Pan American Health Organization

PAHO/ACMR 16/9
Original: English

SIXTEENTH MEETING OF THE
PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

Washington, D.C.
11-15 July 1977

SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES

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WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

TDR/WP/76.4

ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES*

PREFACE

Many millions of the people living in tropical regions of the world are cut off from the mainstream of social and economic progress. Victims of a heavy burden of disease as well as of harsh economic circumstances, they are not free to choose and plan a better future.

There is a growing awareness of these special problems of the tropical countries, and one main channel of response is through the work of the World Health Organization (WHO) and the United Nations Development Programme (UNDP). It is clear that health is an integral part of development; healthy people are more effective and, in turn, development is essential to provide the resources necessary for improved health. Health and development are therefore inextricably interlinked and any strategy for improvement must be based upon this reality.

There is a wide range of existing knowledge and technology to be coordinated and exploited. A new dam to improve water supplies and provide irrigation and power, training in practical ways to avoid disease, better use of available drugs and vaccines, and a more favourable social and economic climate - these are some of the factors which will bring change and benefit. But in considering all the efforts now being made, it is clear that there is one aspect which, although of high priority, is not receiving adequate attention. The technical tools which are now available to control many of the tropical diseases are inadequate, or ineffective. It has, for example, repeatedly been shown that the insecticides and drugs which are available for malaria control are unable to stop transmission of the disease throughout very large areas of Africa. Present remedies for other major tropical diseases -- schistosomiasis, filariasis, trypanosomiasis, leprosy and leishmaniasis -- are not practicable for large-scale control in many tropical countries. New tools are therefore needed.

WHO and UNDP recently launched a new Special Programme for Research and Training in Tropical Diseases to obtain these new tools. Fundamental to this Programme is the involvement of the world's best scientists and research institutes. But of equal importance is the fullest possible involvement of the tropical countries themselves so that they may become competent, through training and research, to deal with their own disease problems.

*Presented by Dr. Adetokunbo O. Lucas, Director, Special Programme for Research and Training in Tropical Diseases, World Health Organization, Geneva, Switzerland.

The Special Programme has been described in non-technical terms in the booklet "Tropical Diseases", available from WHO. The present books provide a detailed technical account, including evaluation of disease problems and approaches to control, and a description of organizational and financial aspects of the Programme. The success of the Special Programme will depend on the work of many people. It will demand not only commitment, determination and talent, but a broad vision, a willingness to adapt, and a spirit of both cooperation and competition to achieve the desired goals. In the final analysis, the Special Programme is a framework for human cooperation, which must be flexible enough to promote initiative and enterprise, realistic enough to respond to urgent needs, and effective enough to achieve its goals. The plans here described have been evolved through much consultation; we believe that they provide a basis to begin.

Dr Halfdan Mahler
Director-General
World Health Organization

Mr Bradford Morse
Administrator
United Nations Development Programme

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TDR/WP/76.5

ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES

1. INTRODUCTION TO THE SPECIAL PROGRAMME

Malaria and other parasitic and infectious diseases are a major impediment to the alleviation of poverty in developing countries of the tropics. Several of these diseases are increasing in prevalence, notably malaria in the Indian sub-continent, and schistosomiasis in association with irrigation schemes. The tools which are at present available to control these diseases are too crude, too cumbersome and too costly for effective widespread use. As costs continue to escalate, application of present technologies, inefficient as they are, will advance even further beyond the economic means of the poorer countries. Strategies to improve the living conditions of the many millions of poor people in developing countries must include the control of tropical diseases. Strategies for disease control must, in turn, include the development of new and more effective tools.

The present level of research and development to obtain the tools which are needed is inadequate. For example, no major new drugs for the treatment of any of the tropical diseases appeared within the past three decades, and there are no vaccines. To promote this research, the World Health Organization and the United Nations Development Programme have jointly sponsored a Special Programme for Research and Training in Tropical Diseases (hereafter called the Special Programme). This is designed to equip health services in tropical countries with new, effective and low-cost tools for the control of tropical diseases. The Special Programme is global in concept and in plan, and has been developed in response to a demand for coordinated research on control of the diseases first expressed in the World Health Assembly resolution WHA 27.52 of 1974. The strategies to be used were re-examined in 1976 and endorsed by the World Health Assembly resolution WHA 29.71. The Special Programme described here has been evolved on the basis of numerous consultations; it is one of cooperation with and service to governments.

The sponsors of the Special Programme recognize the health and socio-economic burdens which these and other diseases impose on the peoples of the tropical countries. They also recognize the complexity of the problems of the control of these diseases. The tools which will be developed must be appropriate to control disease in the varied social, economic and environmental circumstances of the tropical regions. Research in the Special Programme will, therefore, be based on studies in tropical countries, which will identify needs and specify the tools which are required to meet these needs, as well as assessing the effectiveness of new tools in a variety of tropical environments. All relevant aspects of biomedical science will be applied to develop the new tools. Thus, research and development will be carried out in any place in the world where it can be most effectively pursued.

Integrated with the research programme, a training programme will be established to increase the self-reliance of tropical countries in research on technological aspects of disease control. There is a scarcity in many tropical countries of indigenous scientists and technicians to work on disease control problems. The Special Programme

will incorporate training into its research activities and will strengthen specific centres in tropical countries to carry out research and training. In this way, the Special Programme will assist in developing the key manpower needed to enable these countries to develop their own policies and programmes for research on disease control. The initial major focus of these strengthening activities will be in the continent of Africa.

The Special Programme calls for a major effort in research and training on a global scale. Although technical advances and the creation of new research potential in tropical countries may well be achieved in the early years of the Programme, the full benefits of the control of disease cannot be expected to arise within a short period of time. The Programme is conceived as a long-term endeavour lasting twenty years or more.

2. OBJECTIVES

The Special Programme has two interdependent objectives.

2.1 Development of improved tools needed to control tropical diseases - To develop new preventive, diagnostic, therapeutic and vector control methods specifically suited to prevent, treat and control selected tropical diseases in the countries most affected by them. The new methods must be susceptible to implementation:

- at a cost that can be borne by developing countries;
- requiring minimal skills or specialized supervision; and
- in a manner which allows their integration into the health services, especially the primary health care systems of developing countries.

2.2 Strengthening of biomedical research capability in tropical countries - To strengthen research capability in the countries most affected by tropical diseases through training in biomedical sciences and various forms of institutional support. Biomedical research capability in tropical countries must be strengthened because major activities in the specification, development and testing of new tools must occur in the tropical countries where the diseases are endemic, to ensure that these tools are effective in controlling the target diseases in these countries.

3. SCOPE OF OPERATIONS

3.1 Diseases - The initial six diseases which the Special Programme embraces in its scope, in order of priority, are:

- malaria
- schistosomiasis
- filariasis (including onchocerciasis)
- trypanosomiasis (including African sleeping sickness and South American Chagas' disease)
- leprosy
- leishmaniasis

3.2 Technical approaches - The activities of the Special Programme are directed towards the development of any practical tool needed to solve the problems of the selected

diseases. Development will be focused on the following:

- drugs
- vaccines
- methods for biological control of vectors
- diagnostic tests which are simple to perform

Research will therefore concentrate on:

- chemotherapy and chemoprophylaxis
- immunotherapy and immunoprophylaxis
- biological control of vectors
- diagnostic aspects, especially immunodiagnosis

To bring all relevant biomedical knowledge together in a goal-oriented multidisciplinary attack on these diseases will involve researchers from all relevant areas of the biomedical and social sciences. All avenues will be considered in the development of new tools. Full attention will be given to the application of new advances in fundamental biological sciences such as immunology, cell biology and biochemistry. Epidemiology and operational research will serve both to provide specifications of the tools to be developed and to assess their effectiveness in use. Research will also be undertaken in other relevant areas of the biomedical, clinical and social sciences including nutrition, economics, anthropology and education.

3.3 Manpower and institution strengthening - Tropical diseases, especially those transmitted by insect vectors, are intimately related to many aspects of human society and the environment. Disease problems and opportunities for control vary according to social, economic and ecological factors. The strategy of the Special Programme is therefore to base research on practical problems and opportunities for disease control as they occur in different countries. Fundamental to this strategy is emphasis on the maximum possible involvement of workers in the tropical countries, to increase national competence in research on disease control. At the same time, the technical competence of the industrially developed countries is required.

The policy of the Special Programme with respect to training and manpower development is based on national requirements and career opportunities. The Programme will identify and strengthen specific centres for research and training in tropical countries, based so far as possible on existing institutions. These centres will train workers in key disciplines, who themselves will later train others to provide a "multiplier" effect. The centres involved in research and training, both in the tropics and elsewhere, will be linked together in a network to achieve a common goal, thereby making the best use of resources for training and research.

3.4 The extent of research and development activities - The Special Programme will strengthen, coordinate and supplement relevant existing research and training programmes. The Special Programme will develop new tools, to the point where they are proved effective by clinical and field trials. The tools will then become available to national programmes, with advice and assistance in their use available from WHO, for example, through such programmes as the Expanded Programme for Immunization. WHO will ensure that the research is directed towards priority problems in disease control and provide continuity between the development of a tool and its utilization.

4. OPERATIONAL STRATEGY

4.1 Research planning, implementation and evaluation will be the responsibility of Scientific Working Groups, composed of leading scientists selected on a world-wide basis for their competence in disease and research fields. The research will itself be performed in the most appropriate facilities in the world, with a preference for the tropical countries. Whenever possible, research projects will include a training component.

4.2 Training and institution strengthening to promote research competence will be based so far as possible on existing institutions in tropical countries, and will be developed in relation to national plans for research and career structures. Training needs will be identified for all types of manpower necessary to achieve the goals of the Programme, including both scientists and technologists. A variety of training methods will be used, including on-the-job training, courses, and fellowships.

4.3 WHO provides manpower to develop and operate the Special Programme. This is a co-ordinated activity involving all relevant existing Divisions of WHO, including the Divisions of Malaria and other Parasitic Diseases, Communicable Diseases, Vector Biology and Control, and the Office of Research Promotion and Development. A small group (Tropical Diseases Research) is responsible for overall scientific coordination and management.

4.4 The entire Special Programme will be subject to annual review by a Scientific Technical and Advisory Committee, which will determine priorities and evaluate progress.

5. CONCLUSIONS

How may such a Programme be conducted most efficiently on a world-wide scale? Clearly some aspects such as training and epidemiological and operational research will differ according to the needs of different countries and regions. For these, so far as possible, activities must be nationally or regionally based so as best to respond to problems and opportunities. The Regional Offices of WHO are now establishing research priorities and plans for their regions and so far as these concern the diseases included in the Programme, they will be coordinated within the activities of the Programme.

