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RESEARCH AND TRAINING IN TROPICAL DISEASES (TDR)



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INTRODUCTION TO THE REPORT OF THE TENTH MEETING
OF THE SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-10)

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During its tenth meeting held from 29 February to 3 March 1988, the Scientific and Technical Advisory Committee (STAC) addressed the following items:

- Transfer to National Health Services of Technology Developed with TDR Support
- Scientific Progress in 1987-1988
- New Approaches to Research Capability Strengthening
- TDR Project Funding in Developing Endemic Countries
- New Approaches to Field Research and a New Initiative for the Implementation of Biotechnology
- In-depth Reviews of the Leprosy, Malaria and Social and Economic Research Components
- Second External Review and Evaluation of TDR
- Mode of Operation of STAC
- Programme Budget

In submitting the report of STAC-10 to the Joint Coordinating Board, I would like to draw special attention to the following findings, considerations and developments regarding the Special Programme.

Dr H. Mahler, Director-General of WHO, in his opening address to STAC-10, noted that the Programme's main objectives were the development of new tools and the strengthening of research capability in tropical countries to improve the control of tropical diseases. The Programme has kept these aims in focus and has responded appropriately to changing circumstances such as population movements which expose people to new disease risks. Dr Mahler briefly traced the history of TDR. In its first five years, the tasks were defined and projects started. During the second quinquennium, TDR functioned as a promoter of highly innovative research and now, as the Programme enters its second decade, there is increasing emphasis on field-testing of new products and transfer of technology which require community involvement as well as strong ties with national disease control programmes.

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Transfer to National Health Services of Technology Development with TDR Support

Examples of the successful transfer of technology developed with TDR support were presented in a symposium of lectures by four eminent experts.

Multidrug therapy for the treatment of leprosy is or has been successfully administered to 2.1 million patients in 88 countries and in several instances a substantial decline in the prevalence of the disease is evident.

The operational introduction of mefloquine in combination with sulfadoxine/pyrimethamine to combat chloroquine-resistant falciparum malaria and prevent appearance of mefloquine-resistant parasites in Thailand has involved 300 000 patients. Side effects possibly related to sulfadoxine treatment are now being monitored on a large scale.

The microfilaricide ivermectin, which by a single-dose treatment effectively keeps onchocerciasis patients free from microfilaria over a 12 month period, was first tested in 1981. The drug is now approved for treatment of onchocerciasis. By the time the drug is released for more general use in endemic areas within the next year, between 80 000 and 140 000 patients will have been treated in trials. The discoverer and manufacturer of ivermectin, Merck & Co., Inc., has indicated that it will supply ivermectin free of charge for use in onchocerciasis control programmes.

The use of Bacillus thuringiensis H-14 as an effective insecticide in the Onchocerciasis Control Programme in West Africa since 1980 was also presented. Improved formulations are needed if this insecticide is to be used at reasonable cost.

The symposium illustrated the importance of the commitment of national governments and/or their agencies for the deployment of the tools developed by TDR.

STAC was highly appreciative of the position paper provided by the Director of the Special Programme on the policy to be followed by TDR in the transfer of technology developed with its support to national health services. In general, TDR should be responsible for research and development of new tools up to and including the stage of field-testing in the intended setting of use, after which national governments, with assistance of WHO technical programmes, should take over. The smooth transfer of technology should be worked out on a case-by-case basis by establishing suitable links with appropriate national agencies.

Scientific Progress in 1987-1988

The scientific progress was highlighted in the Director's report and included details on increased understanding of the biochemistry of parasite-host relationships, important advances in the development of malaria and leprosy vaccines, dramatic increases in the sensitivity of diagnostics with the aid of recombinant DNA technology, and improvements in vector control. STAC commended Director TDR for the further excellent progress achieved by the Programme.

