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Strategic Plan

for

Applied Field Research in Tropical Diseases

Developed during a Planning Meeting on Applied Field Research in Tropical Diseases held from 26-28 May 1993 in Geneva

UNDP/World Bank/WHO Special Programme for Research and Training for Tropical Diseases

and

Division for Control of Tropical Diseases
World Health Organization

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1. THE NEED FOR APPLIED FIELD RESEARCH

The tropical diseases remain a major global problem. More than half the world population is at risk, half a billion are infected with at least one of these diseases, and millions die annually or are affected by severe disability. For most tropical diseases the epidemiological situation is expected to worsen during the next decade unless major new efforts for research and control are undertaken. Fortunately, there are examples to show that the development of new control tools and strategies through research, combined with concerted national and international efforts for control, can greatly reduce the burden of tropical diseases. Good examples of this can be found for leprosy, onchocerciasis, sleeping sickness and Chagas disease.

The World Health Organization plays an important role in the area of tropical diseases control and research through its Division of Control of Tropical Diseases (CTD) and the Special Programme for Research and Training for Tropical Diseases (TDR).

The mandate of CTD is to prevent and control major parasitic infections of global, regional or national public health importance. In collaboration with the Ministries of Health of the endemic countries, national programmes are supported by technical advice, regional or national training activities and assistance in preparation of requests for NGO, bilateral and multilateral support of control activities including operational research to resolve site-specific problems in control.

The objectives of TDR are to develop new and improved methods for the control of tropical diseases, and to strengthen the relevant research capacity in disease endemic countries. During the first 14 years of its existence, the Special Programme has been highly successful. Its research has resulted in the development of many new tools for use in tropical disease control, some of which have enabled significant improvements in control.

It is becoming increasingly clear, however, that the introduction of a new tool does not automatically lead to improved control. Several new tools, as well as old ones, are under-utilized and have limited impact on the target diseases. The development of new tools is not enough, and there is a growing need for applied field research to develop and evaluate comprehensive solutions to the problems of tropical diseases, especially to problems of a generic nature. There is in particular a need for more research to develop cost-effective and sustainable control strategies and for more operational research to facilitate the implementation and subsequent improvement of these strategies.

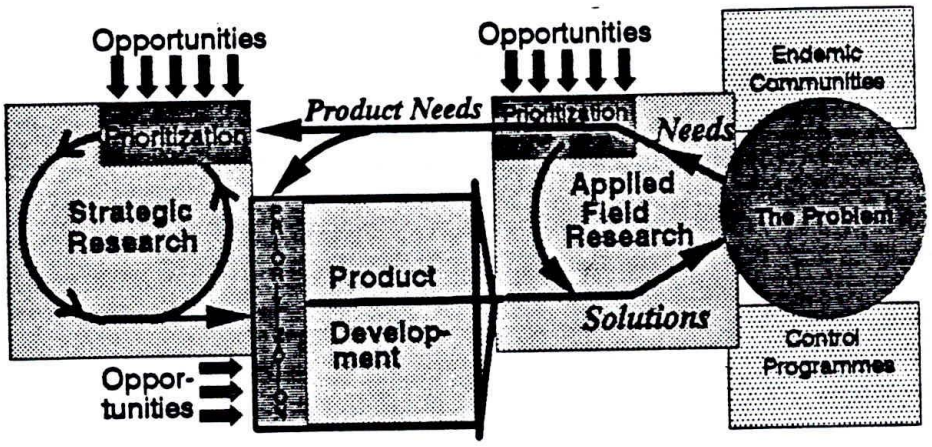
It is also accepted that tropical diseases research should become more driven by the priority needs in the field. These needs are two-fold, (1) the needs of endemic communities and (2) the needs of control programmes operating at the district or national level. These needs may or may not coincide (Figure 1). The proper understanding of these needs requires adequate information on the public health and socio-economic importance of the tropical diseases, the availability and use of health facilities in endemic countries, both modern and traditional, and on current problems in control strategy development, implementation and evaluation. Such information is often lacking, but there is an increasing recognition of the importance of field research aimed at clarifying these issues.

2. REORGANIZATION OF TDR AND ESTABLISHMENT OF AFR

2.1. Reorganization of TDR

Following a review of TDR and its ability to meet its mandate most effectively during the next decade, the Scientific and Technical Advisory Committee (STAC) recommended in March 1993 that the structure of TDR be changed in order to achieve the right balance between its efforts in basic or "strategic" research, product development and field research. One of the major motivating factors was the recognition of a growing demand for applied field research, and the need to develop a flexible structure which could develop rapid solutions to field problems. STAC recommended that TDR's current disease-specific Steering Committees be phased out and replaced by three main components covering Strategic Research, Product Development and Applied Field Research (AFR). Disease-specific issues should still continue to be addressed under the new structure.

Figure 1: Phases in Tropical Diseases Research



Strategic research would be concerned with furthering the understanding of host-parasite/parasite-vector and parasite biology in order to develop leads toward more effective disease control tools. Product development would be responsible for taking the leads once identified through to Phase III trials. AFR would be concerned with applied field research for improved disease control. It would incorporate the activities of the current Social and Economic Research component of TDR (see Annex 2) and would also include operational research and the field testing of new products in their intended setting of use. The recommendations of STAC were accepted by the Joint Coordinating Board of TDR during its session in June 1993 and the new strategy and structure of TDR will formally come into effect on 1 January 1994.

2.2. Organization of AFR

As recommended by STAC, an Applied Field Research component has been created in TDR which covers all six TDR diseases. The activities of this component will be directed by a steering committee (SC/AFR, see section 2.4.) which will meet once per year to review progress and identify priorities for new AFR activities. The committee will be supported by the TDR secretariat in a new Unit (TDR/AFR), which

will initially consist of the secretariat previously in the Social and Economic Research (SER), Field Research in Malaria (FIELDMAL) and the Epidemiology and Field Research (EFR) components of TDR.

In May 1993 a planning meeting on Applied Field Research was held to review field problems and needs, recommend the priorities for AFR, and to make suggestions on the structure and organization of this research. The meeting developed the Strategic Plan for Applied Field Research described in this document. The participants in the meeting are listed in Annex 1.

2.3. The objectives of AFR

The objectives of AFR are:

1. To identify the major problems and needs of endemic communities and control programmes relating to tropical diseases.
2. To develop solutions to these problems
3. To identify the most cost-effective way of introducing the solutions in the health systems and policies, and to facilitate their implementation, evaluation and timely updating.
4. To inform the other R&D components of TDR on priority needs for new products, and on the expected utility of potential new products.

2.4. AFR Steering Committee

The AFR steering committee will consist of 14-16 members. Half of these should be scientists involved in tropical disease control, with the other half consisting of experts in the various AFR disciplines, with a strong representation of the social and economic sciences. For each of the TDR diseases there should be at least one expert on the Committee (at least three for malaria). All WHO regions with endemic tropical diseases should be represented; the number of committee members depending on the tropical diseases burden in the region. At least two-third of committee members should be from disease endemic countries.

The committee will meet once per year for a period of 4-5 days. The Secretary to the Steering Committee will be the TDR/AFR Unit Coordinator. Other members of the WHO secretariat to the Committee will include the TDR/AFR Unit staff, the CTD responsible officers for disease control, and representatives of the RCS, Product Development and Strategic Research components of TDR.

The AFR Steering Committee will at each session review (see also Figure 2):

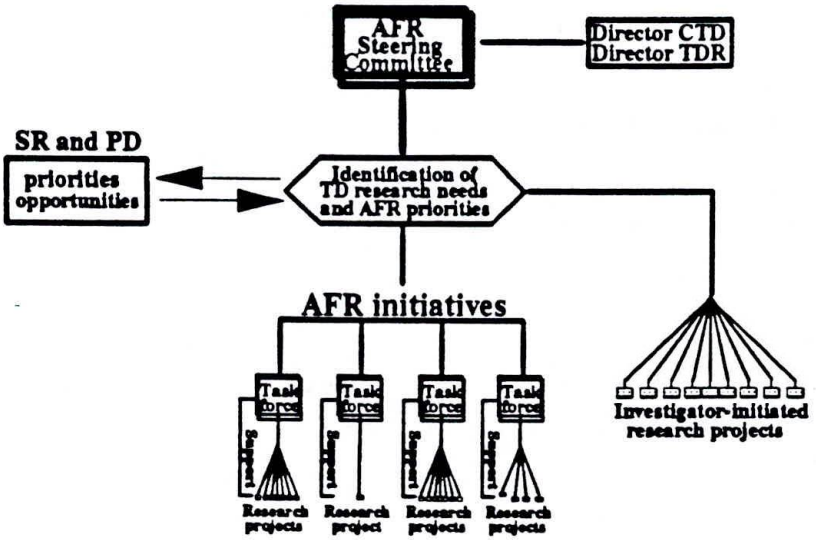
i. the strategic plan, including the identification of research needs in tropical diseases (see section 3.1.) and priorities for Applied Field Research (see section 3.2.).

ii. proposals for new AFR initiatives and the progress of ongoing AFR initiatives (see section 4.).

iii. investigator-initiated proposals for Applied Field Research (see section 5.) and small grant programmes (see section 6.1.)

iv. the relative budget allocation between (1) AFR initiatives, (2) investigator-initiated proposals and (3) small grants programmes.

Figure 2: Organization of Applied Field Research



2.5. CTD/TDR joint management of AFR

As an important objective of AFR is to fund research that will be of practical use to disease control programmes, close collaboration and coordination with CTD will be imperative. Such collaboration should ensure greater relevance and effectiveness of applied field research through more CTD input on control needs, by providing disease-specific expertise and by facilitating the feedback of research results, and their adjustment and implementation at the country level. Seeking site-specific solutions in a national context will remain the research function of CTD (see Annex 3.), but it will be closely linked to the more generic field research funded through TDR.

To ensure optimal collaboration and coordination between CTD and TDR, the Directors of CTD and TDR intend to jointly manage the TDR/AFR Unit, including the joint review and approval of the AFR workplan during annual planning meetings. Furthermore, both Directors will jointly review the recommendations of the AFR steering committee, and jointly appoint the members of the Steering Committee and of AFR taskforces (see section 4.).