Some aspects of the Programme clearly require work on a global level, including many aspects of the development of vaccines and drugs, and administration and financial management. The Special Programme will use the resources of WHO to operate wherever appropriate in the world to attain a given objective most quickly and effectively.

A question has been raised concerning the possible hazard of success. Tropical diseases may be important factors in the balance between populations and their environments. If tropical diseases were controlled, would there not be an excessive growth of population with consequences perhaps more harmful to human development than the diseases themselves? The premise of this question is by no means generally established. WHO is responsible for the promotion of human health, and does not subscribe to the view that disease is either a necessary or an effective factor in population control. The Special Programme aims to improve the control of tropical diseases. The large WHO Human Reproduction Programme aims to make reproduction a matter of choice rather than chance. These two programmes are to be seen together as a balanced response by WHO to meet the needs of tropical populations.

This introduction has aimed to give a brief overview of the Special Programme, and in so doing, has summarized many aspects which are presented in detail in subsequent papers in these books.

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TDR/WP/76.5a

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PREPARATION OF THE DISEASE AND TRANS-DISEASE POSITION PAPERS

The disease and trans-disease position papers were prepared by WHO staff and consultants and are substantially based on discussions with experts and on prior reports of WHO and other meetings. The papers show the nature and extent of the diseases and of the problems of their control. They also indicate specific lines of research to obtain improved tools. In some cases, e.g., the immunology of leprosy, the indications are firmly based on the programme of an existing Scientific Working Group. In other cases, the proposals are provisional, and will be further developed by the Scientific Working Groups when they meet.

All papers were sent to a panel of experts for reviews and comments. The names of the panelists are indicated on each paper. The great majority of panel members gave a general endorsement of the views expressed in the papers. Many members provided helpful detailed criticism and suggestions which were incorporated so far as possible into the final text. However, the final texts were not seen by members before printing, and no member is responsible for any or all of the statements made in these pages.

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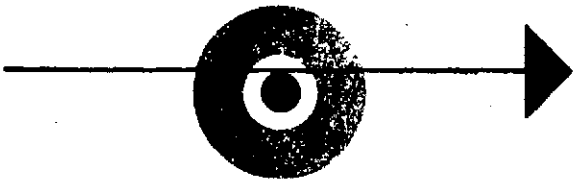

special programme for research and training in tropical diseases

TDR/PK/76.1
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AIMS AND ATTRIBUTES OF THE SPECIAL PROGRAMME

1. INTRODUCTION

In 1973, the seed of an idea for a Special Programme for Research and Training in Tropical Diseases was sown in WHO. After considerable discussion and refinement, the Programme's aims were endorsed by the World Health Assembly, and at a meeting of participating agencies held in Geneva in October 1975, it was launched for a phase of more detailed planning and pilot activities in 1976, with WHO and UNDP as joint sponsors.

The idea of the Special Programme arose in response to the fact that, in the field of tropical diseases, certain major problems gravely hamper progress:

- Despite the remarkable advances in medical science over the past half century, parasitic diseases still threaten more than a thousand million people in the tropical countries, and in many regions they appear to be increasing in both prevalence and severity;

- The technologies at present available for control of these diseases fall far short of the ideal. For example, in malaria, chloroquine-resistant strains are now widespread and no really satisfactory substitute drug has been identified. Similarly, the range of safe and effective chemicals for the control of disease vectors is very limited. Furthermore, there is no vaccine available to protect human populations from any of the parasitic diseases;

- Among the academic community and the pharmaceutical industry, there is diminishing rather than increasing research activity in the field of tropical diseases;

- Neither the funds available to WHO in its regular budget, nor the funds granted by national research councils, philanthropic organizations and other research funding bodies, appear adequate to support the research and training effort required to remedy the situation. An estimated $30 million per year is presently available for world biomedical research in tropical diseases, a sum surely not commensurate with the magnitude of the task, particularly when compared with the estimated 50-fold amount spent annually on cancer research;

- In addition to the pressing need for new and more cost-effective means of control technologies, there is also a requirement for short-term operational research to find more effective ways of applying the present knowledge so as to reduce disease transmission and control disease incidence.

In October 1975, many experts in tropical disease, national and international aid, medical research and economic development met to consider the Programme. They were united in a desire to alleviate the human suffering caused by these diseases and to aid the economies of tropical countries by providing their citizens with better health. WHO and UNDP were heartened by the encouraging preliminary responses and by the constructive criticisms of the draft proposals received at that meeting. Over the past two years, with the aid of generous financial support from some of the donors, WHO has been able to conduct an extensive and coordinated review of the tropical health situation through consultations with eminent scientists and other experts from outside the organization. This process of consultation and review is continuing throughout 1976; the revised plans presented in December 1976 to the meeting of Programme participants will represent the synthesized views of over a hundred outside experts, including many of the most prominent workers in tropical disease research, thus lending great scientific authority to the research content of the Programme.

In October 1975, at the WHO/UNDP meeting of heads of agencies, two documents of a preliminary nature were presented: one on the disease problems, the other on the strategy for research and training. These documents were scrutinized by the participants and recommendations made for the development of a work plan, one for structural management and a budget presentation.

To meet these requirements, new documentation was prepared; this document explains in summary:

- why the Special Programme for Research and Training in Tropical Diseases is urgently needed;
- why six diseases (malaria, schistosomiasis, filariasis, trypanosomiasis, leishmaniasis and leprosy) have been given priority over other common tropical problems;
- what the objectives of the Special Programme are; and
- what measures are being taken to achieve them.

The Special Programme calls for a major effort of research and training to be put into effect on a global scale, with the initial emphasis on the African continent, and with an estimated annual budget of the order of US $20 million. The Programme will be a long-term one. Although technical advances and the creation of new research potential in tropical countries may well be achieved in the early years of the Programme, the full benefits for the control of disease cannot be expected to arise within a short period of time. Therefore, from the outset, the Programme must be seen as a long-term endeavour lasting 20 years or more.

In recent years efforts in the field of tropical diseases research have been directed towards stimulating and coordinating promising lines of research. Much scientific progress has been made in this way, and the results have already been applied against parasitic diseases in some endemic areas. However, when attempts were made to apply them on a nation-wide scale, many of the new control methods developed proved to be beyond the financial and manpower resources of tropical countries. The continuing demand for stop-gap control efforts, chemoprophylaxis, and hospital and out-patient services against parasitic diseases, will remain a heavy burden on the health budgets of tropical countries until new, more effective, and economically feasible methods for mass control become available.

In the field of tropical diseases, it is clear that the present research scene is far from ideal. The effort is disconnected, unnecessary duplication of work exists, and above all many potentially important leads are not being imaginatively explored.

A New Approach

Over the past decade, several nations have embarked on more structured and planned, goal-oriented medical research programmes. The WHO Special Programme will be a well planned, coordinated and international research programme having sharply focussed objectives. It will retain the flexibility and imaginativeness of investigator-initiated research by harnessing leading scientists into Scientific Working Groups, charged with both planning and implementing functions, and ready and able to modify the strategy as changing circumstances and unexpected breakthroughs demand. WHO, this community of 150 nations, is in a more favourable position than is any individual nation or philanthropic group to mount a truly major effort in tropical disease research. Through its Advisory Committee on Medical Research (ACMR) and the recently-established regional ACMRs, as well as its Expert Panels, it has access to the research leaders of many nations. Through its activities of helping Member States in disease control, WHO can ensure that research proceeds along lines relevant to the needs and capacities of all the afflicted countries. Its international status places it in a good position to embark on clinical trials that may have to cross national barriers, and it can provide assurance to Member States on questions of safety, efficacy and ethics. WHO's experience in world-wide disease eradication programmes prepares it for the speedy and efficient application of new technology arising from the research.

2. OBJECTIVES OF THE SPECIAL PROGRAMME

The Special Programme aims to develop methods specifically suited to the countries affected by tropical diseases, which will both cure tropical diseases and protect populations from infection with the proviso that, as far as possible, the methods devised shall be capable of implementation:

- at a cost bearable to the poorest country;
- while requiring minimal skills and supervision; and
- in a manner that permits them to be easily integrated into health delivery systems and/or the public health service.

The Special Programme also aims to strengthen biomedical research capabilities in tropical countries so that they can solve these disease problems.

3. REASONS FOR SELECTION OF THE SIX DISEASES

The six diseases chosen for attention in the Special Programme include most of the major human parasitic infections encountered in the tropical zone. They are the root-evils of tropical pathology. All are infections of long duration, except when they end abruptly in death. They are widespread and may affect every member of the community. Although they are now almost unknown to those living in the industrialized countries of the temperate zones, the total number of people suffering from their effects in the developing regions of the tropics runs into several hundreds of millions, many of whom have multiple infections.

Five of the diseases are in fact groups of diseases. There are four species of malaria parasite which attack man, four schistosome species, eight different filarial parasites (including the one causing onchocerciasis), three forms of trypanosomiasis, and at least three types of leishmaniasis.

Some of the diseases are killers, rapidly fatal in a matter of hours, as in the case of falciparum malaria, which remains the main cause of infant and child mortality in the tropics. Others will kill after a few weeks or months of illness, as African trypanosomiasis (sleeping sickness), which remains a constant threat capable of repeating the terrible epidemic at the beginning of this century. Others may kill only after a long drawn-out illness, as in kala azar (leishmaniasis), Chagas' disease (South American trypanosomiasis) or intestinal schistosomiasis. Finally, there are those which never kill directly, but lead to chronic, debilitating, disabling or disfiguring conditions - urinary schistosomiasis, filarial infections causing river blindness and elephantiasis, espundia (American leishmaniasis), and leprosy.

The six diseases interfere also with the development of tropical countries. The wet season, when the farms must be worked, coincides with the peak of malaria transmission. Irrigation projects are beset by the hazards of increased transmission of schistosomiasis. Hydro-electric schemes may increase the risks of onchocerciasis (river blindness) which may itself prevent cultivation of fertile riverine lands. Trypanosomiasis continues to prevent the effective use of vast areas of potential pasturage in Africa. All these infections thus contribute to malnutrition in the population, while at the same time malnutrition decreases resistance to the diseases themselves.

The six diseases are caused by a variety of parasites with complex life cycles, representing several distinct models of disease: insect-borne protozoa (malaria parasites, trypanosomes, Leishmania), insect-borne helminths (the filariae), snail-transmitted helminths (schistosomes), and contagious intra-cellular bacteria (leprosy bacilli). Most of them can be transmitted naturally only in the tropics, where the ambient temperature is high enough to permit their development in the intermediate host. But the very fact that invertebrate vectors are involved means that the parasites are susceptible to attack both inside and outside the human host.