New Approaches to Research Capability Strengthening

With the new booklet Tropical Disease Research. A Global Partnership at Work: New Approaches to Research Capability Strengthening, TDR presents the mechanisms by which the Research Strengthening Group (RSG) will operate in the strengthening of research institutions and in the development of human resources in developing countries. STAC sees this new approach as a successful beginning in the strongly recommended integration of TDR's research capability strengthening and research and development activities. STAC found especially relevant the establishment of the new programme-based grants to help institutions in developing countries to carry out high-quality research focused on clearly defined objectives related to one or more of the TDR target diseases. These

grants will also allow the establishment of central facilities for services such as monoclonal antibody production or social and economic research activities. Equally welcomed by STAC were the Joint TDR-Rockefeller Foundation grants, and the career development grants to provide support to outstanding investigators who might be prevented from continuing their work by the harsh conditions prevailing in many developing countries.

TDR Project Funding in Developing Endemic Countries

The decline in TDR project funding in developing endemic countries noted for 1986 and 1987 had been analyzed by Director TDR. It appeared to be due partly to decreased promotional activities during the period 1981 to 1985 and a consequent decline in grant applications. STAC was satisfied with the initiatives being taken to increase TDR's scientific activities in developing countries, in particular the introduction of project development grants to encourage developing country researchers to submit project proposals to TDR.

New Approaches to Field Research

STAC was impressed by the top priority initiatives to carry out on-the-spot development of study designs and protocols in field projects as an important part of training and an invaluable way of building research capability in field research within developing endemic countries.

In-depth Reviews of the Leprosy, Malaria and Social and Economic Research Components

The in-depth reviews of the Leprosy, Malaria and Social and Economic Research Components were accepted by STAC and led to a series of recommendations.

There are still 10-12 million cases of leprosy in the world, one third of which progress to an advanced, disabling state of the disease. STAC recommended that high priority should be given to close collaboration between immunology and chemotherapy projects, not only in molecular biological approaches but all field projects as well. The excellently conceived vaccine trials now underway need monitoring for another decade but at the same time contingency plans for different outcomes must be made in relation to the availability of vaccines, target group identification and second-generation vaccines. Provision of *M. leprae* for research, development of sensitive methods of identifying leprosy bacilli in patients, and development of new antileprosy drugs are important research targets, while field trials in leprosy constitute unique opportunities for training.

STAC was acutely aware of the global malaria situation with increased incidence of the disease in some areas and with more than 2500 million persons at risk of infection. Development of resistance of the vectors to insecticides and of the parasites to drugs continue to cause serious handicaps in the fight against the disease. Important results and impressive progress were reported during the in-depth review on malaria. Major recommendations by STAC concern the maintenance of three clinical trial centres in Africa, Asia and South America, early Phase II clinical trials of new promising artemisinin derivatives, and development of trioxane-based drugs. Epidemiological assessment of serological and cell-mediated immune responses and selection of vaccine candidates among the newly characterized blood-stage molecules of the parasite are important research targets. Early notice by the Steering Committees to STAC of planned clinical trials of new drugs and vaccines is necessary for the appropriation of funds. Molecular and biochemical studies of the *Plasmodium* parasite and of host cells provide encouragement that several avenues for vaccine development will be viable if due consideration is given to the diversified antigenic variability of the individual molecules.

The social and economic research disciplines relevant to TDR include sociology, anthropology, geography, economics, psychology and political science. Knowledge, attitudes and beliefs of target populations must be taken into account when introducing new vaccines, drugs or other disease control measures. The Social and Economic Research (SER) Component has mounted 67 research projects in 25 countries over the past nine years, which above all elucidated the complexity and the utility of applying social and economic research to the improvement of disease control. Given the limited resources of TDR, STAC recommended that a member of the SER Steering Committee be involved with each of the disease-oriented Steering Committees in order to pose at the earliest appropriate stage of research and development the relevant social and economic questions. Training in ongoing field research projects in the disciplines mentioned above is considered most appropriate. The extension of SER responsibilities will require strengthening of the Secretariat and a substantial budget increase.

Second External Review and Evaluation of TDR

The second external review and evaluation of TDR has been conducted by a seven-member External Review Committee (ERC). STAC discussed the findings of the Committee with its Chairman Dr E. Otero, its Vice-Chairman Professor H. Danielsson and the Executive Secretary Dr R. Widdus.