There will be active collaboration between CTD and TDR staff at the task force level. On each task force, there will be at least one CTD staff member and at least one member of TDR/AFR, thus ensuring full participation of both CTD and TDR in the most important AFR operations. Furthermore, the CTD responsible officers for disease control will participate as members of the WHO secretariat in the AFR Steering Committee meeting, and provide relevant information resulting from Expert Committees on Tropical Diseases and from other meetings sponsored by CTD.

3. TROPICAL DISEASES RESEARCH NEEDS AND AFR PRIORITIES

3.1. Identification of research needs

An important task of AFR will be to identify the major research needs in the field, and to help ensure that TDR funded research, be it strategic research, product development research or applied field research, is driven by those needs. Special efforts should be undertaken to ensure that the identified research needs properly reflect the needs as perceived by endemic communities themselves and by those involved in disease control at the local and national level. This will require active and continuous communication between AFR on the one hand and Ministries of Health, control personnel and field researchers on the other.

The AFR Steering Committee will prepare and regularly update a list of the major research needs in tropical diseases on the basis of the information obtained through mechanisms such as AFR funded field research on needs at the community level, feedback from disease controllers and field researchers, recommendations from WHO Expert Committees and other relevant meetings, field visits by Committee members and/or secretariat, and feedback from WHO Regional Offices.

Because of its composition, with a strong representation of scientists and public health administrators from disease endemic countries involved in tropical disease control and applied field research, the Committee should be in a relatively good position to review the needs for tropical diseases research. Nevertheless, there will be many situations where the information available to the Committee is insufficient. In such cases the Committee may promote additional research or organize specific activites to clarify specific needs of communities and control programmes.

A list of research needs and AFR research priorities (see below) should be circulated widely among the scientific community and Ministries of Health in endemic countries, together with a request for comments and feedback to the steering Committee. Furthermore, the Committee should experiment with alternative communication approaches to improve the information flow to and from the field, and ensure a close linkage between research and control.

The identification of research needs is not restricted to field research needs, but also concerns the need for new products. The relevant information will be communicated to the Strategic Research and Product Development components of TDR and will assist TDR in its overall research planning and priority setting. The interaction with PDU could also greatly benefit the priority setting and planning process for product development in TDR by discussing at an early development stage with the AFR Steering Committee the likely utility of potential new products and their required characteristics.

3.2. Setting of research priorities for AFR

The Committee will identify AFR research priorities, and review and update these priorities during each session of the Steering Committee. The AFR priorities should be clearly defined and regularly communicated to scientists concerned with tropical disease control and research, who will be invited to submit proposals for AFR initiatives or for separate research proposals on these priority issues. The AFR priorities will also form the basis for the selection of AFR initiatives to be funded, and for the monitoring and evaluation of AFR and its achievements.

In setting the priorities the following factors need to be taken into account:

- the needs of communities, and the needs of control programmes and the health care system
- the expected impact of the research findings on tropical disease control
- the availability of resources
- the expected spin-off in terms of research capability strengthening in endemic countries
- the role of other funding agencies and the comparative advantage of TDR
- opportunities, whether in the 'field' or arising from product development
- the need for phase IV field testing of newly developed products
- the prospects for new products over time

3.3. Current priorities for Applied Field Research in Tropical Diseases.

The AFR planning meeting identified the current research priorities for applied field research in tropical diseases. In addition to *'Gender and Tropical Diseases'* and *'Tropical Diseases and Health Financing'*, which were already established TDR priority areas and the subject of ongoing initiatives, the meeting identified as AFR priorities the topics which are listed in Annex 4 in order of priority. These priority topics cover both disease-specific and cross-disease issues. After extensive discussion, the meeting grouped these priority research topics into five main priority areas as shown below.

Disease Control within Health Care Delivery Systems

- Preventive measures for malaria infection and disease at individual and community levels*
- Optimal combination of measures to interrupt *T. cruzi* human transmission**
- Cost-effective preventive/treatment strategies and managerial tools for schistosomiasis control*
- Strategies for ivermectin use in onchocerciasis control in Africa**
- Malaria case management at peripheral-hospital levels focussing on children and women*
- New strategies to improve the organization and management of control programmes
- Improved detection and subsequent treatment of leprosy
- Integrated control of visceral leishmaniasis through school children
- Feasibility and cost-effectiveness of control tools and strategies for lymphatic filariasis
- Integration into Primary Health Care and sustainability of control programmes
- Improvement of health care delivery systems as relating to tropical disease control
- Drug delivery systems for diseases requiring repeated mass-treatment
- Ivermectin-based control strategies for the elimination of onchocerciasis in the Americas*
- Field-testing of new tools for lymphatic filariasis control**
- Feasibility and cost-effectiveness of alternative treatment regimens in leprosy*
- Optimization of current treatment regimens in African trypanosomiasis
- Prevention of deformities by early identification and appropriate management of nerve function impairments in leprosy

Environment and Demographic changes

- Leishmaniasis, migration and environmental changes (incl. GIS)
- Tropical disease control within rapid socio-economic, demographic and environmental changes
- Effect of ecological changes on transmission of vector borne diseases
- Agricultural development and rice cultivation as relating to malaria and schistosomiasis

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**: already an ongoing TDR initiative

*: partly covered by an ongoing TDR initiative

Information, Education, Communication (IEC) from perspectives of Communities and Policy Level

- Information, education and communication strategies for tropical disease control
- Community compliance and participation in control activities
- The school as entry point for tropical disease control*
- Health promotion through leishmaniasis control with women as the key health providers*

Development of Rapid Assessment Procedures (RAP)

- RAP for distribution of diseases requiring intervention at community level
- RAP for monitoring and evaluation of control
- Cost-effective community and individual diagnostic strategies in schistosomiasis*

Surveillance and Impact Assessment

- Surveillance and health information systems for local and national levels, especially for malaria
- Epidemiological modelling for surveillance and control
- Methods and managerial tools for cost-effective surveillance and control of African Trypanosomiasis**
- Identification of risk factors for Chagas disease among those infected with *T.cruzi**
- Socio-economic and public health importance of lymphatic filariasis**
- Epidemiological assessment of morbidity and of the impact of control in schistosomiasis

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**: already an ongoing TDR initiative

*: partly covered by an ongoing TDR initiative

4. AFR INITIATIVES AND TASKFORCES

In AFR there will be two main approaches to applied field research: a new approach referred to as "AFR initiatives" and the current TDR approach of investigator initiated research. The AFR initiatives will be the most important research activity and receive the major share of the AFR operations budget.

4.1. General principles of AFR initiatives

Definition

An AFR initiative is a focussed applied field research effort which addresses a priority issue for tropical disease control. It aims to develop, within a time-limited period, a practical solution to an identified priority problem and to ensure that this solution can be, and in a number of important situations actually is, applied. The ultimate objective for each AFR initiative is to have a significant and demonstrable impact on disease control.

Research issues

AFR initiatives may address disease specific issues, such as phase IV trials of new drugs or operational research for improved effectiveness of specific disease control programmes, or cross-disease issues such as the improved management of the sick child, gender biases in health care delivery, and helminth control through the school system. The proposed AFR structure should facilitate cross-disease initiatives which were not commonly funded under the previous disease-specific steering committee structure of TDR, but which may have a broad impact.

Competition for funding

Proposals for AFR initiatives are submitted on a competitive basis to the AFR Steering Committee (SC/AFR). During its annual meeting, the Committee will review all submitted proposals and select a limited number of AFR initiatives for funding. The major criteria for selection of AFR initiatives are:

- the potential for impact on disease control
- collaboration with and integration in existing health services
- involvement of local investigators and health service managers
- the potential for covering more than one disease
- the use of multi-disciplinary approaches

Taskforces

For each approved AFR initiative, a taskforce will be appointed which will plan, initiate and supervise the operations. The taskforce will be multi-disciplinary in nature and consist of members with the relevant expertise and interest in the research problem in question, and with good links to disease control. The taskforce will operate in a very pro-active way and will be given considerable freedom and adequate funds to execute its task. Each year, the taskforces report back to the SC/AFR on their progress.

Time limit

At any given time, only a limited number of AFR initiatives will be operational. This will ensure that adequate financial resources and other support can be made available to each active taskforce to give it a fair chance to meet its objective within a limited period of time. The time limit is important for two reasons. First, to avoid that taskforces become self-perpetuating and thus block the availability of resources for new initiatives on other priority issues for control. Secondly, because results of field research, and particularly of operational research, become less relevant with time when the control problem evolves or when, in the absence of new research results, solutions may be implemented which are inappropriate but which become nevertheless established. AFR taskforces will have to encourage a rapid research cycle, with immediate feedback of the research findings to control, in order to achieve optimal impact of the initiative.

Involvement of scientists from endemic countries

The relevance of an AFR initiative will also depend on the extent to which it will achieve the active involvement of scientists and public health administrators from endemic countries. It is often said that there is a great shortage of good field researchers in the endemic countries and that therefore only few endemic scientists participate in applied field research in tropical diseases. However, this is a somewhat biased point of view. There are still many field researchers in endemic countries who, though maybe not well known internationally, are competent in various AFR disciplines, understand the endemic communities well and are active at the local level. These researchers, many of who have been trained with RSG support, should be involved in the AFR initiatives.

Particularly in the area of AFR, it makes sense to give preference to local researchers and provide them with an important opportunity to broaden their experience in advanced field research. In many cases this may require additional input through training workshops etc, but this should be a very efficient way of research capability strengthening which clearly falls under the TDR mandate. The AFR will promote 'learning by doing' and within the context of the AFR initiatives there needs to be a very close interaction with RSG and with the CTD programme on tropical diseases training (CTD/TDT).

Link to disease control

To ensure the relevance of the research activities and optimum utilization of the research findings, attempts should be made to create a direct link between the AFR initiative and related disease control programmes and responsible officers in Ministries of Health. This may be achieved by enlisting staff of disease control programmes as task force members, by execution of the field research under the umbrella of a control programme or a district health plan, preferably by incorporating disease control staff as investigators, or by organizing joint workshops for identifying research questions and for reporting research findings. Other approaches of linking research to control should be actively explored.

