with international organizations, governments, non-governmental organizations, foundations and industries collaboration with the Special Programme. Since TDR is dependent on voluntary contributions for most of its income, major emphasis is placed on fund-raising and relations with contributors. Major activities include the provision of information to contributors and potential contributors, periodic visits by the Programme Director and senior Programme staff. During 1987-89, the JCB Ad Hoc Committee on TDR's Financial Prospects reviewed in detail TDR's fund-raising and public relations activities and recommended a number of improvements and innovations in these areas.

The Programme's communications activities include both scientific and technical publications directed primarily to scientific audiences, and more general information about tropical diseases and TDR's activities aimed at the general public and those interested in TDR in governments, organizations, foundations and industry.

TDR's computerized management information system provides information on a wide range of Programme activities, especially related to research proposals submitted to TDR and funded by the Programme. Recent activities have emphasized the expansion of office automation through the introduction of microcomputers for both professional and support staff, and the linkage of management information data with project management microcomputer applications.

Planned Activities 1990-91

During the forthcoming biennium, Programme Management will continue to implement recommendations of the Second External Review Committee, which reported to the JCB in June 1988, and the recommendations of the JCB Ad Hoc Committee on TDR's Financial Prospects. Improvements will be made in fund-raising and public relations, and emphasis will be placed on the provision of relevant and timely information to current and potential contributors, and on making tropical diseases and the role of the Special Programme better known among the general public in contributory countries. Regular contact will be made with media representatives, especially those interested in health matters. The Programme will produce attractive and easily understood publications for general audiences and will make increasing use of audio-visual media.

Budget provisions cover personnel requirements of the Office of the Programme Director, Programme Management, and information and communications, as well as TDR personnel located in the WHO Regional Offices for Africa, the Americas, Eastern Mediterranean, Southeast Asia and Western Pacific. No increased staff is envisaged for Programme Area IV; the increase in Personnel Services relates to a transfer of existing staff (see section 7). Following the major investment in microcomputer technology in 1988-89, a decrease in the provision for equipment and development is proposed, since major emphasis will be placed on full utilization of existing equipment, including the development of effective microcomputer applications using in-house resources. For the reasons explained in section 2, Geneva-based costs under General Support, including premises, postage and telecommunications and other common services, continue to increase substantially.

TABLE 6 Programme Area IV: Programme Management

<i>Component/Budget Item</i>	1988-89		1990-91	
	Approved Budget (1)	Revised Budget (2)	Proposed Budget (3)	Increase (Decrease) (3)-(2)
<i>Personnel</i>				
Personnel Services	2 760.0	2 760.0	2 976.2	216.2
Temporary Assistance	200.0	342.4	350.0	7.6
Consultants/Temporary Advisors	50.0	50.0	80.0	30.0
Overtime	25.0	25.0	50.0	25.0
Subtotal - Personnel	3 035.0	3 177.4	3 456.2	278.8
<i>Operational Support</i>				
Informations Systems - Equipment & Development	250.0	250.0	200.0	(50.0)
Services & Maintenance	200.0	200.0	200.0	0.0
Public Information	50.0	100.0	100.0	0.0
Duty Travel	80.0	80.0	100.0	20.0
Office Supplies & Equipment	50.0	50.0	50.0	0.0
Audit Fees	20.0	20.0	50.0	30.0
Subtotal - Operational Support	650.0	700.0	700.0	0.0
<i>General Support</i>				
Administrative Support Costs	689.0	689.0	738.0	49.0
Common Services & Premises	1 160.0	1 160.0	-	(1 160.0)
Premises	-	-	700.0	700.0
Postage and Telecommunications	-	-	300.0	300.0
Other Common Services	-	-	400.0	400.0
Subtotal - General Support	1 849.0	1 849.0	2 138.0	289.0
<i>Regional Offices</i>				
Personnel Services	913.0	913.0	1 002.3	89.3
Duty Travel	40.0	40.0	50.0	10.0
Subtotal - Regional Offices	953.0	953.0	1 052.3	99.3
<i>Total</i>	6 487.0	6 679.4	7 346.5	667.1

7. PERSONNEL REQUIREMENTS

In June 1988 the Standing Committee and the Programme Secretariat proposed the establishment of seven posts, effective 1 January 1989, to meet increased workload requirements in several areas: research capability strengthening, social and economic research, epidemiology and communications. The Joint Coordinating Board approved the establishment of two Professional posts, one for research capability strengthening and one for social and economic research, and one General Service post for epidemiology. The Board also agreed to reconsider proposals for the establishment of additional posts in research capability strengthening, social and economic research and communications following an analysis of future TDR staff needs to be presented to JCB(12) together with the Proposed Programme Budget for the 1990-91 Biennium. In addition, the Board noted that the proposals to be presented to JCB(12) would show a higher proportion of General Service posts.

In the light of the analysis of future staff needs (document TDR/JCB(12)89.8), the Proposed Programme Budget for 1990-91 recommends the establishment of two new General Service posts, both in Research Capability Strengthening (Programme Area III).