These are diseases which, except in certain special and limited circumstances, have not yet been successfully controlled with the means currently available. For some of them, the present methods of control and treatment are frankly inadequate; for others they tend to be too costly for widespread practical application, or there is insufficient trained manpower to put them into effect, or they are not acceptable to the population. For most of the six diseases, vector control methods are hampered by the increasing cost of pesticides, by insecticide resistance, and by the risk of environmental pollution.

Curative treatment with the drugs at present available is prolonged, difficult, and often fraught with danger for the patient. For some, means of prevention by chemo-prophylaxis are non-existent; for others, notably malaria, drugs are becoming increasingly ineffective, due to resistance. As already noted, no vaccine has yet been developed

against any of them. To a great extent, this is because most of the organisms involved cannot yet be cultivated in vitro although very important advances have been made recently. Thus, in contrast to many bacteria and viruses, these organisms are difficult and costly to manipulate in the laboratory, for either the development of vaccines or the screening of drugs. Some of them cannot yet be transmitted to experimental animals, other than certain higher primates.

4. JUSTIFICATIONS FOR THE SPECIAL PROGRAMME

Economic Aspects

The sixth and seventh special sessions of the UN General Assembly dealt with the need to establish a new international economic order capable of better serving the needs of the developing countries. It stands to reason that a work force plagued by chronic ill health will be handicapped in its attempts at economic progress. Surely any new economic approach should include the provision of better health, even though it may be difficult to quantify the probable benefits.

Epidemiological, sociological and economic baseline data on the six diseases are lacking in most of the countries afflicted by them. This lack, combined with inadequacy of methods presently available for assessing the economic consequences of ill health in the tropics, makes it impossible to present the economic impact of the diseases on a "profit and loss" basis. It is also difficult to calculate the total amount of money spent by the various governments on the cure, prevention and control of these diseases. However, the following general points appear germane.

In the light of present knowledge of the morbidity, disability and mortality caused by the six diseases, and of the resulting need for medical treatment, disease control and prevention, there can be no doubt that the size of the problem is formidable. It is the more so since the younger productive section of the population is often that which is worst affected. This reduces earning potential and actual work outputs to a substantial degree and, in turn, aggravates poverty.

The Programme should secure and utilize funds over and above those that countries would allocate for their own internal interest. The research should be planned efficiently, keeping the costs of communication and application as low as possible so that full advantage can be taken of new knowledge. A reduction in the cost of tropical diseases control should be a product not only of biomedical research and development, but also of changes in methods of delivering direct services. It would not be a step towards efficiency if the research programme were to develop complex approaches that would be expensive to deliver to the masses of the people. An efficient research effort should develop methods that could be applied widely and at low cost per person in terms of manpower and equipment. It should complement improvements in the organization of primary health care, the end product of both being widespread health protection for the people.

Research in Relation to Disease Control

It must be emphasized that in the struggle against tropical diseases the two activities of research and control are continuous and indivisible. Each disease control project depends, for its operational justification, on the biomedical and biological research activities which preceded it. In turn, each control project poses further questions, the answers to which will be found only by additional research, often in other fields of investigation. Neither in practice nor conceptually should there be any dichotomy between the complementary elements of research and control.

One must also recognize the essential unity of the many components that make up what is loosely termed "research". In medical research, laboratory-based, clinical and field activities are all inter-related in the sense that an advance in one frequently leads to subsequent advances in the others. In addition, the basic sciences, such as biochemistry, immunology and genetics, are closely inter-related, and activities in these disciplines provide essential background components for the totality of research. There is thus a broad continuum of investigatory effort, which may be labelled at one stage as "research" and at another stage as "control".

Parasites, whether unicellular or multicellular, are highly complex. Their interactions with the defence mechanisms of their hosts are complicated, and not yet thoroughly understood. Whereas immense progress has been made over the last two decades in the fields of cell and molecular biology, little attention has been given to the vital relationship between parasitic organisms and their hosts' defense mechanisms. Thousands of scientists in temperate lands are working on cell biology, using the most refined and sophisticated tools. All too few of them are working on the complex nature of parasites and, of these, only a limited proportion are engaged in work on the parasites of man which have such important practical applications in the tropics.

During the past 25 years, WHO has both catalyzed the international research effort and sponsored control measures in tropical diseases. The technical tools at the disposal of the Organization have been used to the fullest extent possible. Weak links in the complicated transmission cycles of tropical parasitic infections have been located, and control efforts have been concentrated at these points. Undoubtedly, some major successes in disease control have resulted. Malaria has been controlled in parts of Central and South America and in some other tropical countries. Onchocerciasis has been eradicated from the main foci in Kenya, and Bancroftian filariasis controlled on some islands in the Pacific Ocean. Trypanosomiasis has been held in check since the early 1920's by continuous control efforts in several countries. However, schistosomiasis has so far been controlled only in sub-tropical areas, such as Japan and the People's Republic of China.

Unfortunately, in other circumstances, technical inadequacies and the constraints imposed by operational, socio-cultural, political and economic factors have contributed to failure. This, in turn, indicates that new methods need to be developed which will be acceptable and practicable in the circumstances under which they have to be used.

Herein lies the justification for the Special Programme for Research and Training in Tropical Diseases, which will represent an intensive, innovative and long-term goal-directed research effort, exploiting promising breakthroughs towards new knowledge and new control methods. It will mobilize the world-wide scientific community and, by bringing the powerful influence of biomedical research to bear on tropical diseases, should make significant contributions to knowledge in this field. It will supplement the current WHO research programme, which is based on small grants-in-aid, comparable perhaps to seed-money and used largely in prospecting for new leads. It will not be accompanied by any reduction in WHO's current operational control efforts, such as the Onchocerciasis Control Programme in West Africa, or the UNDP/WHO project to control schistosomiasis in man-made lakes. On the other hand, as the results of the research efforts of the Special Programme become available, they will be incorporated into the control programmes continuously pursued by the Organization. The Special Programme and WHO's current research and control programmes are thus complementary and not exclusive. Through coordinated planning and action, each will reinforce the other, and control technology can thus be expected to benefit both in degree and in rapidity of application.

5. CHARACTERISTICS OF THE SPECIAL PROGRAMME

How will the Special Programme for Research and Training in Tropical Diseases be planned and carried out so as to solve the real problems of tropical disease control?

Planning, Co-ordination, Monitoring, and Evaluation of Research

The Special Programme will coordinate its activities with international, national and philanthropic research agencies already active in the same fields. Scientific Working Groups (SWGs), whose membership will be selected from among the world's best scientific minds, will be responsible for planning and monitoring the research programme, to be carried out in a world-wide network of participating laboratories, in such a way as to supplement and strengthen existing efforts. These SWGs will be a novel feature of the Special Programme. They will comprise "peer groups" of international experts in the subjects concerned, who will be able to promote communication between those versed in the newer biological sciences and those concerned more directly with the problems of disease control in the tropics. An SWG will be established to cover each field where the knowledge required to control the diseases appears to be lacking, so that an intensified research effort can be focused thereon under the Special Programme. The SWGs will define the problems to be attacked, plan and implement research projects, and monitor and evaluate them as they proceed.

The proper monitoring and evaluation of the Special Programme will be assured by a two-fold mechanism:

- A Scientific and Technical Advisory Committee (STAC) composed of individuals with broad knowledge of the diseases and their socio-economic impact in tropical countries, will determine priorities among the different diseases and allocate funds accordingly. This top-level body will ensure an authoritative and balanced overall approach.

- Within each disease, and for trans-disease research areas, the "peer group" SWGs will judge the scientific merit, soundness, and probability of success of each research project, before it is included in the Programme. They will also undertake regular periodic evaluations of the projects.

The research programme of each SWG will thus be reoriented periodically in the light of what has been achieved and of the new possibilities opened up as a result of Special Programme or other research. The reorientation may take the form of a shift in the research strategy within an SWG or the disestablishment of some Scientific Working Groups and the establishment of others. In this way, whenever a line of research has been well tried but has not proved fruitful, it will be stopped. Likewise, unexpected discoveries can be immediately exploited.

A network of collaborating laboratories will carry out the research programmes of the SWGs. Existing laboratories, wherever situated, will be selected for their competence to carry out the proposed research programme, and these will be in the developed world, as well as in developing countries. As an integral part of the programme, a partnership with all developing countries is envisaged and thus there will be a strengthening of laboratories in tropical countries with an initial emphasis on Africa. Qualification, competence and experience in the research discipline concerned, as well as physical capacity, will be principles governing the allocation of research tasks.

The Promotion of Research Skills in the Tropical Countries

At the outset and for some time to come, it will be necessary for many workers from temperate countries to become involved in the Programme, but more important in the long run will be the need for increased and active participation by scientists from the tropical countries concerned. It would be naive to imagine that parasitic diseases in the tropics will rapidly be brought under control. An acceptable containment of the six diseases will demand a continuing effort by the tropical countries themselves over a

prolonged period of time. This will require increasing numbers of scientists, and the provision of facilities for their work. The Special Programme aims to assist the tropical countries in their plans to develop their own scientific resources by supporting effective formal and in-service training of clinical and laboratory scientists, as well as field and laboratory technical staff. Laboratory capabilities will also be built up.

Since the Special Programme will be world-wide, its manpower requirements may be considered from two aspects -- manpower in the developing countries of the tropics and manpower in the industrialized countries of temperate regions. A keystone in the development of the Special Programme will be the strengthening of research on disease control in tropical countries, so that these countries will themselves become capable of tackling the disease control problems which face them. For this they will require additional scientific manpower, and the Special Programme will assist in the training of scientists and technologists according to plans worked out with national authorities. The aim will be to identify key disciplines and train individuals who will subsequently be active both in research and in the training of others, so as to build up a cadre of scientists specified according to national requirements. These activities will be based on national plans for research on disease control, including provision of career structures for the trained personnel.

With regard to the industrialized countries, it will be necessary to show the scientific communities in these countries that there is a pressing need to apply their scientific skills to the solution of problems presented by tropical diseases. It will also be essential that national career structures be developed for those who are willing to devote the major portion of their working lives to the study of tropical diseases. The Special Programme will promote collaboration in research and training between the industrialized and the tropical countries.

The training component of the Special Programme must be tailored especially to the needs of tropical countries. The traditional use of fellowships tenable at centres of excellence in temperate countries should be minimal. Training will be conducted mainly in a network of centres on a regional basis. The use of regional training facilities will help to minimize the external movement of staff at all levels and thus reduce the loss of trained personnel to their respective countries.

As in the design of scientific studies on the various diseases, the training and institution strengthening aspects of the Special Programme will also be periodically subject to expert planning and review, bearing in mind that scientific training requires more than just the development of skills in the use and maintenance of sophisticated instruments and techniques.