4.2. Mode of operation of AFR initiatives

(a). The first step towards the establishment of an AFR initiative is the preparation of a proposal and its submission to SC/AFR. The proposal should specify the objectives, timeframe and budget of the proposed initiative and the membership profile of the corresponding taskforce. Proposals can be submitted by any person, but it is likely that the preparation of proposals will in many cases require significant input from steering committee members and the AFR secretariat. Following review of the proposal and incorporation of modifications suggested by the committee, an AFR initiative starts with a recommendation by SC/AFR for its creation, and subsequent approval by Directors CTD and TDR. The taskforce members will then be identified and appointed, and be made responsible for the execution of the initiative. The taskforce will be given optimal freedom and support to undertake its task as long as this remains within the general operating principles and regulations of WHO. The progress of the initiative will be reviewed during each subsequent meeting of SC/AFR which will report to Directors CTD and TDR, and make recommendations concerning the continuation and funding of the initiative.

(b). To facilitate smooth operation, the taskforces should be kept fairly small and should not exceed 3-5 members. The profile of the taskforce membership should be relevant to the topic of the initiative and should reflect the general need for multi-disciplinary expertise and strong representation from endemic countries. Whenever an initiative is geographically limited to a single country or a subregion, it should be attempted to recruit most taskforce members from the countries concerned and operate as much as possible at the local level. Other important selection criteria are the willingness and capability of individual members to contribute actively to the initiative, and practical considerations such as access to reliable communications. At least one of the taskforce members should also a member of SC/AFR. Specific suggestions for task force membership should be included in the proposal, and these should be carefully reviewed by the Steering Committee. Task Force members will only be appointed by Directors CTD and TDR upon recommendation of the Steering Committee.

(c). For each taskforce a chairperson will be appointed who will report the progress of the initiative to SC/AFR and who may act on behalf of the taskforce if so required. Furthermore, one TDR/AFR staff member will be attached to the taskforce as secretary to provide the necessary secretariat support. Given the need for rapid action and processing of research grants, travel arrangements, recruiting of consultants etc., a major input from the TDR/AFR secretariat will be indispensable. Other WHO staff members, particularly staff from CTD and TDR, will also be involved in the taskforce activities according to their specific expertise, experience and responsibilities. They will undertake various supporting activities such as linking the initiative with other related research and control activities of WHO, providing the taskforce members with relevant expert advice and access to information from other sources, and facilitate the feedback of the research results to disease control.

(d). The taskforce will decide on its strategy and its implementation, a mechanism for selecting researchers on the basis of objective and specified criteria, and will decide on the funding of research projects and supporting operations. It will determine the appropriate way of advertising the initiative, and to ensure the active involvement of the research community in endemic countries. It will identify the research approaches to be followed, select field researchers to be included in the initiative and decide on the funding of the research. Major decisions concerning the initiative must be considered by all taskforce members if possible, and will require the approval of a majority of taskforce members. However, the decision making process should not obstruct the smooth running of the taskforce and mechanisms should be worked out to allow the taking of decisions without having to await a full meeting of the taskforce.

(e). On the average the duration of an AFR initiative will be in the order of three years, excluding the start-up period during which the taskforce is formed, develops its plan of action, advertises the initiative and selects the researchers to be involved. However, the acceptable duration for different AFR initiatives may vary considerably depending on their objectives. An AFR initiative may be extended beyond the duration initially approved, but it will have to compete for such an extension with other proposals for AFR initiatives. In general, extensions should be discouraged for the reasons given in section 4.1..

(f). The taskforce will need to operate in a highly pro-active way and undertake various activities to ensure optimal participation of scientists from endemic countries and input from disease control programmes. These activities may involve small planning meetings with experts in the relevant disciplines and staff from disease control programmes, preparation and distribution of information materials describing the initiative and inviting field researchers to apply, visits of taskforce members to disease control programmes to establish active links, and protocol development workshops with active participation of prospective researchers.

(g). The taskforce will also be responsible for organizing in collaboration with the RCS component of TDR and the training component of CTD the supporting research capability strengthening activities. These may involve training workshops in specific skill required for the initiative such as anthropological field research techniques, methods for economic data collection, and computerised data processing and analysis. In the case of multi-centre studies, it may be advisable to organize an initial workshop for the joint development of a standard protocol, record forms and data processing systems, and toward the end of the studies a workshop for joint data analysis. These workshops, often to be undertaken with the help from experts in the relevant disciplines, will also have an aspect of research capability strengthening. Many of these activities may be funded and/or organized by the RCS component of TDR which should be kept closely informed of the plans and activities of the taskforce, especially through the respective taskforce secretary.

(h). At the start of the initiative, the approximate budget for its total duration will be indicated. However, the actually available budget will be decided upon on an annual basis following SC review and final decision by Directors CTD and TDR. Each year the taskforce will submit a budget proposal to SC/AFR with a breakdown of the proposed expenditures for research operations and for supporting activities such as meetings, travel, consultants etc. Once the budget for a given year is approved, the taskforce is free to utilize the funds for research and supporting activities as long as these fall within the limits of the approved budget and the funded activities are in accordance with the approved proposal and the general guidelines from the steering committee. Funds for specific activities can be disbursed at any time of the year. In accordance with general TDR rules, funds should be used as much as possible for funding research activities. However, it is understood that the need for being pro-active and for research capability strengthening activities will require the allocation of a greater share of the funds to supportive activities than is usual in TDR. Supporting activities include meetings of the taskforce, communications between members, recruitment of consultants, organization of workshops etc. The costs of such activities may rapidly become disproportionately high and all efforts should be undertaken to keep them at a minimum.

(i). The taskforce should explore alternative ways of reducing the costs and try to identify additional resources at the local level where control programmes or ministries of health may assist with providing transport, meeting costs etc, or at the regional or international level by identifying other donors willing to contribute funds for the initiative. It should be investigated if the administration of funds can be subcontracted to an institution other than WHO as this could significantly reduce many expenditures, such as on airfares, and greatly increase the operating flexibility of the taskforce. Travel costs of WHO staff involved in the initiative will be paid from the regular operational support budget for the staff members concerned.

(j). For all research projects to be funded under an AFR initiative, a project proposal needs to be developed using the standard TDR proposal forms for collaborative research projects or a similar format. All standard TDR guidelines and instructions for collaborative research projects will apply, including those for ethical and government clearance. The taskforce can at any time submit selected proposals to WHO for clearance and funding. In certain specific situations, when the administration of the initiative and ethical clearance can be delegated to an institution other than WHO, such as a Ministry of Health in a country where the initiative is operating, the procedures may be further simplified, and funding and clearance of research and supporting activities may often be handled at the local level. For reasons of efficiency, the delegation of administrative procedures is usually preferable as long as it can be assured that they will continue to comply with the relevant WHO rules and regulations.

5. INVESTIGATOR INITIATED PROPOSALS

It is important that the new AFR structure retain a balance between funds for AFR "initiatives" and funds for investigator initiated proposals on all TDR target diseases. The rationale for devoting considerable funding to special initiatives is that it will allow AFR to address high priority disease control issues in a concerted manner, with considerable flexibility and within a defined time frame. On the other hand, many important new ideas are initiated from the field and adequate funds must be kept to allow for these.

It is proposed that the Steering Committee recommend, on a biennial basis, an amount of funds to be appropriated for investigator initiated proposals. As a guideline it is proposed that approximately $1,500,000 be appropriated for a maximum of 50 proposals to be funded during 1994-95. For 1994-95 the TDR proposal forms will continue to be used, but the Committee should discuss whether it recommends any changes in format. Also, the Committee should be responsible for drafting guidelines for the submission of proposals for new initiatives. Eventually, a brochure or information package should be prepared describing AFR priorities and mechanisms of working.

Investigator-initiated proposals will be reviewed by the AFR Steering Committee at its regular meetings, as will ongoing AFR initiatives and proposals for new initiatives. Experience in other TDR steering committees has shown that the review of investigator-initiated proposals can take a disproportionate amount of time, partly because committee members tend to be particularly interested in this aspect of the work, thus leaving insufficient time for review of priorities and development of a workplan. A similar development should be prevented in the AFR Steering Committee, especially because of the important other responsibilities of this committee, such as the review of AFR initiatives and the identification of research needs and priorities, which will require a considerable amount of time during committee meetings and the active participation of all committee members. It is therefore recommended that the scientific review of investigator-initiated proposals is undertaken during parallel sessions of SC sub-groups who each review only a proportion of the proposals, and that a maximum of one day is allocated for this review. The recommendations of the sub-groups will be reported to plenary without discussing the details of different proposals. Based on the recommendations of the sub-groups, the full Steering Committee will then decide on the proposals to be funded. This plenary session should not take longer than half a day, bringing the total time available for review of investigator-initiated proposals to a maximum of one and a half days.

6. OTHER AFR ACTIVITIES

6.1. Small Grant Programmes

SER has funded two Small Grants Programmes, one in Latin America and one in Africa. The former has completed its first three-year round, and is currently starting a second round. The African programme is just beginning its first round.

The initial aim of Small Grants was to attract new researchers into the field of social and economic research on tropical diseases. As such, projects were funded on any relevant topic, as long as the quality of the proposals were sufficiently high. In the second round of the Latin American programme there is a growing tendency to focus research on particular themes (e.g. housing and Chagas disease; gender and tropical diseases) and on operational research on issues related to disease control. Similarly, the African programme will concentrate several projects in the area of severe and complicated malaria.

With the growth in more focused activities under the Small Grants initiatives, it is expected that they will become increasingly complementary to AFR activities. For example, a task force on a particular theme within AFR could be complemented by a group of studies on a similar theme in Latin America or Africa. AFR workshops related to the common theme could be attended by both AFR-funded investigators, as well as by Small Grants project grantees. This could be an effective way to share resources and to allow junior investigators to interact and learn from more senior researchers.