Staff years approved for the 1988-89 biennium totaled 156 (including staff years for the three posts approved in June 1988). Proposed staff years for the 1990-91 biennium total 162, an increase of 6 staff years over 1988-89 (Table 7.1).

TABLE 7.1 Summary of Programme Personnel Requirements

<i>Programme Area</i>	Personnel Requirements in Staff Years			
	1988-89 Approved		1990-91 Proposed	
	P	GS	P	GS
I Technical and Administrative Bodies	-	-	-	-
II Research and Development	29	30	28	28
III Research Capability Strengthening	11.5	11.5	14	18
IV Programme Management	18	24	18	24
Regional Offices	10	10	10	10
Administrative Support Services	-	12	-	12
Total	68.5	87.5	70	92
Total Staff Years	156		162	

The Proposed Programme Budget reflects three types of changes in personnel requirements from the Budget for the 1988-89 Biennium:

- Three new posts approved by JCB(11) in June 1988 for establishment from 1 January 1989. In the tables, the staff for these posts are included in the approved staff years for 1988-89 and in the proposed staff years for 1990-91.
- Redeployment or reassignments of existing posts and staff with no increase in the number of posts or staff years.
- The two additional posts proposed for establishment from 1 January 1990.

The following sections describe briefly changes in personnel for each Programme Area.

Programme Area II: Research and Development (Table 7.2)

- One Professional (P) post (two staff years) and one GS post (two staff years) have been transferred from *Biological Control of Vectors* to *Epidemiology and Field Research Support* (PA III).
- One P post (two staff years in 1990-91) has been added to *Social and Economic Research* from 1 January 1989 in accordance with the decision of JCB(11) approving a second professional post for SER.

Programme Area III: Research Capability Strengthening (Table 7.3)

- Two posts approved by JCB(11) for establishment from 1 January 1989 are included the 1988-89 Approved Staff Years and the 1990-91 Proposed Staff Years: one Medical Officer/Scientist P post (two staff years) for *Research Capability Strengthening*; and one GS post (two staff years) for *Epidemiology and Field Research Support*.
- Two additional secretarial/clerical GS posts (four staff years) are proposed for Research Capability Strengthening (further details and explanation are provided in document TDR/JCB(12)/89.8).

Programme Area IV: Programme Management (Table 7.4)

- There are no changes in the staff requirements of Programme Area IV.

TABLE 7.2 Personnel Requirements, Programme Area II: Research and Development

<i>Component</i>	Personnel Requirements in Staff Years			
	1988-89 Approved		1990-91 Proposed	
	P	GS	P	GS
General Activities	-	4	-	4
Chemotherapy of Malaria	4	2	4	2
Immunology of Malaria	2	2	2	2
Applied Field Research in Malaria	2	2	2	2
Schistosomiasis	2	2	2	2
Filariasis	2	2	2	2
African Trypanosomiases	2	2	2	2
Chagas Disease	2	2	2	2
Leishmaniases	2	2	2	2
Immunology of Leprosy	2	2	2	2
Chemotherapy of Leprosy	2	2	2	2
Biological Control of Vectors	4	4	2	2
Social and Economic Research	3	2	4	2
Total	29	30	28	28

TABLE 7.3 Personnel Requirements, Programme Area III: Research Capability Strengthening

<i>Component</i>	Personnel Requirements in Staff Years			
	1988-89 Approved		1990-91 Proposed	
	P	GS	P	GS
<i>Research Capability Strengthening</i>				
Responsible Officer	2	-	2	-
Medical Officer/Scientist	3.5	-	4	-
Technical Officer	2	-	2	-
Secretarial Staff	-	8.5	-	12
<i>Epidemiology and Field Research Support</i>				
Medical Officer/Scientist	4	-	6	-
Secretarial Staff	-	3	-	6
Total	11.5	11.5	14	18

TABLE 7.4 Personnel Requirements, Programme Area IV: Programme Management

<i>Component</i>	Personnel Requirements in Staff Years			
	1988-89 Approved		1990-91 Proposed	
	P	GS	P	GS
<i>Office of the Programme</i>				
<i>Director</i>				
Programme Director	2	-	2	-
Secretarial Staff	-	4	-	4
<i>Programme Management</i>				
Responsible Officer	2	-	2	-
External Relations Officer	2	-	2	-
Secretarial Staff	-	4	-	4
<i>Communications</i>				
Communications Officer	2	-	2	-
Editors	4	-	4	-
Secretarial Staff	-	4	-	4
<i>Information Systems</i>				
Management Officer (Information)	2	-	2	-
Programmer/Analyst	2	-	2	-
Clerk/Coder	-	4	-	4
Secretarial Staff	-	2	-	2
<i>Operations and Finance</i>				
Management Officer (Finance)	2	-	2	-
Technical Assistant	-	4	-	4
Secretarial Staff	-	2	-	2
Subtotal	18	24	18	24
<i>Regional Offices</i> (One Medical Officer and one Secretary at AFRO, AMRO, EMRO, SEARO and WPRO)				
	10	10	10	10
<i>Administrative Support Services</i>				
	-	12	-	12
Total	28	46	28	46