6. PARTICIPATION IN THE SPECIAL PROGRAMME

Country Participation

Participation of a country in the Special Programme will depend on:

- one or more of the six diseases being a significant health problem in that country and/or
- the availability in the country of suitable facilities for research and training in tropical parasitic and communicable diseases, and, of course
- a willingness of the country to be involved.

For a successful operation, it is essential that national staff at all professional levels be assigned to the Programme for the full duration of an individual research project. If a scientific or medical research council exists in a country where cooperative research is to be carried out under the Special Programme, its close cooperation and guidance will be sought. When required, the Special Programme will assist national health authorities in the study of diseases of public health importance that are relevant to the objectives of the Programme.

Participation of the Academic Community

The Special Programme seeks to involve the world's biomedical research community in the fight against tropical communicable diseases. Happily, all indications are that there exists within the universities and medical research institutes, a fund of expertise and idealism ready to be tapped. The pilot activities of the Special Programme have already received unstinting support from outside scientists, and there is a long tradition which ensures that the calls of WHO upon the resources of academia are accorded the highest priority. The Special Programme will doubtless benefit from the high standing of WHO in this respect throughout the world.

Participation of the Pharmaceutical Industry

WHO has always had good relations with the pharmaceutical industry, especially at the technical level, where continuous communication exists between those sections of WHO concerned with the control of parasitic diseases and the representatives of industry concerned with the research and development of pharmaceuticals and pesticides.

There is no substitute for the facilities and expertise of industry in the search for new chemotherapeutic agents to control those parasitic diseases which concern the Special Programme. On the other hand, WHO can provide facilities for the clinico-pharmacological evaluation of new drugs, thereby demonstrating to industry that an outlet exists for their products, and at the same time minimizing the delay between pre-clinical experimentation and clinical use.

The Special Programme, by providing the necessary assurance to the pharmaceutical industry that WHO has a continuing interest in anti-parasitic drugs, may serve to halt the accelerating decline in the research and development of these essential products.

WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

TDR/WP/76.20

ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND
TRAINING IN TROPICAL DISEASES

THE ROLE OF BIOMEDICAL RESEARCH IN THE OVERALL STRATEGY OF THE SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES

by

Professor G. J. V. Nossal
Member, ACMR; Consultant to the Special Programme
for Research and Training in Tropical Diseases

EXPERT REVIEW PANEL:[1]

Dr N. Ansari, formerly Chief, Parasitic Diseases, Division of Communicable Diseases, WHO, Geneva, Switzerland

Professor C. de Duve, ICP International Institute of Cellular and Molecular Pathology, Brussels, Belgium

Dr J. H. Humphrey, National Institute for Medical Research, London, England

Professor J. Lederberg, Stanford University Medical Center, Stanford, California, United States of America

Professor I. Molenaar, University of Groningen, Groningen, Netherlands

Professor D. F. H. Wallach, Tufts New England School of Medicine, Boston, Massachusetts, United States of America

Professor L. M. Deane, Universidade de São Paulo, São Paulo, Brazil

Professor V. Ramalingaswami, All India Institute of Medical Sciences, New Delhi, India

[1] For details concerning the procedure of review, please see INTRODUCTION: PREPARATION OF THE DISEASE AND TRANS-DISEASE POSITION PAPERS.

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CONTENTS

1. Summary

This paper deals with the future role of basic biomedical science in parasitism research. Fundamental biology has made enormous strides in the last quarter century and our knowledge of cellular and molecular functioning is now profound. Although a number of pioneers have applied the concepts and tools of the new biology to problems of parasitism with good results, the overall effort in fundamental aspects of tropical disease research remains poorly funded and coordinated, particularly by comparison with basic research in fields such as tumour biology.

We are concerned here with just five examples from among the kinds of basic biomedical research which could flower into application in the coming 10 to 15 years:

(a) growth of parasites or parasite-derived molecules in tissue cultures;

(b) novel drug approaches such as the targeting of drugs which kill parasites to the particular cells and tissues which harbour the parasites;

(c) identification and isolation of antigens, the parasite cell membrane molecules which would help in making antiparasite vaccines;

(d) ecological methods of destroying parasite vectors or the parasites themselves; and

(e) investigation of the disease producing side-effects of the body's immune attack against parasites.

Other subjects of outstanding promise include characterization of parasite biochemistry and metabolism; exploitation of any metabolic quirks for the intelligent design of new drugs; modern approaches to the molecular biology and genetics of parasite life cycles; and vector genetics. These could all profit from examination by the sharp tools of the "new biology", but have not been dealt with at length for reasons of space.

As many other broad areas could be promoted with equal merit, it will be the task of an appropriate group or groups of advisers to plan and fund the biomedical research proposals. One possible administrative mechanism, involving the creation of a Biomedical Science Working Group, is briefly discussed. For purposes of discussion, an annual budget of US$ 2 million is suggested for this working group, US$ 1.5 million being for research and US$ 0.5 million for training. Obviously, a more detailed budget will have to be prepared following the establishment of a management structure for the programme.

2. Introduction

> "Science always has its two aspects, its intellectual aspect as knowledge and its practical aspect as control . . . every science arrives at a stage during which it makes its main broad contributions to practical human affairs. Biology is clearly on the verge of such a phase."
>
> Julian Huxley, 1931

Looked at half a century later, Huxley's words have a truly prophetic ring. Over this pivotal period in the history of medicine, deep insights have been gained into the nature of life processes. This new knowledge of the functioning of the healthy body has in turn led to discovery of the causes of many diseases. As a result, both preventive medicine and therapeutics have at last reached the level of objective sciences. What has been the harvest? Infectious diseases have lost most of their terror in the developed world, thanks to vaccines and antibiotics. The triumphs of anaesthesiology, surgery and obstetrics, resting on an infrastructure of science, have minimized the impact of trauma, both external and internal. Rational replacement therapy has made possible the control of endocrine disturbances, including diabetes, of vitamin deficiencies and certain inherited defects. The discovery of antidepressants, major tranquillizers and other neuroactive drugs, though not yet definitively curing mental illness, has substantially reduced suffering

For the residual major killers of the developed world - heart and arterial diseases, cancer and chronic degenerative diseases - research has so far produced only partial answers, but massive programmes of attack on them are underway in many countries.

In most cases, these practical advances have resulted from efforts over a wide spectrum of endeavour. Fundamental scientists such as biochemists and physiologists have revealed how cells and organs function. Microbiologists, pathologists, entomologists and clinicians have put together the pieces of knowledge for an understanding of the causative mechanisms in disease. Organic chemists and pharmacologists have produced and tested the new miracle drugs. Physicians, epidemiologists and statisticians have chosen the best amongst competing remedies. Thus Huxley's prophecy has come true, not by chance, but out of a conscious, planned commitment of skilled manpower and resources to medical research, as defined in the broadest sense.

The field of tropical diseases has, of course, been touched by this revolution. Some valuable control measures have become available through research, and knowledge about the diseases and the organisms causing them has increased considerably. However, the current medical research effort in parasitic diseases is only a tiny fraction of that in, for example, cancer or heart disease. Obviously, then, the comparatively modest progress in the development of new control technologies for tropical diseases is in no sense an indictment of the small number of dedicated professional researchers in this field. Rather, it is because they are so few, a lack due to unbalanced global priorities in health research. A change in the scale of global thinking about research into parasitism is required. This research will involve both a search for new weapons and studies of how to make better use of the existing technologies. For the purpose of this paper, the term parasitic diseases refers to all six diseases of the Programme, including the bacterial disease leprosy.

3. Biomedical science as a tool in practical progress

The WHO Special Programme for Research and Training in Tropical Diseases is conceived as a giant step towards rectifying this imbalance. It does not seek simply to augment the existing, and vital, control efforts of many countries. Rather, it seeks to provide new and more effective weapons through modern research, a need amply documented in accompanying papers pointing up the benefits of vaccines; of safer, cheaper drugs; and of ecological methods of vector control. The purpose of the present paper is to show that, while clearly defined short- and medium-term research projects may provide some of these tools, the programme will not succeed without the important element of long-term fundamental biomedical research to provide new and more cost-effective "high technologies".

The fact is that, in many instances, we simply do not know enough about the biology of the parasite and the mechanisms by which it eludes the defences of the human host to allow us to plan intelligent intervention. We know much about the life cycles of the parasites and the ecological habitats of the vectors, about modes of transmission and the clinical features of human disease. In contrast, we know relatively little about the molecular organization and metabolic peculiarities of the parasites, of how to find the chinks in their biochemical armour. Moreover, our knowledge of detailed pathological mechanisms in parasitic disease is limited. We know that in the majority of instances the patient mounts some kind of an immune attack against the parasite, but usually without totally eliminating the infection. What are the limitations in immune defences against parasitic diseases? By what evolutionary tricks has the parasite learnt to evade host immunity? These are the types of questions which must be answered by applying recent advances in fundamental research to this field.

4. Multidisciplinary research involving newer biosciences

The tropical medicine expert cannot perform this research alone. To understand and describe phenomena in the continuum of knowledge, we break problems up into arbitrary segments to be solved by diverse professional disciplines. A comprehensive view, then, requires an integration of these specialized fragments of knowledge. In sharp contrast to the fructification of virology, parasitology has so far had little concerted input from fundamental scientists working in the newer, frontier disciplines. One aim of the Special Programme is to assure this input by involving in parasitism research the keenest minds in sciences such as molecular biology, cell biology, genetics and cellular immunology, thereby providing the depth of insight and integrated knowledge required. The recently-developed and powerful technologies of these disciplines have not yet been applied to any great extent in parasitism. Tools such as the scanning electron microscope, capable of determining sub-microscopic shapes in minute detail, and the transmission electron microscope, for immunoelectron microscopy study of parasite protein, both helping us to understand how parasites may penetrate host cells; fractionation methods which can separate different classes of cells from one another, and could thus help in isolating pure parasites from infected tissue; microradiochemical methods for analyzing the structure of proteins, which could help to identify the antigens important for vaccine production; genetic techniques for fusing cells to each other or for introducing foreign genetic materials - all of these represent resources waiting to be harnessed to the task of understanding parasites and identifying their Achilles' heels.

We are conscious of the need to ensure the most efficient coupling of these new tools to public health requirements. The Programme will enlist key leaders in the important fundamental biosciences to join with tropical disease experts in scientific working groups to define the lines of necessary research and to involve the appropriate scientists in carrying it out, a concept expanded later in this text.

This type of interdisciplinary research is already the norm in fields such as cancer and organ transplantation. The WHO Advisory Committee on Medical Research has stated clearly and unequivocally that the time is ripe to take a similar approach to tropical communicable disease. The scientific community is geared to respond to the challenge. It remains only to begin the operation.