In 1992, a new initiative called the EMRO/TDR/CTD Small Grants Programme, was launched to stimulate control-oriented research projects in countries of the Eastern Mediterranean Region where leishmaniasis represents an important public health problem. This initiative has stimulated new research projects from investigators, who were not involved before, created new perspectives for control and addressed priority areas for leishmaniasis research in the region. The experience so far has been a success, and the Programme will now be extended to schistosomiasis. The small grants programme clearly illustrates the value of combining the complementary expertise of TDR and CTD.

It is proposed that the Coordinators of Small Grants programmes be members of the AFR Steering Committee in order to allow for smooth communications between these groups. Furthermore, the steering committee should regularly review the activities and plans of action for all small grants programmes, whether they are fully or only partly funded by TDR, in order to ensure that they are consistent with, and form a logical part of, the overall AFR effort.

6.2. Research Capability Strengthening and AFR

The greater emphasis on applied field research will require greater efforts in research capability strengthening in the area of AFR, and TDR plans therefore to increase the proportion of the RCS budget will be devoted to capacity building activities in relation to the needs of applied field research. It is estimated that during the 1994-1995 biennium, over 40% of RCS funds will be dedicated to AFR research capacity building.

There will be increased interaction between RCS and AFR, and closer integration of their activities. Since AFR initiatives will operate in Disease Endemic Countries (DECs) and involve DEC scientists, they will result in capacity building in the area of AFR. AFR taskforces will be encouraged to utilize institutional and human resources developed through RCS grants and a computer data base of TDR trainees is being developed for this purpose. RCS support for skills training within the context of AFR initiatives is expected to be a very effective way of training. Furthermore, the AFR initiatives may provide opportunities for research training (short- and long-term) which should be explored. In selected DECs with limited capacity for AFR, '3 plus 2' grants in flexible mode or small grants could be employed.

Annex 1. Participants in the AFR planning meeting

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Annex 2. Evolution of SER in relation to AFR

TDR's Social and Economic Research (SER) component was established with the ultimate aim of improving the effectiveness of disease control programmes through the incorporation of social, cultural and economic factors. In its initial years SER funded mainly descriptive studies focusing on the impact of sociocultural and economic conditions on disease transmission and control; in the more recent past, SER has funded mainly intervention-oriented research from the perspectives of social acceptability and cost-effectiveness of disease control tools and strategies. It has also embarked upon operational research in close collaboration with disease control programmes. Thus, SER has steadily moved towards the realization of its ultimate aim, and in doing so has worked increasingly closely with biomedical researchers, including epidemiologists, parasitologists, clinicians and other public health specialists.

Throughout its history, an underlying objective of SER was the strengthening of capacity in social sciences in developing endemic countries in relation to tropical disease research needs. Today a well trained cadre of social scientists with experience in tropical diseases can be found in many endemic areas, with the possible exception of health economists. Whereas a decade ago it would have been difficult to conceive of social scientists working with biomedical scientists as equal partners in multidisciplinary research projects, today such partnerships have become the foundation of most SER studies.

Given this evolution, the integration of social sciences into the broader AFR framework is a logical next step. As an increasing number of disease control tools become available for use in the field, there is a growing demand for research on practical questions such as cost-effective drug distribution strategies, utilization of health services to which many TDR products will be disseminated, the perceived importance of signs and symptoms of disease in relation to prevalence, and the development and testing of rapid assessment diagnostic and treatment strategies. All of these issues require collaboration among specialists in different field research disciplines. As social and economic considerations are of the utmost importance in such interdisciplinary research, the SER Steering Committee will form the nucleus of the proposed new AFR Steering Committee.

Annex 3. CTD Research in support of local disease control

CTD promotes research that is directly relevant to local disease control needs. These needs may be epidemiological, clinical, managerial or operational. Such applied field research is viewed as an integral part of all plans of actions for disease control.

The support provided by CTD is to assist programmes in the preparation of action plans with research components which can attract resources from national, regional or global sources. Preference is always given to the involvement of national researchers and national research institutions. Where problems are common to neighbouring countries, intercountry coordination and collaboration is encouraged. Modest financial support from CTD may be provided to facilitate this process. These grants are selected on the basis of local priorities rather than global priorities or specific technical merits.

At the global level CTD provides standardized reagents for monitoring resistance against antimalarial drugs and insecticides for use in applied research as well as in control programmes. In addition, the WHO pesticide evaluation scheme (WHOPES) organizes operational research for testing and evaluation of new pesticides in view of their possible use in the control of vector borne diseases.

The extensive network of WHO Collaborating laboratories in the area of tropical disease control, built up over the last decades and regularly brought up to date, will continue to serve country programmes for ad hoc specialized investigations such as identification of parasites or animal reservoirs, parallel evaluation of diagnostic tests and quality control of reagents and drugs.

In promoting national control programmes, CTD has coordinated with bilateral and NGO donors in providing technical support and funding of large scale control programmes with an operational research component. These programmes are integrated into the national health care system and in certain instances, involve more than one disease.

CTD will continue these activities and will present overviews of all these activities to the AFR Steering Committee and to the AFR taskforces concerned.

Annex 4. Priority needs for Applied Field Research in Tropical Diseases

List in order of priority ranking as given by the AFR planning meeting

1. Preventive measures for malaria infection and disease at individual and community levels*
2. Leishmaniasis, migration and environmental changes (incl. GIS)
3. Optimal combination of measures to interrupt *T. cruzi* human transmission**
4. Cost-effective preventive/treatment strategies and managerial tools for schistosomiasis control*
5. Tropical disease control within rapid socio-economic, demographic and environmental changes
6. Information, education and communication strategies for tropical disease control
7. Strategies for ivermectin use in onchocerciasis control in Africa**
8. Surveillance and health information systems for local and national levels, especially for malaria
9. Malaria case management at peripheral-hospital levels focussing on children and women*
10. Effect of ecological changes on transmission of vector borne diseases
11. Agricultural development and rice cultivation as relating to malaria and schistosomiasis
12. Epidemiological modelling for surveillance and control
13. New strategies to improve the organization and management of control programmes
14. Improved detection and subsequent treatment of leprosy
15. Methods and managerial tools for cost-effective surveillance and control of African Trypanosomiasis**
16. Community compliance and participation in control activities
17. RAP for distribution of diseases requiring intervention at community level
18. Identification of risk factors for Chagas disease among those infected with *T.cruzi*
19. RAP for monitoring and evaluation of control
20. The school as entry point for tropical disease control*
21. Integrated control of visceral leishmaniasis through school children
22. Socio-economic and public health importance of lymphatic filariasis**
23. Feasibility and cost-effectiveness of control tools and strategies for lymphatic filariasis
24. Integration into Primary Health Care and sustainability of control programmes
25. Improvement of health care delivery systems as relating to tropical disease control
26. Drug delivery systems for diseases requiring repeated mass-treatment
27. Ivermectin-based control strategies for the elimination of onchocerciasis in the Americas*
28. Field-testing of new tools for lymphatic filariasis control**
29. Feasibility and cost-effectiveness of alternative treatment regimens in leprosy*
30. Epidemiological assessment of morbidity and of the impact of control in schistosomiasis
31. Cost-effective community and individual diagnostic strategies in schistosomiasis*
32. Health promotion through leishmaniasis control with women as the key health providers*
33. Optimization of current treatment regimens in African trypanosomiasis
34. Prevention of deformities by early identification and appropriate management of nerve function impairments in leprosy

Annex 5. Tropical disease burden, status of control and related research needs

Tropical disease burden and problems in control

The tropical diseases targeted by CTD and TDR cover the most important communicable diseases of parasitic origin, as well as leprosy, found in the tropical and sub-tropical belt. The heavy burden of tropical diseases occurs in a background of economic and social under-development, very low investment in health and related sectors, malnutrition, environmental deterioration, insufficient recognition of the havoc being caused by tropical diseases, and the lack of know-how on the appropriate use of current tools for control, resulting in poor political commitment and low priority.

The tropical disease burden extends to over 100 countries with a total population at risk of over 2500 million. The population size involved in sub-clinical infections range from 18 million in Chagas disease to 200 million in schistosomiasis. The number of clinical cases ranges from 12 million in leishmaniasis to 190 million in malaria. While mortality is a major cause of concern in diseases like malaria with over a million annual deaths, physical deformities and blindness are important concerns in diseases such as leprosy and onchocerciasis.

This annex provides for each of the tropical diseases a short overview of the disease burden, status of control and related field research needs.

I. MALARIA

Malaria risk of varying degree exists in 99 countries or areas. Accurate information on the global incidence of malaria is difficult to obtain because reporting is particularly incomplete in areas known to be highly endemic. The global incidence of malaria is estimated to about 190 million clinical cases each year.

Disease burden and distribution

Countries in tropical Africa are estimated to have more than 80% of all clinical cases and more than 90% of all parasite carriers. The vast majority of malaria deaths occurs in Africa; estimates vary greatly: a figure of 800 000 deaths per year in African children has been quoted in 1991 by the WHO African Region. Severe malaria and mortality are caused by *Plasmodium falciparum* which is the predominant species of malaria in tropical Africa, while in the rest of the world it is far less common.

The number of cases recorded annually in the countries of Asia and the Americas is approximately 5 million. It is estimated, however, that the real number is nearly four times as high. About 80% of these cases are found in Asia, where, except for China, the situation is worsening particularly in the Indochina peninsula which is affected by extremely severe problems of parasite resistance to drugs. It is estimated that malaria claims more than 100 000 lives per year outside Africa - these deaths occur in all age groups.

There are only a few countries from which the resistance of *P. falciparum* to chloroquine has not been reported and the rapid evolution of this resistance in Africa threatens to hamper the provision of adequate treatment in rural areas. Resistance to sulfadoxine-pyrimethamine has developed in South-East Asia, South America, and focally in Africa. In Thailand, there are indications that up to 50% of cases in certain areas no longer respond to mefloquine therapy, while the sensitivity to quinine is also diminishing in areas of Thailand and Viet Nam.

Status of control

Areas where endemic malaria remains basically unchanged are inhabited by 500 million people, mainly in tropical Africa. 1.7 billion people, or 32% of the world's population, live in areas where endemic malaria was considerably reduced or even eliminated by the existing national malaria control programme, but transmission has been reinstated and the situation is unstable or deteriorating.