It is easy for STAC to concur with many, if not all, of the conclusions and recommendations given in the report, which is most comprehensive and gives a strong endorsement of the basic strategies of TDR.

According to the report, TDR "has fulfilled its mission laudably by identifying rational objectives and pursuing them through appropriate, well-managed mechanisms. It is now a central and indispensable feature of global research and development efforts to find new and better tools for tropical disease control".

STAC noted the ERC's conclusion that TDR has an impressive record of accomplishments in research and training and in promoting and speeding the development of products for disease control.

STAC noted that many ERC recommendations regarding field studies, social and economic research, research capability strengthening and linkages of other research and development efforts with these activities were already being implemented.

STAC made the following recommendations:

- a) As recommended by the ERC, the diseases falling within TDR's mandate should continue to be only the six target diseases, and the situation with regard to the hazards of these tropical diseases fully justifies the continuation of the Programme for at least another decade.
- b) Continued efforts should be made to link research and development activities with social and economic research and with research capability strengthening. Such links are now the key to the success of the Programme and will provide the basis for long-term tropical disease control. STAC, on the other hand, will monitor the expansion of social and economic research and the linkage with research capability strengthening to ensure that the scientific quality of the research effort in developing new tools for combating the diseases is not jeopardized.
- c) TDR staffing requirements would need to be considered within the context of the global and goal-oriented nature of the Programme's activities, with attention being given to demands on the number and expertise of the staff. In this connection STAC noted that Director TDR had already streamlined the management and reorganized the staff to adapt to the new situation.

- d) With regard to the expansion of SER activities, a scientist with expertise in health economics should be appointed.
- e) Because of the role of Scientific Working Groups (SWGs) in coordinating activities within a disease-specific Component and with WHO disease control activities, there should be only one SWG for each disease-specific Component, i.e. one SWG might relate to several Steering Committees.
- f) With regard to the ERC's detailed suggestions on Steering Committee review procedures for incoming proposals, existing procedures had evolved under the close scrutiny of STAC and continued to meet requirements effectively. Some flexibility was needed, however, in special situations and was indeed essential in dealing with proposals submitted by scientists inexperienced in the preparation of formal research proposals.
- g) STAC supported the ERC's proposal to expand the Director's Initiative Fund from US\$ 262 000 to US\$ 1 million per year and agreed that limits should not be set for the amount which could be granted from this fund for start-up activities or increases of a Component's budget.

Mode of Operation of STAC

STAC examined in detail its procedures for review of Programme Components and resolved that greater efficiency of this process was now needed.

STAC therefore decided that in order to increase the effectiveness of STAC's biennial review of all Components, in 1988 each STAC member will attend the meetings of one of the Steering Committees or of the Research Strengthening Group and will prepare a report for STAC-11 on the activities of the assigned Committee or Group.

The Filariasis and Schistosomiasis Components will submit their five-yearly reports on their activities to STAC-11. After reviewing these reports, STAC will decide whether an in-depth review by a Scientific and Technical Review Committee (STRC) is necessary in each case and, more generally, whether to continue this modified five-yearly review process.

In order to enhance the scientific direction given by STAC to the Programme, STAC introduced "Prospective Thematic Reviews" (PTRs). Their purpose would be to examine problems and new scientific advances relevant to a number of Programme Components. Ad hoc committees to conduct these reviews will be chaired by members of STAC and include international experts.

In 1989, a PTR on "New Directions in Research on Methods for the Control of Vectors", chaired by Professor J. Duarte de Araujo, and another on "New Directions in Drug Development", chaired by Professor A. Cerami, will take place.

Programme Budget

STAC noted with great satisfaction the improvement of TDR's finances which would allow the implementation of the scientific and technical programme as recommended by STAC-9 to JCB in 1987 for the 1988-1989 biennium. STAC noted with pleasure that the JCB had established an ad hoc committee to review TDR's financial prospects and requirements. STAC supported the recommendation of the External Review Committee that TDR's budget should increase by at least 25% over the next five years. There are excellent opportunities to do more for research and training in tropical diseases and STAC will be happy to support, in whatever manner is deemed appropriate, the fundraising activities of TDR.