Though axiomatic to the working scientist, the continuum between fundamental and applied research and the dependence of major practical advances on an infrastructure of basic scientific knowledge are still unfamiliar concepts to most non-scientists. Concrete examples will therefore be particularly illuminating and will comprise the greater part of this paper.

The author of this paper is an immunologist, and thus the examples given are in no sense intended to be representative of what biomedical research in its totality can offer to this subject area. In particular, the examples almost totally ignore the discipline of biochemistry, which is the dominant discipline in biomedicine. Readers with chemical or pharmacological backgrounds are asked to excuse this deficit. A biochemically-oriented paper of equal length could readily have been generated by another consultant. The involvement of the world's biochemical community (most of which is only peripherally aware of the existence and scope of this study area) will be one of the early tasks facing the Biomedical Sciences Working Group (see Section 11).

5. Mass growth of parasites outside their hosts

The principle of immunization, so spectacularly successful in the control of many viral and bacterial diseases, depends on injecting micro-organisms or their components into the body to stimulate the antibody-forming system. Various tricks are used to render the injection itself harmless. The microbe may be killed, as is the case for whooping-cough vaccine; a non-virulent relative may substitute for the actual disease-causing organism,

as in smallpox vaccine; or the toxin of the particular bacteria may be produced by culturing the microbes, and then rendered harmless prior to injection into the body, as is done for tetanus toxoid. For all these tricks, the vaccine developer faces the problem of attaining the requisite purity. To begin with, we must have available in bulk a source of micro-organisms free from contaminating molecules. This is relatively easy to attain in the case of bacteria, which grow in artificial media of simple chemicals. It is less easy for viruses, which grow only inside living cells. One of the great advances making possible the development of poliomyelitis vaccine came through purely academic research when, after a painstaking period of development, scientists succeeded in growing mammalian cells outside the body in glass or plastic vessels, a technique known as tissue culture. This, in turn, allowed viruses to be grown inside tissue cultured cells, under controlled conditions and to high concentrations. With an assured source of virus, the way towards vaccine development was open, though much further research was needed to separate the virus from the host cells and attenuate it, that is, to render it less virulent, or to kill it.

(a) Tissue culture growth of parasites

There are as yet no vaccines available for the control of parasitic diseases of man. The reasons for this are many, and their development will be no simple task. One limiting factor is the lack of large-scale sources of pure parasites to act as antigenic material. It is here that growth of parasites in tissue culture could fill a critical gap.

Most parasites undergo complex life cycles, their different life stages developing in different hosts. One logical vaccine approach would be to immunize against that particular life stage of the parasite which is injected into the body through the bite of the insect vector. This would mean culturing the insect stage of the parasites in the insect host's cells. Unfortunately, however, tissue culture of insects' cells is not yet developed to near the degree of sophistication which has been achieved for mammalian tissue culture. Moreover, the part of the life cycle which takes place inside a particular vector forms only a portion of the complex totality of events leading to the perpetuation of the parasite species. Hence, mass tissue culture growth may require growing the parasites to different life stages in different tissue cultures.

Reviewing developments in malaria immunology, a recent WHO Scientific Group recommended high priority for research on tissue culture of different malarial stages in various appropriate cell types. This would require the close collaboration of parasitologists and cell biologists reminiscent of the productive collaboration between virologists and cell biologists a quarter of a century ago which resulted in development of a vaccine for poliomyelitis.

(b) Heterokaryons as antigen sources

Straightforward tissue culture is not the only feasible approach to mass production of parasite antigens. Some newer techniques of cellular and molecular biology could provide even more spectacular approaches to the problem, one such technique being cell fusion. Cells are bounded by a rather oily outer layer or membrane, and when two cells are brought into close contact, as for example by glueing them together with a sticky virus, they sometimes fuse, much like two oily droplets would do. Amazingly, even when the two cells are from sources as different as man and mouse, the fused cell, or heterokaryon, not infrequently continues to grow, making proteins and other molecules characteristic of both the original cells. It is not yet certain whether it will be feasible to fuse single-celled parasites with other cells known to grow well in tissue culture, or whether, following that, such heterokaryons would then grow well and in addition express the particular parasite's antigenicity. If this could be done, a convenient source of antigen would emerge through the relevant basic research.

(c) Parasite antigens and recombinant DNA

Even more advanced research could lead to genetic techniques of making parasite antigens with still faster-growing entities, such as harmless bacteria. Very recently a new research technology has emerged which can create recombinant DNA molecules. This means recombining the molecules comprising the genes from two different organisms to produce a gene with a new combination of characteristics. With these methods, it has proved feasible to insert genetic specifications for the production of certain proteins into species quite different from those that formed the proteins in nature. Thus far the new technology has been used mainly for research into bacteria and viruses, but among the logical extension of its application now widely predicted is production of human proteins by the modification of simple gut bacteria called E. coli.

Little is known at present about the genetic constitution of parasites. Once this knowledge builds up, however, it would not be far-fetched to imagine the day when parasite genes coding for important antigens could be transferred to harmless bacteria such as E. coli, thus making these fast-growing bacteria the source of antigenic material.

For this reason, research into the genetics and molecular biology of parasites represents the type of long-term research which would merit planning and support under the Special Programme.

6. Golden bullets through cell biology

In the early years of this century, Paul Ehrlich dreamed of "golden bullets", drugs that would find and destroy pathogenic micro-organisms without harm to the host. Antibiotics and some other compounds come close to Ehrlich's vision but, unfortunately, many of the drugs in current use for treatment of tropical diseases fall far short of the ideal. Indeed, some exhibit so much toxicity and side-reaction in man that it is doubtful they could pass the licensing standards for new drugs required by most drug regulatory agencies today.

Much of the search for new, better and safer drugs will follow the traditional approach of the pharmaceutical industry, the systematic screening of promising organic chemicals in artificial model systems mimicking the human diseases. Nevertheless, there is good reason to attack the problem from another direction at the same time: using new knowledge in cell biology to design new modes of treatment which exploit the special metabolic and molecular characteristics of the parasite.

(a) Lysosomotropic drugs

One illustration of the latter approach is the research being performed at the new International Institute of Cellular and Molecular Pathology in Belgium as a Special Programme pilot project under the direction of Professor C. de Duve. This is based on the concept that the golden bullet may be found through lysosomotropic drugs. These are drugs linked to molecular carriers which behave much as guided missiles, naturally and preferentially "homing" to the tiny, submicroscopic stomachs inside cells, known as lysosomes. These lysosomes contain enzymes capable of digesting the food or foreign particles consumed by the cell. In the case of a lysosomotropic drug, the enzyme would split the drug off from its carrier, releasing it inside the cell. Single-celled parasites such as the trypanosomes are known to feed mainly through taking in particles from their surroundings and digesting them in lysosomes. They are probably more greedy than most of the cells of the host, and thus a lysosomotropic drug could be designed to reach a higher concentration in them than in the host cells. Furthermore, it is quite possible that different parasites have special tastes, and the inert carrier portion of the drug could then be "seasoned" to appeal to such tastes.

Amongst the greediest cells of the host, and thus the ones in the normal human body in which lysosomotropic drugs would reach the highest levels, are the macrophages. These are

scavenger cells whose duty is the sequestering of foreign particles, of dead or dying body cells, and of the invading micro-organisms in lysosomes. There exists a group of diseases, amongst them tuberculosis, typhoid fever, leprosy and some parasitic diseases such as Chagas' disease and leishmaniasis, in which the invading micro-organisms defy the scavenger cells. They are indeed taken up into macrophage lysosomes, but instead of being digested there, they neutralize or otherwise foil the threat of the digestive enzymes. As a result, the macrophage becomes a refuge and a breeding ground for the pathogen, and consequently a possible target for lysosomotropic drugs.

The lysosomotropic drug concept has its limitations and is not equally applicable to all parasitic diseases. As single-celled parasites spend little time outside host cells, in most cases drugs need to go first into the host cell and thence to the parasite. Thus, for the red cell forms of the malaria parasite, the approach would be limited, as red cells lack lysosomes. Other ways by which drugs may be selectively concentrated inside cells need to be considered.

In the short time during which pilot projects have been in operation under the Special Programme, Professor de Duve, Professor A. Trouet and their colleagues have made exciting progress towards validating the usefulness of the lysosomotropic drug approach to trypanosomiasis in animal models. It is hoped that this type of research can be extended considerably as the Special Programme moves into high gear.

(b) Liposomes

Liposomes are small artificial sacs of fluid surrounded by a layer of fatty material similar to that of cell membranes. They are made in the test tube and the composition of the fluid and fatty components can be varied. For example, the charge on the surface of the liposome can be controlled, and various substances can be incorporated into either their fatty or watery parts.

Liposomes can be used as carriers of drugs and, by varying their composition, it is possible to control their fate in the body. For example, liposomes coated with certain proteins are concentrated in the mononuclear phagocytic system, where Leishmania protozoa and leprosy bacilli multiply; and liposomes with certain other compositions are taken up by liver parenchymal cells, the site where some malaria parasites multiply at certain stages of their life cycle. This concept may, therefore, be applicable to parasite chemotherapy, concentrating the drug in tissues where the parasites are present, so that toxic side effects are reduced.

Moreover, when liposomes come into contact with living cells, their fate varies. Liposomes of certain compositions fuse with the plasma membranes of the cells, discharging their contents directly into the cytoplasm. Liposomes of other compositions enter secondary lysosomes where they are digested and their contents released. This too may be useful in chemotherapy. For example, some rickettsiae multiply in the cytoplasm whereas mycobacteria multiply in secondary lysosomes, and liposome-associated drugs may be used to achieve concentration of drugs in the cellular compartment where they are needed.

Another application of liposomes is as adjuvants, or stimuli to enhanced immune reaction. Antigens associated with liposomes are found to elicit higher defensive antibody levels than are elicited by antigen alone. Since the liposomes do not provoke any reactions in tissues at the site of injection and are completely biodegradable, they can be safely used in humans whereas the traditional Freund's adjuvant, based on mineral oil, cannot because it causes severe inflammation.

Originally designed as model membrane systems for academic studies of membrane permeability, liposomes have emerged as interesting biological tools with promising applications to practical situations.

(c) Drug-antibody complexes as golden bullets

It is frequent in clinical medicine to find that neither one of two treatments completely controls a disease, but that a combination of the two succeeds. In some parasitic diseases, we know that antibody molecules, made by the host against the parasite, can limit the havoc, but they frequently fail to totally eliminate the parasite. We know that drugs can also help, but often only in doses that cause toxicity. One approach, already being extensively explored in the cancer field but not yet in parasitism, is to construct a complex of drug and antibody.