The countries of the world affected by malaria today can be classified with respect to malaria control into two major categories: those which did not come within the global malaria eradication efforts to end the transmission of infection (Category I), and those which did and in which large-scale programmes of house spraying with insecticides have been in operation since the 1950s or 1960s (Category II). Most countries of the first category are in Africa south of the Sahara, while countries in the second category are in the Americas and Asia.

Major problems in control

The major problems faced by malaria control programmes are as follows:

- In most countries of Africa south of the Sahara, where 80% of malaria mortality in the world occurs, the quality and coverage of disease management provided by existing health services are inadequate. Lack of funds further compounds the malaria problem in these countries.
- Many control programmes in Asia and the Americas lack the managerial and epidemiological capabilities for reorienting their activities according to the Global Malaria Control Strategy.

- Some countries, particularly those in the Western Pacific and South-East Asia with focal and very severe malaria problems, lack funds for implementing their malaria control programmes.

- In all malaria control programmes there is an inadequate capability for applied field research due to which programme activities cannot be more effective.

Applied Field Research Priorities

The AFR planning meeting identified as the three top priority areas for applied field research in malaria the following:

1. Malaria case management at peripheral and hospital levels focusing on children and women

2. Preventive measures for infection and disease at the individual and community level.

3. Surveillance and health information systems

II. LEISHMANIASIS

Disease Burden

Global distribution: 88 countries (16 developed - 72 developing countries of which 13 are among the least developed) in 4 countries affected. The overall prevalence of infection is estimated at 12 million people out of a population at risk of 350 million people. The annual incidence is 1 to 1,5 million cases of cutaneous leishmaniasis and 500 000 cases of visceral leishmaniasis

Leishmaniases are important in terms of morbidity and some are severe in terms of mortality. Visceral leishmaniasis is the most severe form. The mortality rate is usually 100% if untreated. Mucocutaneous or "espundia" produces an extensive destruction of the oral, nasal and pharyngeal cavities, and is highly disfiguring. Cutaneous leishmaniasis with multiple lesions leads to disabling and disfiguring scars. Diffuse cutaneous leishmaniasis never heals spontaneously with occurring relapses after treatment. It is recognized as a special public health problem.

There has been a recent and significant increase in the morbidity and mortality rates together with a geographic spread of the leishmaniases worldwide. This increased severity is frequently correlated with the economic development of the countries (new agro-industrial projects, unplanned urbanization, man-made environmental changes (dams, irrigation) and new settlements in endemic areas. Outbreaks frequently occur when large-scale population movements take place, as in rural development schemes, in areas of civil unrest or military operations.

Major Problems in Leishmaniasis Control

- Reluctance to recognize the gravity of the situation to cover-up inaction, e.g., notification is compulsory in only 30 countries out of the 88 which are considered to be endemic.

- Relatively low priority ranking, short-term commitments, lack of resources, lack of full-time qualified personnel available for field work.

- Poor reporting system.

- Treatments based on pentavalent antimonials as injectables are costly (100-120 US$). Cost of the drug delivery is high, as most of the foci are in remote dispersed areas leading to frequent 'interruptions in treatment and appearance of resistance.

- Within countries, those affected are people of the lowest socio-economic class without means to assume the costs of the disease.

- Most of the nosogeographical entities are zoonotic (difficulty to control animal reservoir hosts).

Status of Control

- Leishmaniases represent completely different nosogeographical entities; some could be controlled by present available tools, others require new ones. Unfortunately available tools are often badly used or/and incorrectly evaluated. Currently, there are 21 ongoing vector control programmes and 19 ongoing reservoir control programmes around the world.

Priorities for Control

1. In most of the endemic countries, implementation of a basic level of control called "minimal operations":

   - passive case detection (availability of trained personnel and basic diagnostic facilities);
   - improvement of reporting system;
   - treatment (permanent availability of first line drug at peripheral level).

2. Vector control: high priority is given to the comparative evaluation of alternative vector control methods

   - to reduce morbidity in the main foci of anthroponotic cutaneous leishmaniasis of the Old World (South-Western Asia);
   - to reduce mortality in the main foci of anthroponotic visceral leishmaniasis of the Old World (Indian Subcontinent).

3. Evaluation of feasibility of integrated vector control approach (e.g.visceral leishmaniasis/malaria).

4. Evaluation of new tools relevant to the main eco-epidemiological entities, through the implementation of demonstration projects in countries where the problem is particularly severe.

5. Application at national scale of those tools providing technical and managerial expertise.

6. Elaboration of technical documentation, especially maintenance of a worldwide data base on the distribution, prevalence and public health impact of the various forms of leishmaniasis, and on HIV/leishmaniasis co-infections.

Applied Field Research Priorities

The AFR planning meeting identified as the three top priority areas for applied field research in leishmaniasis the following:

1. Leishmaniasis, migration (urban and rural) and environmental changes including the use of GIS for epidemic predictors.

2. Integrated visceral leishmaniasis control through school children in anthroponotic foci with emphasis on alternative vector control approaches.

3. Health promotion in remote rural communities through leishmaniasis control with women as the key health providers

III. CHAGAS DISEASE

Disease Burden and Public Health Impact

Chagas disease, named after Dr Carlos Chagas the Brazilian physician who first described it in 1909, exists only in the American Continent. It is caused by a flagellate protozoan parasite, *Trypanosoma cruzi*, transmitted to humans by a blood sucking triatomine bug and by blood transfusion.

There are two stages of the human disease : the acute stage appears shortly after the infection. After several years of an asymptomatic period, 27% of those infected develop cardiac lesions which may lead to sudden death, 6 % develop digestive damage mainly megaviscera, and 3% will present peripheral nervous impairment. The remainder 64% will not present any symptomatic clinical picture.

Transmission through vectors

It is estimated that the overall prevalence of human *T.cruzi* infection on the continent reaches 16-18 million cases. Some 90 million people i.e 25% of all the inhabitants of Latin America are at risk of contracting *Trypanosoma cruzi* infection.

Transmission via Blood Transfusion

The rural/urban migration movements that occurred in Latin America in the 1970's and 1980's as a consequence of the urban industrialization and the need for labour force changed the traditional epidemiological pattern of Chagas disease as a rural condition and transformed it into an urban infection that could be transmitted by blood transfusion.

The prevalence of infected blood in selected cities of the continent between 1960 and 1989 varies between 1.7 and 63.0 % which shows that it is much higher than that of Hepatitis or HIV infection. In Santiago, Chile, for instance, the prevalence of Hepatitis-infected blood is 0.4% (ten times lower than the *T.cruzi*-infected blood) and the frequency of HIV-positive blood samples is only 0.01% (400 times lower than the *T.cruzi*-infected blood).

The transmission of Chagas disease via blood transfusion is a threat even for countries where it is not transmitted by vectors as is the case of the USA and Canada where two cases of acute Chagas disease have been reported . In addition, migration of persons infected by *T.cruzi* to non-endemic countries poses a public health problem for the safety of blood transfusions.

Control Targets: 1993 - 1998

Vectorial Transmission

* To interrupt vectorial transmission of *T.cruzi* in the countries of the Southern Cone (Argentina, Brazil, Bolivia, Chile, Paraguay and Uruguay) through the use of chemical vector control tools such as

insecticides, insecticide paints and fumigant canisters, housing improvement and health education within the context of a sustained development of the rural and peri-urban areas.

* To identify areas of high transmission where control measures could later be implemented in the Andean Region (Ecuador, Colombia and Peru) and the Central American countries (El Salvador, Costa Rica, Guatemala, Honduras, Mexico, Nicaragua, and Panama).

Transfusional Transmission:

* To develop legislation requiring screening for *T.cruzi* antibodies of all blood donors from the endemic countries of the Americas where it does not exist (Compulsory legislation for blood screening of *T.cruzi*-infected blood currently exists only in Argentina, Brazil, Honduras, Uruguay and Venezuela.), and to strengthen the current infrastructure within the health services for universal blood screening (HIV, Hepatitis B and *T.cruzi*)

Applied Field Research Priorities

The AFR planning meeting identified as the two top priority areas for applied field research in Chagas disease the following:

1. Evaluation optimal combination of measures to interrupt T.cruzi human transmission, including use of insecticides, improvement of housing, blood bank control and health education, identified and applied in rural and peri-urban areas, in the frame of multinational initiatives (South Cone-on going- Andean and Central American Countries).

2. Identification of risk factors for disease for improving management of 18,000,000 currently infected persons in order to ensure commitment by decision makers.

IV. AFRICAN TRYPANOSOMIASIS

Disease burden and distribution

African trypanosomiasis, or sleeping sickness, is endemic in 36 sub-Saharan African countries. It occurs in some 200 discreet foci, where the resurgence of the disease occurs. At the local level it is an important public health and socio-economic problem with a continuous threat of severe epidemics, which are difficult and costly to control.

Between 15,000 to 20,000 new cases of trypanosomiasis are reported annually. The actual numbers of people suffering from the disease is not known, but considering that less than 10 per cent of the 50 million people at risk are under any form of surveillance at present, a true estimate would likely be in the range of 200 000 to 300 000 per year.

Sleeping sickness is currently a major concern among many countries, particularly in East and Central Africa. The recrudescence of old foci and geographic spread in certain areas have been reported in recent years in the Cameroon, Chad, Congo, and the Republic of Central Africa. In Zaire, where 10 000 patients have been diagnosed annually (about half of the total number of cases reported to WHO) control activities have virtually ceased following the withdrawal of external technical and financial aid, as a result of political problems, and there is a permanent potential risk of a major epidemic. In Sudan, due to the civil and

2. to determine the feasibility and cost-effectiveness of control tools and alternative control strategies.

3. the field testing of new tools for control (drugs, diagnostic and vector control).

VII. ONCHOCERCIASIS

Disease burden

Onchocerciasis or river blindness is endemic in large parts of Africa and in isolated foci in America and Yemen. In many endemic countries, it is a very important public health and socio-economic problem, and recognized as such by the governments concerned. Some 18 million people are believed to be infected with the parasite, *Onchocerca volvulus*, and more than 95% of those infected live in Africa. The disease causes dermal, lymphatic and systemic complications, the most severe of which are eye lesions which may ultimately lead to blindness. It is estimated that more than 40,000 people go blind every year as a result of onchocerciasis, and that their life-expectancy is thus reduced by 10-15 years.

In the savanna, onchocerciasis is not only a major public health problem, but also an significant obstacle to socio-economic development. Fear of the disease has led to the depopulation of relatively fertile river valleys where the vector has its breeding sites and transmission is most intense.

Other, non-ocular, manifestations of onchocerciasis such as skin lesions have received much less attention in the past. Recent studies indicate that onchocercal skin disease can be a very serious social problem, and much more serious than has been appreciated previously.

Disease control and trends

The last decade has seen a decline in the prevalence of onchocerciasis infection and morbidity. This was mainly due to the remarkable success of vector control in the Onchocerciasis Control Programme in West Africa (OCP). The core area of the OCP is no longer under vector control and has entered a new phase without active control and based only on epidemiological surveillance for early detection of possible recrudescence.

The experience of OCP has shown that vector control is feasible but only when it is based on aerial larvicide spraying over a very large area. This makes vector control very costly, too costly to be undertaken by the endemic countries themselves. Until recently, large scale chemotherapy was not an option because of the high risk of severe adverse reactions, and the net result was that the countries outside the OCP had no practical method for onchocerciasis control.

The registration of ivermectin in 1987 as an effective and safe microfilaricide for the treatment of onchocerciasis, and its donation free of charge by the manufacturer, was therefore a major breakthrough. The results of community trials indicated that sustained annual treatment with ivermectin would be sufficient to prevent onchocercal blindness in all endemic areas of the world, even though interruption of transmission may only be feasible in a few areas where the vectors are less efficient. The prevention of severe skin lesions may require a shorter treatment interval but this question needs further study.

Major problems in control

The global impact of ivermectin based control is still unsatisfactory because of the difficulties in providing annual treatment to those who need it. Onchocerciasis is often found in the most remote areas where there are little or no health care facilities. However, the momentum is growing in ivermectin based

control and, with adequate financial and research support, a great reduction in onchocerciasis morbidity is possible during the next decade in all endemic countries of the world.

Applied Field Research Priorities

The AFR planning meeting identified as the two top priority areas for applied field research in onchocerciasis the following:

1. Strategies for ivermectin use, including rapid assessment of endemicity, delivery systems, compliance, monitoring, financing, and long-term epidemiological impact.

2. Ivermectin treatment based strategies for elimination of transmission in the Americas.

VIII. LEPROSY

Disease Burden and Distribution

Leprosy is an important cause of morbidity and consequent physical deformities in most countries of Asia, Africa and Latin America. By the beginning of 1992 there were an estimated 5.5 million cases in the world with about 3.1 million registered for treatment. The number of registered cases at the beginning of 1993 was 2.4 million. Leprosy is endemic with a prevalence of at least 1 in 1000 in over 90 countries where about 2.4 billion people live. Globally, about 500 000 new cases are being detected each year. It is estimated that there are between 2 to 3 million individuals have deformities as a result of leprosy.

Based on registered cases, about 73% of cases are found in Asia, about 13% in Africa, about 13% in Latin America, and less than 1% in the rest of the world.

Status of control

Until the 1980s, leprosy control was based on treating patients with dapsone, with limited results. Based on the recommendations of a WHO Study Group in 1981, the treatment of patients with multidrug therapy (MDT) was introduced in the 1980s in most leprosy endemic countries. By the beginning of 1993, over 4.1 million patients had been cured through MDT and, in addition, about 1.1 million patients were under it. MDT has made a major contribution to the reduction of leprosy prevalence between 1985 and 1993, as reflected by the number of registered cases which came down from 5.4 million in 1985 to 2.4 million in 1993, a reduction of about 55% in eight years. Because of the steady progress being made, WHO is now committed to eliminating leprosy as a public health problem by the year 2000, defining elimination as attaining a level of prevalence below 1 per 10 000 population. Global and regional strategies to attain the elimination goal have been developed and countries have, or are developing, national strategies and plans of action to reach the elimination goal.

Major problems in control

The technology of MDT is working well at present although it is possible that problems such as drug resistance can develop in the future. The impact of MDT on incidence is rather slow due to the long incubation period of the disease. MDT has very little direct impact on the

deformity situation although, together with early case finding, it helps prevent a large number of deformities. National managerial capabilities to organize leprosy control is still weak in several countries and resources, particularly for drugs, is a problem in certain situations in spite of support from international nongovernmental organizations.

Applied Field Research Priorities

The AFR planning meeting identified as the three top priority areas for applied field research in leprosy the following:

1. Improve detection and subsequent treatment of cases of leprosy.

2. Prevention of deformities through early identification and appropriate management of nerve function impairments.

3. Feasibility and cost-effectiveness of alternative treatment regimens.

TDR/SR/INF/94.1

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

Strategic Research in TDR's new structure

A new TDR structure for new priorities

TDR's research targets, and the appropriate management and decision-making structure to reach those targets, have been thoroughly reviewed during 1992-93. A new structure will come into effect from 1st January 1994 to enable TDR to rapidly develop solutions to field problems, to concentrate its efforts on well-focused targets and to respond promptly to new opportunities in science.

TDR's current disease-specific steering committees will be phased out and replaced by a new steering committee and task force structure divided into three main areas: Strategic Research (SR), Product Research and Development (PRD), and Applied Field Research (AFR).

Strategic Research: keeping up with moving targets

Basic research in tropical diseases has to contend with the fact that the characteristics of many of its targets - the parasites and their vectors - are continually evolving, thereby rendering ineffective the tools that have been laboriously developed to control them. In addition, it now has to contend with rapid changes in the environment due to large-scale population movements associated with unplanned or planned development, military conflicts, and many other kinds of disturbance and damage related to human activities.

The resistance of malaria to existing drugs, for example, is developing faster than new drugs are being developed and brought into use. Research has become a race against time which requires continual vigilance in the monitoring of changes in parasites and vectors, and exploration of novel approaches to track these "moving targets" and develop tools to control them.

Jn 6/6/94

However, in parallel with the feverish activity on the part of parasites and vectors, technology for biological research is advancing in leaps and bounds and now offers astounding potential, in molecular biology, immunology and genetic engineering, for the development of more powerful and longer-lasting control tools. TDR needs to keep constantly up-to-date with these new possibilities in order to take advantage immediately of the opportunities which present themselves.

TDR needs to engage the endeavours of the best scientists in all fields, in order to ensure that avenues of research which are likely to lead to discoveries of potential interest for control of the tropical diseases are fully and promptly explored.

Furthermore, knowledge and experience accumulating from disease specific research now needs to be consolidated across diseases, for example, in understanding the interplay of various cytokines. The time has come to exploit the new technologies to unravel the most fundamental molecular intricacies of parasites, their vectors and hosts, with the hope of designing long-lasting control tools.

Goal-directed research

TDR has re-evaluated its priorities in Strategic Research and will focus its support on research which is at the cutting edge of the important new advances and technologies referred to above. TDR's efforts, therefore, will be concentrated in fewer, more targeted areas of basic research. However, in order to ensure the continued generation of research leads for future product development, TDR hopes that the broader areas of basic science underpinning tropical disease research will remain priorities on the agendas of other research organizations.

TDR's basic research programme must ultimately be driven by the needs of endemic communities. For this reason, TDR will support "strategic research" - defined as basic research aimed at developing future tools for the long-term control of the diseases.

Organization of TDR's strategic research

The Steering Committee on Strategic Research (SR) will be responsible for overall management of the work in three areas: the parasite genome, pathogenesis and molecular entomology. (The Coordinator for Strategic Research is F. Modabber.) Each of the SR areas will have its own committee to review proposals:

- Parasite Genome Committee (GENOME), Manager, F.A.S. Kuzoe
- Pathogenesis Committee (PATHO), Manager, N.R. Bergquist
- Molecular Entomology Committee (BCV), Manager, B. Dobrokhotov

The Steering Committee on Strategic Research will meet once a year to review projects and to provide guidance on future priorities.

Priority strategic research in TDR

The major thrust of current activities in TDR's strategic research are outlined below in order that researchers may formulate proposals which are in line with TDR's priorities and which will advance research in the directions indicated. Research proposals which do not appear to fit into any of the areas outlined below but which will contribute significantly to furthering our understanding of the fundamental characteristics and mechanisms of the parasites, hosts and vectors of tropical diseases, will nevertheless be given serious consideration.

Genome mapping

Low resolution physical maps of parasites (1000 units)

With the introduction of high precision robotics, it is expected that the genomes of most, if not all, of the representative TDR pathogens will be sequenced in the next decade. The sequencing of *Plasmodium falciparum, Mycobacterium leprae and Leishmania* is already underway. African trypanosomes are not yet the subject of a large scale sequencing project. Though the *Trypanosoma cruzi* genome has not yet been well characterized, gene targeting experiments have been successfully conducted. The genetic composition of *Caenorhabditis. elegans* has mostly been elucidated and may be useful in mapping other nematodes.

Implementation of new, cost-effective technologies and provision of universally accessible data bases and data management programmes

A group of laboratories, supported by the Wellcome Trust, are collaborating on the malaria genome project and reference libraries are available to all interested scientists. Data are distributed through the Internet, and in printed form for laboratories without access to electronic networks. Similar arrangements are expected to be made for other parasite genome projects. (Data on protein and nucleic acid sequences of *Plasmodium* and *M. leprae* are available through TDR.)

Development of systems for genetic analysis of parasites

The recent advances in genetic manipulation of parasites particularly *Leishmania*, provide a powerful tool for the construction of stable recombinants and for functional analyses. Genetic markers have been introduced into parasites to allow high power selection. Over 20 independent mutants of *Leishmania* have already been obtained through transfection.

Participation of scientists from Developing Endemic Countries, including training.

Participation of DEC scientists is important in all aspects of SR but particularly in genome mapping. The low resolution mapping of selected parasite genomes by developing country laboratories will provide excellent training opportunities for their scientists. With their lower costs, developing country laboratories with the requisite infrastructure and expertise can compete favourably.