This would involve preparation of antibody against the parasite and coupling it to an anti-parasitic drug in such a way as to achieve greatest effectiveness of both drug and antibody at the site of infection, while avoiding a toxic dosage of the drug. This guided missile preparation would "home" to any site in the body where parasites were present, thus making a small dose more effective by getting it to its target without side effect in other organs. A problem here will be to accomplish the coupling of drug and antibody without destroying the delicate antibody vehicle. Such a targeted missile might do its job of destroying the parasite much better than the saturation bombing approach of the drug would do it alone.

(d) Drug combinations

Based on a knowledge of cell biology and biochemistry, drugs of limited efficacy when used by themselves could be used in combination or sequentially. The first antibiotic administered may, for example, be 99.9% effective, leaving 0.1% of live infection because a few of the bacteria were not susceptible to it. This 0.1% is then attacked with another antibiotic, leaving a minimal proportion of it alive, and may be followed by a third or even a fourth drug to obtain a cure of the disease. This principle has already amply proven its value in bacterial antibiosis and more recently in the treatment of leukaemia. It should hold equally well in parasitic diseases, and indeed some progress has already been made as, for example, in the use of pyrimethamine in combination with sulphonamides in the treatment of resistant malaria. However, it could be considerably extended as our knowledge of parasite biochemistry grows.

7. Molecular biology and parasite receptors

Within the specialized world of scientific research, progress is now so rapid and widespread that the word "revolutionary" has become a cliché. Nevertheless, there is no other way to describe the effect molecular biology has had on our perception of virtually every biological phenomenon. The realization of the essential unity, in chemical terms, of all life processes; the universality of the genetic code throughout the whole plant and animal kingdoms; the many common features in the internal organization of different cells - all have been powerful unifying factors in modern biology, transcending sub-specialty barriers and permitting a discovery in one specialty to diffuse rapidly to its neighbours.

One field benefiting greatly from this new approach is that of cell membranes. The outer skin of a cell was once thought of as merely a passive wall. Now we know that the limiting membrane is a dynamic, functional structure, vitally involved in helping the cell to respond to its environment and to interact with its neighbours. In the field of parasitism, it is known that certain parasites attach to host cells by means of specific cell membrane proteins, and if these specific molecules are removed or covered up by coating them with antibody, the attachment can no longer occur. For example, in malaria, the so-called Duffy blood group antigen appears to function in permitting parasites to attach to red cells. If this critical attaching interaction between the receptors of the parasites and those of the red cells containing Duffy antigen is foiled, the parasite is unable to enter the host cell for nourishment, and therefore dies. For this reason, antibodies to key cell membrane receptors of the parasites may be particularly useful in disease eradication. Accordingly, much interest would attach to experimental vaccines consisting of purified receptor molecules, which could induce the formation of anti-receptor antibodies.

The sequential steps required to realize such a hope are readily apparent. Parasites would have to be grown in reasonable numbers. They would then have to be separated from the cells or tissues in which they had grown. Fortunately, sophisticated biophysical techniques exist for separating various kinds of mammalian cells from one another, and these would have to be adapted to the problem. Next, the separated, purified parasite cells would have to be split open, and the outer cell membranes, comprising less than 1% of the cell's weight, would have to be separated from the rest of the cell. Then the many different proteins residing in that membrane would have to be extracted from the oily milieu in which they live and the particular receptor of interest would have to be separated from all the other, irrelevant membrane proteins. Such a purified receptor molecule could itself act as a vaccine. One can envisage, though more distantly, that the most active portion of the molecule, the immunodominant determinants, could be broken off, analyzed as to detailed structure, and then synthetically produced. The type of scenario outlined above is by no means science fiction. Most of the technologies for its component parts are at hand and have already been applied to related problems in mammalian biology.

There is a second reason for devoting special attention to the cell membranes of both parasite and parasitized cells. Should a key event in parasitism be a lock-and-key like recognition of specific molecules on the two respective cell membranes, then this union might be impeded by drugs with an appropriate structure. In fact, drugs could be tailor-made by organic chemists expert in "structure-activity" relationships so that they would interfere with such interaction.

Cancer biology has many similarities to parasite biology. In both cases, cells that are foreign, at least to a degree, are proliferating in the body; yet, the host defences alone are inadequate to conquer the foreigners. In current cancer research, enormous attention is being paid to cancer cell surface antigens and to the tumor cell membrane generally. It would now appear most appropriate to adopt a similarly active approach to the parasitic diseases.

8. Can we invade the invaders?

Viewed in the broadest terms, the enemy in the fight against the parasitic diseases is not only the parasite itself but also the vector - insect, snail, or whatever - that transmits the disease. We must therefore ask whether one can unleash a scourge on the scourge. Is it possible to find biological species to invade either the parasites or their vectors, and thus to discover an ecological method of control?

Many aspects of this fascinating problem are covered in the paper on Vector Biology elsewhere in this volume. We mention it here briefly, however, because previous successful examples of this form of control have involved the closest possible collaboration of fundamental biomolecular scientists and field-oriented ecologists.

Many of the principal handicaps which must be overcome before large-scale research can begin on the development of microbes capable of killing vectors lie in the field of fundamental research. For example, while we know a lot about the diseases of man and domestic animals, knowledge about the diseases to which insects and snails are subject is much less advanced. The field of invertebrate pathology, which seeks to fill this gap, needs strengthening. Recent WHO-sponsored research has already identified a small number of bacteria and fungi which cause disease in important vectors. Though limited, this knowledge provides a spark of confidence for future work.

Two types of biological control agents which are active against mosquitos have reached the stage of application on a limited scale. They are fish which eat mosquito larvae and a nematode worm (Reesimeomis nielseni) which infects and kills larval mosquitos. In both cases, costs of production are reasonably low.

Can we expect ecological control methods ever to be effective on a large scale? If we extend the concept to overall pest control, recent history provides some encouraging examples. One very large-scale experiment, which turned out to be successful and reaped economic benefits measured in thousands of millions of dollars, was the pandemic of myxomatosis virus infection unleashed amongst the wild rabbit population in Australia during the 1950's. Before this continent-wide ecological intervention could take place, great efforts in basic science were required for characterization of the myxomatosis virus and its growth habits, to make sure it was absolutely specific for the rabbit and could not infect other domestic or indigenous animals, let alone man. Genetic enquiry was directed to the question of whether it could mutate or recombine with other viruses to produce potentially dangerous strains. Laboratory research revealed the modes of transmission, degrees of virulence for different types of rabbits, percentage mortality, acquisition of immunity, and dozens of other necessary variables.

Only after these determinations were the first field trials initiated. Following some early discouragement, the right climatic and other conditions for optimal spread occurred, and the disease advanced throughout the rabbit population to an extent surprising even the experts. Of course, 100% eradication was not achieved, and many of the surviving rabbits of the subsequent generation proved to be less susceptible to the virus. The ball was passed back to the basic laboratory for a new solution. It was found that the progeny of the surviving rabbits, though less susceptible, still showed sufficiently high mortality to make a second round of the myxomatosis virus attack worthwhile. Through constant laboratory/field interchanges, the effectiveness of the valuable new tool was optimized.

Any plan to use a similar rationale against a parasite vector should rest on a similar interdisciplinary relationship of close collaboration. The case for further basic research seems strong.

9. Exploiting quirks in host defences

The task which evolution has worked out for the immune system is not an easy one. On the one hand, the lymphocytes and other cells of the system must recognize the presence of foreign antigens, form antibodies and promote acute and chronic inflammation to limit the spread of infection. On the other hand, the lymphocytes must not form antibodies against constituents of their own body itself, even though these constituents may act as perfectly good antigens on injection into another person or animal. Ideally, the system must be geared to spring into action early during infection, that is, when the amount of invading antigen is quite small; in addition, antibody should be formed in a sufficient amount, and for a sufficiently long time, not only to help in the cure of that particular infection but also to prevent reinfection, preferably for a lifetime. In other words, the immune system needs to be subject to exquisite regulation. Bearing in mind the vast range of infections which the system may be asked to face, it is not surprising that immune mechanisms sometimes fail or go awry. In such circumstances, the disease state may be worsened. In fact, a substantial branch of immunology, termed immunopathology, has grown up to describe all the ways by which immune processes can have deleterious effects. One of the most important basic biomedical research areas needing exploration is the immunopathology of parasite diseases. Several examples may illustrate the point.

(a) Immunopathology

In onchocerciasis, larvae called microfilariae accumulate in large numbers in the front of the eye. When they die, they excite a profound local lymphocyte reaction. This chronic inflammatory response, believed to be due to release of antigenic material from the dead larvae, while it does lead to a slow removal of the parasite, is itself the cause of disease, as it produces severe impairment of vision. When drugs such as diethylcarbamazine are given to kill the worms and larvae, there may be a temporary but severe worsening of symptoms in the eye through an exaggeration of the above process.

Today, we have a variety of anti-inflammatory and immunosuppressive drugs which can diminish immunological processes, and it is possible that their administration together with the worm killing drug can minimize this flare-up of symptoms. This is only one example of the immune defences acting in apparently paradoxical fashion, but unfortunately we know so little of the details of the immunopathology of parasitic diseases that, without further basic and clinical research, these potential leads cannot be followed up.

(b) Localized versus generalized disease

A related puzzle in several diseases is why the causative organism sometimes remains localized to one or a few areas of the body, while sometimes it becomes generalized with tens of billions of microbes swarming throughout many tissues. The localized variety, as in the "tuberculoid" forms of leprosy, is generally accompanied by a strong immune response. The generalized disease, such as the "lepromatous" form of leprosy, is marked by absent or grossly deficient immune defence. Analogous examples may exist in the parasitic diseases, though at the moment we do not even know whether both generalized and localized forms of disease are caused by exactly the same strain of parasite. Of course, there are intermediate stages between these clear-cut extremes. We know only too little of the reasons for these different forms of the one disease, and our ignorance is a barrier to more intelligent implementation of control measures. One possibility is that there are innate genetic differences amongst people in their capacity to respond to a particular parasite's antigens. Alternatively, some individuals may have their immune response capacity impaired by malnutrition or other concomitant infection such as malaria. A third possibility is that the generalized form of the disease occurs when the immune system finally becomes worn out or paralyzed by too constant, intensive stimulation with one antigen. A long-term, "horizontal" study embracing both clinical and laboratory research could provide definitive answers to these key questions.

(c) Nutrition and immunity

The nutrition-immunity interface, already the subject of successful WHO-sponsored research, needs further special emphasis. As severe malnutrition may impair lymphocyte function, immunization programmes could be jeopardized if instituted in regions where infant malnutrition is rife, and incorrect conclusions could be reached from such clinical trials. We need much more detailed and quantitative information on this relationship, again requiring both epidemiological and laboratory research. This is the type of investigation which the tropical disease research and training centre at Ndola is ideally suited to perform.