Pathogenesis

Mechanisms of protective immunity and consequences for host pathology

These include factors related to host susceptibility and the pathological outcome of the immune response. Diversion of the immune response towards different subsets of CD4 cells (Th1/Th2) has a profound effect on the outcome of many parasitic infections.

- Cytokine interplay in control of infection and disease processes

The precise roles of different cytokines in pathogenic responses remain to be elucidated. However, it has been shown, for a number of parasites, that pathogenic response can be reduced by depletion of some cytokines; that for example, the process of fibrosis in granulomatous response in schistosomiasis is regulated by cytokines; and that the pathogenesis of cerebral malaria is directly related to factors released by the sequestered parasites which induce host cells to generate inflammatory cytokines (see also entomological factors).

- Parasite and human diversity related to pathogenicity

The heterogeneity of disease susceptibility in populations has been documented for all the TDR target diseases. It is unclear as yet whether genetic, environmental or other factors determine the character of immune responsiveness and consequent pathology. Asymptomatic infection is the rule rather than the exception, with most parasites. The mechanism by which pathology is evaded is not known and should be investigated in the field. The role of scientists in endemic countries is crucial.

- Utilization of reconstructed mice with human cells and genes as animal models

Specifically, the development of totally immunodeficient mice (scid mice), has made possible the study of the reaction of human cells to a variety of agents; and likewise, the construction of mice with desired genetic makeup (deletion of genes responsible for cytokines or transfected with human genes) has made possible the study of mechanisms of immunity at a more refined level. These models should be evaluated and exploited to the maximum.

Identification of critical virulence factors (genes) for new drug and vaccine development

By genetic manipulation of parasites, factors responsible for virulence are beginning to be identified (e.g., in *Leishmania*). Similar approaches are needed to identify targets for chemotherapy or candidate vaccines. Parasites themselves elaborate products that affect the host. A trypanosome-derived lymphocyte triggering factor (TLTF) has been isolated which stimulates interferon-gamma production and causes trypanosomes to proliferate. Similar mechanisms may be at work in the pathology of schistosomiasis and filariasis.

Development of *in vitro* model systems to expedite experimentation for vaccine and drug development

For all six diseases, there is a critical need for the development of model systems for experimentation. The development of new technologies for rapid production of large numbers of peptides at low cost, opens a new avenue for drug and vaccine development. Recent research on ivermectin resistance in *Caenorhabditis elegans* provides a valuable paradigm for studies of parasite drug resistance.

Entomological factors affecting pathogenicity

Elucidation of the role of molecules delivered by insects in the initiation of infection and subsequent pathology produced by the parasites might lead to the development of preventive tools. Work on sandfly salivary exudets have indicated the presence of potent inflammatory molecules which are critical for the initiation of a successful leishmanial infection.

Transformation

- development of transformation systems using autonomous and integrated nucleic acid vectors

Transformation/transfection systems are needed for the functional analysis of genes, mechanisms of drug resistance and virulence factors, for studies of biochemical pathways and various aspects of gene regulation, and eventually for the production of attenuated parasites. A transient transfection system has been developed for malaria which is an important first step.

- development of attenuated parasites (via modification of targeted genes)

Leishmania offers a useful model system for stable parasite transformation. One virulent conditional auxotroph of *Leishmania* has been developed as a prototype candidate vaccine. This has been achieved by selectively knocking out dihydrofolate reductase-thymidilate synthetase (DHFR/TS) genes. Similar approaches are beginning to emerge for other parasites.

Molecular entomology

In the light of recent methodological advances, it has become feasible to manipulate vector genomes with the goal of making them incapable of parasite transmission. The availability of a genome map will greatly facilitate the development of targeted approaches for vector manipulation.

Genetic and physical mapping of *A. gambiae* genome

Using identification and localization of microsatellite markers in a recessive sex-linked mutation (white-eye), and combining it with a cytological map of banding patterns, the X chromosome of *A.gambiae* is being mapped. With similar technology and additional transformation and expression systems with different viruses, it may be possible to map autosomal chromosomes.

Development of transposable elements and transformation systems for use in *A. gambiae*

Current efforts focus on the development of mosquito transformation systems, using murine retroviruses, and densoviruses. In addition, the search is under way to define functional elements (transposones), using high spontaneous mutations.

Population structure and gene flow studies for *A. gambiae* in the field

Population genetic studies on the size of reproductive units and the extent of gene flow will produce information needed for future approaches to vector control. These studies must be performed in the field and the involvement of scientists from endemic countries is encouraged.

Genetic and physioethological studies of host-vector and vector-parasite interactions

The understanding of genetic regulation of insect behaviour is a prerequisite to development of modified vectors. The analysis of oviposition behaviour and mechanisms for assortative versus non-assortative mating is an important research area. Other subjects for study include: patterns of dispersal, determinants of anthrophily, endophagy and endophily, non-blood feeding behaviour and patterns of temporal organization.

How to apply

Types of research grant

Researchers are invited to submit proposals to the Office of the Director, TDR. There are three main types of research grants awarded by TDR:

1. Research and Development Grant (proposal form TDR/RP(B)FORM/91)

This is the main type of research grant awarded by TDR. Proposals for research support are considered at meetings of the appropriate Steering Committee/Task Force (see above). For consideration at any particular Steering Committee/Task Force meeting, proposals must reach the Steering Committee/Task Force Manager at least two calendar months before the scheduled date of that meeting. Dates will be advertised in TDR News.

2. Director's Initiative Fund (proposal form TDR/DIF(B)FORM/92)

The Director's Initiative Fund (DIF) is intended for (1) projects for which rapid funding is essential, (2) projects which may be preparatory to larger scale projects, or (3) projects which focus on new lines of research relevant to disease control that may not fall within the current research plans of TDR's new Steering Committees/Task Forces. Proposals for support from the Director's Initiative Fund may be submitted at any time; they are reviewed by the Director, TDR, in consultation with technical experts. DIF grants may not exceed US$15,000 and are not renewable.

3. Project Development Grant (proposal from TDR/PDG(B)FORM/92)

Project Development Grants are designed to assist scientists of developing countries to formulate technically sound research proposals suitable for consideration for financial support by the various new Steering Committees/Task Forces. The grants may thus be used for collection of baseline or preparatory data, to initiate preliminary research, or to seek the advice of recognized experts. These grants are open only to nationals of developing countries who wish to pursue research on one or more of the TDR target diseases. Proposals for Project Development Grants may be submitted at any time; they are reviewed by the Director, TDR, in consultation with technical experts. Project Development Grants may not exceed US$10,000 and are not renewable.

TDR also supports a range of institutional strengthening grants and training grants. Further information on these are available on request from:

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Switzerland
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TDR/PI/AFR2/93.1
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UNDP/World Bank/WHO Special Programme for Research & Training in Tropical Diseases (TDR)

Applied Field Research in TDR's new structure

A new TDR structure for new priorities

TDR's research targets, and the appropriate management and decision-making structure to reach those targets, have been thoroughly reviewed during 1992-93. A new structure will go into effect from 1st January 1994 to enable TDR to rapidly develop solutions to field problems, to concentrate its efforts on well-focused targets and to respond promptly to new opportunities in science.

TDR's current disease-specific steering committees will be phased out and replaced by a new steering committee and task force structure divided into three main areas: Strategic Research (SR), Product Research and Development (PRD), and Applied Field Research (AFR). There will be greater emphasis on Applied Field Research and the budget allocation for this area will be increased.

Applied field research: from products to solutions

Research undertaken by TDR during the first 18 years of its existence has resulted in the development of many new tools, some of which have led to significant improvements in tropical disease control. However, experience has shown that the mere introduction of a new tool or *product* is not enough, and there is a growing recognition of the need for applied field research to develop and evaluate comprehensive *solutions* to the problems of tropical diseases. This includes multidisciplinary research aimed at the development of cost-effective and sustainable control strategies, and operational research to facilitate the implementation and subsequent improvement of these strategies.

Applied field research also aims to better clarify the priority needs in the field. These needs are two-fold: first, the needs of the endemic communities; and second, the needs of control programmes operating at the district or national level. The proper understanding of these needs requires adequate information on the public health and socio-economic importance of the tropical diseases, the availability and use of health facilities in endemic countries, both modern and traditional, and on current problems in control strategy development, implementation and evaluation. Such information is often lacking, but there is increasing recognition of the importance of field research aimed at clarifying these issues.

Objectives of applied field research

The objectives of TDR's applied field research may thus be defined as follows:

- To identify the major problems and needs of endemic communities and control programmes relating to tropical diseases.
- To develop comprehensive solutions to these problems.
- To identify the most cost-effective way of introducing the solutions into the health system and to facilitate their implementation, evaluation and modification when appropriate.
- To coordinate closely with the SR and PRD areas of TDR to inform them about priority needs in basic research and for new products respectively, and to assess the feasibility of development, and the utility of promising leads and new products.

The organization of applied field research in TDR

To meet the above objectives, an Applied Field Research component has been established in TDR which will cover all six TDR diseases* and will incorporate the activities of the previous Social and Economic Research (SER), Epidemiology and Field Research (EFR), and Field Research in Malaria (FIELDMAL) components.

The activities of this new component will be directed by a Steering Committee which will meet once a year to review progress and identify AFR priorities. The Committee will be supported by the TDR Secretariat in a new unit (TDR/AFR), which will initially consist of the secretariat of the former SER, FIELDMAL, and EFR components.

* The six TDR diseases are malaria, schistosomiasis, the leishmaniases, the filariases including lymphatic filariasis and onchocerciasis, the trypanosomiases, including African trypanosomiasis and Chagas disease, and leprosy.

The AFR Steering Committee itself will consist of 14-16 members, half of whom will be drawn from tropical disease control and half from the various AFR disciplines, with a strong representation of the social and economic sciences. Each of the six TDR diseases will be represented by at least one expert on the Committee. All WHO regions with endemic tropical diseases will also be represented and at least two-thirds of committee members will be from disease endemic countries. The Steering Committee will meet, for the first time in February 1994, for a period of five days to review AFR plans, activities and new proposals.