(d) Non-specific immunity

Children living in areas where malaria is hyperendemic have repeated attacks of the disease between the ages of about six months and three years. These malaria attacks in young children are associated with fever and other manifestations of disease which are often severe, and not rarely fatal. An estimated one million African children die of malaria every year. Nevertheless, the majority survive without treatment, and after the age of about three years they become progressively more immune to the worst symptoms of the disease, though from this time on, they have marked spleen enlargement, indicating the infection has not been totally eliminated.

These observations suggest that protective immunity to malaria is achieved only by repeated natural infections, possibly because there are several different strains of each species of malaria parasite. Relatively little is known about the mechanism of recovery from malarial infection. Recent experiments in mice have revealed a mechanism of immunity which may be applicable to the human situation. It is termed non-specific immunity because it is elicited by one type of organism (a bacterium) and is effective against a different type of organism (a protozoan). When mice are given an intravenous injection either of living,

attenuated tubercle bacilli (BCG) or of killed Corynebacterium parvum, and are then challenged three weeks later with malaria parasites, they show considerable resistance against the latter. The resistance is mediated, not by antibody, but by a soluble factor which is liberated into the blood plasma and inhibits the multiplication of malaria parasites within the red blood cells. Electron microscopic studies show that a high proportion of the parasites in the red blood cells of animals recovering from infections, or protected by prior inoculation with BCG, rapidly develop signs of degeneration and fail to multiply.

The agents which elicit non-specific immunity as, for example, BCG and C. parvum, indirectly increase the number and activity of macrophages suggesting, together with other evidence, that it is macrophages which secrete the protective factor conferring non-specific immunity against parasitic infections.

Injections of BCG of C. parvum have also been shown to increase immunity against Trypanosoma brucei, Toxoplasma gondii, and a strain of Trypanosoma cruzi. The immunity engendered in this way may, therefore, be applicable to a wide range of parasitic infections.

It is conceivable that raising non-specific immunity of this type in young children living in areas where parasitic infections are prevalent could be achieved without harmful effects. Indeed, a part of the observed phenomenon may be a natural manifestation. However, careful experimental work is required to ensure there is no increased risk of lympho-reticular malignancy or other undesirable long-term effects.

Clearly, attempts should be made to identify the protective factor and define its mode of action in the parasitized cell. The factor may have a relatively simple composition. If it could be synthesized, it might become a widely applicable and safe adjunct to disease control.

(e) Antigenic variation in trypanosomes

One of the ways by which parasites such as trypanosomes evade immune attack is by sequential changes in the composition of their surface coats, a phenomenon known as antigenic variation. This phenomenon raises interesting academic and practical questions. The first concerns genetic control of the surface antigens. It may be that the trypanosome has all the structural genes for a programmed variation of the surface proteins, with control of gene expression so that they are transcribed and translated one after the other. Alternatively, perhaps the structural genes for coat proteins undergo mutation, though the available evidence supports the first hypothesis.

A second problem is the nature of the antigens and how they differ in composition. Some major coat glycoproteins are now available in pure form and their compositions are being analyzed.

It has also been suggested that the trypanosomes in the tsetse fly all have the same coat composition, and that the antigenic variation only occurs in the vertebrate host. If this is correct, it should be possible to define the composition of the trypanosome coat in the insect and identify major antigenic determinants. Presumably these would be relatively simple peptides, which might be synthesized and used to immunize humans and cattle so that they would be resistant even to the small inocula of trypanosomes from tsetse flies which cannot themselves induce protective immunity.

A great deal of information has accumulated on immune responses to synthetic peptides, which encourages the hope of such application.

(f) Animal models

The immunology and immunopathology of parasitism present so many facets that not all of the relevant research can be done in man. For this reason, heavy emphasis should be placed on models of the diseases in laboratory animals. While the mouse presents many advantages for biomedical research projects because of its low cost and our profound knowledge of its genetics and immune system, many other species should be involved in this crucial activity of model-building. Special mention should be made of research in primates, whose physiology more nearly approximates that of man. Primate research can proceed in Africa at far less cost than in countries lacking indigenous non-human primates.

(g) Genetics of disease susceptibility

One of the most fascinating aspects of research into parasitism concerns differential susceptibility of people to the various diseases. In a malaria infested region where essentially all the people are exposed to infectious mosquito-bites nearly every day, some individuals develop fatal malaria, others suffer from a chronic or relapsing severe disease, and still others demonstrate little apparent ill health, though the tell-tale large spleen gives evidence of the parasite load they carry. One important factor contributing to these differences is the genetic makeup of individuals. It has long been known that a gene coding for haemoglobin of a particular type reaches unexpectedly high frequencies in African and certain Mediterranean peoples, even though the possession of a "double dose" of the gene causes a fatal disease known as sickle cell anaemia. Why has natural selection allowed this to happen? Simply because a single dose of the gene confers on the red blood cells of the person concerned a substantial partial resistance to malaria. It is now believed that this is only one example amongst many of the interactions between human genetics and the epidemiology of parasitism. One new area of excitement relates to the so-called immune response genes. It has recently been discovered that the strength of the antibody response mounted against a particular vaccine molecule is regulated by a number of different sets of genes, some of which are beginning to be well understood. It is now important to institute comparative surveys of the immune response genes of sufferers from different parasitic diseases and of people in the same region displaying relative resistance, to determine whether the possession of certain genes is statistically related to disease resistance. Indeed, the whole field of genetic polymorphism in relation to differential susceptibility now calls for exploration.

This section and the preceding one have placed great emphasis on immunology, but animal models are equally important for chemotherapy research. Indeed, a parallel list of examples showing that basic research could help in the design of many new drug approaches could readily be constructed. Finally, it must not be forgotten that the history of science gives many examples of powerful new tools emerging from some totally unexpected discovery. Chance favours the prepared mind, and the basic research envisaged will prepare many keen minds to think about tropical disease problems.

10. Research training and institution strengthening: biomedical research aspects

The spectrum of research envisaged for the Special Programme ranges from basic, long-term studies, such as the examples outlined in this paper, through medium-term applied research endeavours, to short-term operational research. On balance, it is to be expected that the research to be performed in Africa and elsewhere in the developing world will initially be weighted towards the more applied end of the spectrum, and that the majority of the more basic work alluded to in this paper will be performed in established laboratories, chiefly in the developed countries. Nevertheless, the dichotomy is not sharp, and substantial basic work will also be performed in tropical countries. Moreover, as time passes, it is expected that the capacity of laboratories in tropical countries to undertake fundamental research will progressively increase. In the meantime, continued interactions will be needed at many levels to ensure that the main thrust of the biomedical research remains closely related to programme objectives and to other programme elements.

As regards research training, it is envisaged that trainees, at widely varying levels of experience, will be chosen from all over the world to work as integral members of the various biomedical research teams. Appropriate administrative mechanisms are described elsewhere in this documentation. As for institution strengthening, it is not envisaged that a portion of the biomedical research budget be specifically set aside for this purpose. Rather, it is believed that the support of specific trainees and specific research projects in the basic biomedical sciences will in itself lead to a more creative and interactive atmosphere in the institutions concerned. It is recognized that it may be a decade or longer until some of the new tropical research and training centres will be self-sufficient in their basic research capacity.

11. Resource allocation for biomedical research in tropical diseases

In developing basic research related to diseases of the Special Programme, careful attention must be given to the deployment of financial, institutional and human resources to achieve maximum cost-effectiveness. It will be especially important for the programme to explore possibilities of initiation and coordination of this research into the programmes of the world's major scientific research institutions.

This paper has dealt with several examples of possible research avenues, each of them broad and illustrating the kinds of long-range, multidisciplinary efforts in basic science which could build an infrastructure for future applied research and development. The possibilities outlined are intended as examples only: it remains for a scientific advisory committee to determine the detailed mechanisms by which particular research projects are to be selected and funded. Similarly, the present paper is in no way intended to pre-empt the future decisions on organization which must be the prerogative of the top management of the programme once it is operational. However, it may be useful to give, again as an example, one possible option.

A central Scientific and Technical Advisory Committee of the Special Programme (STAC) would be responsible for advising on priorities among the programmes presented by various Scientific Working Groups (SWGs). These SWGs would, in the main, be concerned with particular approaches to particular diseases, e.g., an immunology of leprosy SWG would be charged with developing a leprosy vaccine, a chemotherapy of malaria SWG with the responsibility for new prophylactic and therapeutic drugs, etc. Such SWGs would certainly perform some basic research, including work similar to that outlined in the present paper. In many cases, however, the goal-oriented SWGs may not be in a position to deal with protective mechanisms of potential common importance to several or all of the individual diseases. Furthermore, some ideas may be of too exploratory a nature to concern the goal-oriented SWGs. Therefore, the STAC could appoint a Biomedical Science Working Group (BIOSWG), being a group of experts from disciplines such as parasitology, immunology, cell and molecular biology and genetics. BIOSWG could:

(a) itself identify promising areas of research, as above, and make appropriate grants and contracts;

(b) receive from the various disease-oriented scientific working groups (IMMLEP; THELEP, IMMAL, etc.) proposals for review which these SWGs believe to fall more appropriately into BIOSWG's area of responsibility;

(c) develop a plan to attract and enlist those groups of biomedical scientists such as biochemists and pharmacologists, who are not fully aware of the magnitude of the problem of tropical diseases or of the need for more research on them. BIOSWG, if constituted of scientists of sufficient status, could perform a valuable educational function amongst the biomedical research community. Wide discussion and availability of funding has recently drawn scientists from a broad diversity of disciplines into the cancer field. BIOSWG should try to achieve the same for tropical disease research. An active programme of symposia and training courses would be a major BIOSWG responsibility.

It is possible that BIOSWG would wish a proportion of the funds to give substantial support to a whole research unit or units. For example, a highly effective unit entirely devoted to tropical disease problems, has received some support through the pilot phase of the Special Programme. In other cases, full or partial support of a single investigator and his technical staff would be involved. Funding levels would depend on many factors, including alternative sources of support, geographical location, need for expensive equipment or consumables, etc. Taking guidelines from national research council experience, a budget of US$ 1.5 million might be distributed in supporting two or three substantial units (total costs US$ 500 000) and approximately 30 research projects in amounts varying from US$ 5000 to US$ 50 000 per annum (total costs US$ 1 million).