As an important objective of AFR is to fund research that will be *of practical use* to disease control programmes, there will be close collaboration and coordination with the WHO Division of Control of Tropical Diseases (CTD). The Directors of CTD and TDR will jointly manage the TDR/AFR component.

A dual approach to project funding

A detailed Strategic Plan for Applied Field Research - available on request from TDR Communications (see address on the last page) - was developed during a major interdisciplinary meeting held in Geneva in May 1993.

In accordance with the Plan, the *majority* of AFR activities will be undertaken through a new approach referred to as **AFR Initiatives**, which will be managed by expert **Task Forces**; the *remainder* will be undertaken through the current TDR approach of **investigator-initiated research proposals** (see page 6).

AFR Initiatives

AFR Initiatives will be the most important of AFR activities and will receive the major share of the AFR operations budget. The ultimate objective of each **AFR Initiative** is to have a *significant and demonstrable impact* on disease control.

An Initiative aims to develop a practical solution, within a time-limited period, to an identified priority problem and to ensure that this solution can be, and to the extent possible, actually is, applied to combat the problem.

For each **AFR Initiative**, a multidisciplinary **Task Force** of experts will be appointed to plan, initiate and supervise the operations. Members of the **Task Force** will not themselves carry out research. But they will both directly commission research, and review proposals for research which fall within their remit. Each **Task Force** will follow a *workplan* which will be made available from TDR Communications to potential applicants.

The first AFR Initiatives, together with brief highlights of their workplans, are listed in Table 1.

TABLE 1

The first AFR Initiatives and highlights of their workplans

Gender research - Secretary: C. Vlassoff
Development and testing of a "Healthy Women's Counselling Guide". Determination of the nature and extent of genital complications of urinary schistosomiasis and lymphatic filariasis, and ways of improving medical workers' understanding, detection and treatment of these. Determination of ways of decreasing special risks of pregnancy and tropical diseases. Investigation of women's knowledge, attitudes and practices regarding leishmaniasis.

School-aged children - Secretary: D. Evans
Rapid assessment of the prevalence of helminths using school-based questionnaires. Communication strategies for the control of helminths and other conditions. Optimal treatment/re-treatment schedules, methods of measuring morbidity and the impact of treatment on morbidity.

Tropical diseases and health financing - Secretary: D. Evans
The impact of changes in financing mechanisms on: treatment seeking behaviour, provider behaviour, perceptions of providers and patients about these changes. Comparison of patterns of health service use for treatment of tropical diseases with general patterns of use, and comparison of vulnerable groups with others. Mechanisms for achieving more appropriate control using a mix of public/private sectors as necessary.

Tropical diseases and environment - Secretary: M. Gomes
Correlation between changes in agricultural systems and risk of tropical diseases. Identification of options for interventions, such as land management practices which bear systematic risks. Economic valuation of the impact of environmental changes on social welfare and human health. Identification and assessment of policies that reduce or minimize the negative health effects of environmental change or stimulate the joint pursuit of environmental and health improvements.

Operational research on anti-malarials in South-east Asia - Secretary: M. Gomes.
Improvement of treatment and compliance with existing multi-dose anti-malarials; evaluation of operational experience with artemisinin (qinghaosu) derivatives.

TABLE 1
(continued)

Operational research on onchocerciasis - Secretary: H. Remme
Operational research in support of ivermectin-based control, including the development of rapid methods for assessing and mapping endemicity; cost-effective delivery mechanisms; social and public health importance of skin disease; effect of repeated treatment on ocular and skin disease; rapid methods for monitoring of control; elimination strategies in Latin America.

Bednets - Secretary: J. Cattani
Evaluation of the impact of impregnated bednets and curtains in various locations in Africa; following resolution of efficacy issues, operational research to assess implementation issues and the potential role of this intervention in control strategies at national, district and local levels.

Sick child - Secretary: J. Cattani
Development of integrated case management strategies and training materials for health workers, for the five illnesses (pneumonia, diarrhoea, malaria, measles and malnutrition) responsible for four out of five deaths in under-fives in developing countries.

Filariasis field trials - Secretary: C.P. Ramachandran
Effect of existing chemotherapeutic tools on micro- and macrofilariae. Simple, sustainable strategies for morbidity and transmission control. Quantitative relationships between vectors, parasites and hosts. Public health importance of filarial disease.

Operational research on Chagas disease - Secretary: A. Moncayo
Improved methods of vector control and blood bank control in multi-country comparative studies; cost-effectiveness and acceptability studies of new vector control tools; methods for rapid assessment of public health impact of control activities.

African trypanosomiasis surveillance - Secretary: F.A.S. Kuzoe
Development of cost-effective methods of surveillance of populations at risk, using available tools of diagnosis and vector control, and their integration into health care systems. Optimization of current treatment regimens of available drugs.

Leprosy field studies - Secretary: S.K. Noordeen
The search for generic solutions to problems of accessibility of multidrug therapy in certain geographic areas and among certain population groups.

8/11/96 ? write to TDR to get list of publications & reprints of possible regarding implementation issues

Investigator-initiated research proposals

Despite the prominence that AFR will give to its own AFR Initiatives, and in recognition of the importance of new ideas generated and initiated from the field, AFR will take care to remain open to **investigator-initiated research proposals** which fall outside the precise areas of the AFR Initiatives themselves.

Although the largest share of the AFR budget will be allocated to AFR Initiatives, adequate funds will be kept to allow for investigator-initiated proposals.

Among investigator-initiated proposals, first priority will be given to those falling within a broader list of AFR priority topics for applied field research (see Table 2).

Four steps to apply for AFR grants

Step 1: Consult the table of *The first AFR Initiatives and highlights of their workplans* (Table 1) to determine whether your research interest is already covered by an AFR Initiative.

Step 2: If you *believe* your interest *may* be covered by an Initiative, do not submit a proposal immediately but *first request the relevant workplan* from the appropriate task force secretary (named in Table 1). In your request for the workplan, it would be useful if you would, at the same time, indicate your own areas of interest and expertise. In this way, task force secretaries may be able to propose particular research projects, already planned by the task force, that you might like to undertake.

Step 3: If you believe your research interest is *not* covered by an AFR Initiative, consult the list of AFR priority topics (see Table 2) for guidance on AFR's wider priorities. You may then develop a proposal which should be submitted directly to the AFR Steering Committee (Secretary: H. Remme). Your proposal will be reviewed by the Steering Committee during its annual meeting.

Step 4: If you still have a great idea for *a research topic which may significantly contribute to tropical disease control*, but do not see it covered by any of the priority topics listed in Tables 1 or 2, AFR will nevertheless give it serious attention. Proposals for such research should be submitted to the AFR Steering Committee as for **Step 3** above.

Research proposals to be reviewed during the next AFR Steering Committee meeting in February 1994 should reach TDR no later than 7 December 1993. Decisions by Task Forces, on the other hand, will be made according to timetables described in their workplans, or available from the Task Force Secretary.

Applications for TDR grants should be made in English or French.

TABLE 2

Priority topics for Applied Field Research

Disease control within health care delivery systems

- Preventive measures for malaria infection and disease at individual/community levels.
- Optimal combination of measures to interrupt *T.cruzi* human transmission.
- Cost-effective preventive and treatment strategies, and managerial tools for schistosomiasis control.
- Strategies for ivermectin use in onchocerciasis control in Africa.
- Malaria case management at peripheral-hospital levels focusing on children and women.
- New strategies to improve the organization and management of control programmes.
- Improved detection and subsequent treatment of leprosy.
- Integrated control of visceral leishmaniasis through school-children.
- Feasibility and cost-effectiveness of control tools and strategies for lymphatic filariasis.
- Integration into Primary Health Care and sustainability of control programmes.
- Improvement of health care delivery systems as related to tropical disease control.
- Drug delivery systems for disease requiring repeated mass treatment.
- Ivermectin-based control strategies for the elimination of onchocerciasis in the Americas.
- Field-testing of new tools for lymphatic filariasis control.
- Feasibility and cost effectiveness of alternative treatment regimens in leprosy.
- Optimization of current treatment regimens in African trypanosomiasis.
- Prevention of deformities by early identification and appropriate management of nerve function impairments in leprosy.

Health care financing

- The impact of changes in financing mechanisms on the availability of funds for tropical disease control, on treatment seeking behaviour and on prevention.
- Provider and community perceptions of these impacts.
- The role of the non-government sector in tropical disease control.
- Developing more effective and efficient control using a mix of public and private sectors, where appropriate, in both provision and financing.

Gender and tropical diseases

- Research on women's recognition and understanding of disease, including malaria, schistosomiasis, African sleeping sickness and Chagas disease.
- Operational research to improve services and care provided to women at health centres.
- Cultural factors impeding women's access to and use of treatment facilities.
- Gender differences in stigma associated with tropical diseases (leprosy, cutaneous leishmaniasis, lymphatic filariasis, schistosomiasis), that hamper early detection.

TABLE 2
(continued)

Environment and demographic changes

- Leishmaniasis, migration and environmental changes (including use of geographical information systems)
- Disease control within rapid socio-economic, demographic and environmental changes
- Effect of ecological changes on transmission of vector-borne diseases.
- Agricultural development and rice cultivation as related to malaria and schistosomiasis.

Information, education, communication (IEC) from perspectives of communities and policy makers

- Information, education and communication strategies for tropical disease control.
- Community compliance and participation in control.
- The school as entry point for tropical disease control.
- Health promotion through leishmaniasis control with women as the key health providers.

Development of rapid assessment procedures (RAP)

- RAP for distribution of diseases requiring intervention at community level.
- RAP for monitoring and evaluation of control.
- Cost-effective community and individual diagnostic strategies in schistosomiasis.

Surveillance and impact assessment

- Surveillance and health information systems for local and national levels, especially for malaria.
- Epidemiological modelling for surveillance and control.
- Methods and managerial tools for cost-effective surveillance and control of African trypanosomiasis.
- Socio-economic and public health importance of lymphatic filariasis.
- Epidemiological assessment of morbidity and of the impact of control of schistosomiasis.

* * *

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