As the STAC has not yet met to consolidate a global research strategy, and as BIOSWG itself has not yet met in order to assess its brief and debate its modus operandi, it is impossible to construct an accurate budget for this segment of the Special Programme. Clearly, BIOSWG is not the only group charged with undertaking the approaches outlined in this paper, and indeed many of the research ideas generated through the trans-disease orientation of BIOSWG may find their most appropriate funding source through one of the disease-oriented SWGs. BIOSWG's own funds should be oriented towards concepts relevant to parasitism as a whole, but its influence should be felt widely throughout the programme. An order of magnitude for the BIOSWG budget could be suggested to allow substantial activities to begin, namely US$ 1.5 million for research and US$ 0.5 million for training. The research segment of the budget would support specific research projects, both investigator-initiated and generated through the efforts of BIOSWG itself.

A training budget of US$ 500 000 per year would allow approximately 40 fellows of pre-doctoral and post-doctoral levels to receive support, as well as allowing a reasonable number of training courses, workshops and symposia to be held. Arrangements would also have to be made for an adequate supply allowance for the host laboratory as an integral part of each fellowship. If an average duration of a fellowship were two years, then 20 fellowships could be awarded per year, sufficient to make a very significant impact on the research manpower situation in tropical diseases over a period of one to two decades. The question of training is more fully discussed elsewhere in this documentation.

Obviously, these estimates are first approximations only, and detailed plans would have to be formulated by STAC and BIOSWG themselves.

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WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

TDR/WP/76.24
ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND
TRAINING IN TROPICAL DISEASES

THE STRENGTHENING OF RESEARCH INSTITUTIONS AND RESEARCH TRAINING WITHIN THE SPECIAL PROGRAMME

PANEL ON MANPOWER DEVELOPMENT

Dr Hamad El-Neil, Assistant Director of Health Services, Regional Office for Africa, Brazzaville, Congo

Professor H. M. Gilles, Department of Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, England

Mr G. W. Park, Secretary/Registrar, Institute of Medical Laboratory Technology, Yaba, Nigeria

Dr P. Tukei, East African Virus Research Institute, Entebbe, Uganda

Dr Adetokunbo O. Lucas, Director, Special Programme for Research and Training in Tropical Diseases

Dr F. M. Katz, Educational Evaluation, Division of Health Manpower Development

Dr H. G. Kupferschmidt, Assessment and Training, Division of Malaria and other Parasitic Diseases

Dr D. K. Ray, Health Manpower Planning, Division of Health Manpower Development

Dr David S. Rowe, Special Programme for Research and Training in Tropical Diseases

Dr A. R. Zahar, Planning and Programme Development, Division of Malaria and other Parasitic Diseases

The above panel held an Informal Discussion on Manpower Development for the Special Programme in Geneva from 24 to 26 May 1976. This paper takes into account the panel's conclusions as well as the recommendations made by a WHO symposium on Training in Epidemiology and Management of Parasitic Diseases held in London, 29 November - 1 December 1971.

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CONTENTS

GENERAL INTRODUCTION

1. Objectives of the Special Programme

The Special Programme has two interdependent objectives:

- DEVELOPMENT OF IMPROVED TOOLS NEEDED TO CONTROL TROPICAL DISEASES - to develop new preventive, diagnostic, therapeutic and vector control methods specifically suited to prevent, treat and control selected tropical diseases in the countries most affected by them. The new methods must be susceptible to implementation:

  - at a cost that can be borne by developing countries
  - requiring minimal skills or specialized supervision
  - in a manner which allows their integration into the health services, especially the primary health care systems of developing countries.

- STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY IN TROPICAL COUNTRIES - to strengthen research capability in the countries most affected by tropical diseases through training in biomedical sciences and various forms of institutional support. Biomedical research capability in tropical countries must be strengthened because major activities in the specification, development and testing of new tools must occur in the tropical countries where the diseases are endemic, to ensure that these tools are effective in controlling the target diseases in these countries.

Fundamental to the Special Programme is the concept that a continuing process of research and development is an essential element of health programmes in tropical countries. In the past, some research in tropical countries has been carried out by institutions staffed by teams of skilled scientists from non-tropical regions, isolated from national bodies such as universities or research councils, and without provision for the training of indigenous scientists and technologists. Such research is of strictly limited value; it fails to realize the great potential benefit which training through involvement in the work could bring to the tropical host country. A number of institutions became non-viable for this reason, following withdrawal of external support.

The Special Programme aims to extract the greatest benefit from its investment by combining research and training in tropical countries. In this respect, the WHO Immunology Research and Training Centre, which was established in the University of Ibadan in Nigeria, is a model. The table shows how this Centre progressed from initial support by WHO to full incorporation and support by the University. Thus, a relatively small WHO contribution - one scientist, one technologist and US$ 10 000 per annum - sowed the seed for the development of a major biomedical discipline in the country and the region, and this was recognized by national authorities as relevant to their health programmes.

POSTGRADUATE CERTIFICATE/DIPLOMA COURSE IN IMMUNOLOGY

Immunology Research and Training Centre
Department of Chemical Pathology
University of Ibadan, Nigeria

Year	No. of students	Course organized by
1965	3	WHO
1966	8	WHO
1967	No course	
1968	6	WHO
1969	4	WHO
1970	4	WHO
1971	No course	
1972	7	WHO/Department of Chemical Pathology
1973	9	Department of Chemical Pathology
1974	11	Department of Chemical Pathology
1975	11	Department of Chemical Pathology
	Total = 63	

2. Specific Objectives of Institution Strengthening and Manpower Development in Tropical Countries

The specific objective of institutional strengthening is to enable institutions in tropical countries to assume their appropriate roles in analysing and solving local and regional health problems. The institutional support and training opportunities provided through the Special Programme will ensure an increasing involvement of research scientists and institutions in tropical countries in the research and development activities of the Special Programme. A further benefit of such strengthening will be to increase national competence in health research, so equipping countries to tackle other health problems of high national priority.

Special Programme support, with regard to promotion of research, will thus:

- assist research institutions in tropical countries to play their essential role in developing, testing and applying new control methods or refining existing ones
- strengthen the national capability of tropical countries for health research.

With regard to the manpower component, the Special Programme will promote:

- the training of manpower at all levels needed to carry out research to identify the problems and develop the new tools required to improve prevention, diagnosis and treatment of tropical diseases
- the development of research training programmes to meet national needs within health service manpower development programmes
- the planning and implementation of appropriate national programmes for biomedical research and training.

These two components of the Special Programme, strengthening of institutions and training of research manpower, are interdependent. The Special Programme will operate in such a way that one will be used to promote the other.

3. The Rationale for Institution Strengthening and Manpower Development

The need for strengthening research institutions in the endemic areas and carrying out research training for scientists from these areas is dictated by the following considerations:

- Specification of new tools. If new tools are to be of value, they must be applicable to disease control in endemic areas. Thus, scientists and health planners from the endemic areas must be involved in drawing up specifications for potential new tools and in assessing the problems which must be overcome to develop tools with such specifications.

- Research and development. A new method of disease prevention or control, be it a new drug, a vaccine, a diagnostic test or a vector control method, will require careful testing in endemic areas. Although the fundamental biomedical research necessary to develop new tools will initially take place chiefly in sophisticated laboratories outside the endemic areas, clinical and field trials can take place only in the endemic areas. Scientists in the endemic areas must participate increasingly at all levels of this research.

- The adaptation of new methods to local situations. This will often require local operational studies prior to application. Epidemiological, clinical, genetic and other differences may necessitate modifications, for example, in dosage of drugs or in schedules of immunization. Differences in the local system of health care and local cultural and social factors may also require special assessment. Such local assessments are often best carried out by local scientists.

- The utilization of existing institutions in the endemic area. This is usually a more cost-effective and rational approach than the creation of new facilities. Selected existing institutions may be suitably strengthened and expanded to carry out research and development and strengthen the basis of national research. If institutions were nationally supported, they would have a higher probability of continued operation should there be, in due course, a phasing out of the support from the Special Programme.

- The involvement and training of local scientists in the endemic areas. The provision of training opportunities and the involvement of local scientists at all levels of research and development is designed to enable the tropical countries to assume increasing responsibility for health research.

THE GUIDING PRINCIPLES FOR INSTITUTION STRENGTHENING AND MANPOWER DEVELOPMENT IN TROPICAL DEVELOPING COUNTRIES

The following principles will guide the evolution of institution strengthening and of training:

- The institution strengthening and training activities must be relevant to regional and national priorities.

- The institution strengthening and the training of research scientists must occur within the context of national health services and in appropriate relationship to existing health service and training programmes

- Existing institutions should be strengthened by providing the necessary additional resources. So far as possible, no new institutions would be built specifically for the Special Programme.

The support for institution strengthening provided by the Special Programme will be flexible according to needs, and subject to periodic review. It will be particularly appropriate if Special Programme support to an institution leads to increasing national support, so that in time some or all of the additional functions introduced through the Special Programme become supported and funded from national resources. In most cases, long-term support over 5-10 years may be required before institutions and countries can effectively take over these functions.

It is recognized that strengthening of institutions and training activities are closely interlinked. However, they will be separated for convenience and clarity of description. The following Section A describes the institutional component; Section B outlines the training activities.

A. THE INSTITUTIONAL COMPONENT

1. Strategies in Strengthening Research Institutions

The following information is necessary to determine the scope and extent of research institution strengthening:

(a) Specification of the research activities

The possible range of research activities includes:

(i) Definition of the magnitude and severity of health problems created by the six diseases in specific areas, based on epidemiological and clinical research

(ii) Development of alternative approaches to deal with the health problems through:

- the improved application of existing methods, i.e., operational research.

- the technical improvement or adaptation of existing methods and their application, including the identification of constraints, i.e. developmental and operational research.

- goal-oriented research to develop completely new tools, i.e., research to fill gaps in scientific knowledge, leading to the development of new cost-effective and efficient methods.

- fundamental research aimed at increasing the scientific basis of knowledge of medical practice.

In defining research priorities it is important to note that some research findings may be widely applicable, whereas others may be mainly of local significance. Thus, new tools such as vaccines or drugs, and knowledge of the biology of parasites, their hosts and their interactions may have wide application, while epidemiological studies designed to assess the frequency and the distribution of a disease, and the determinants of patterns of morbidity and mortality may be relevant only in restricted areas and may be invalid if projected to another community or district. Similarly, the best methods of application of existing tools may depend upon local socioeconomic, cultural and geographical factors, or may need modification to suit local administrative mechanisms.

It follows, therefore, that each country should undertake a significant part of the epidemiological and operational research relevant to its national health problems, whereas responsibility for developmental research to fill essential gaps in scientific knowledge can often best be carried out on a regional or global basis. Furthermore, epidemiological and operational research work can be carried out with relatively simple tools, while developmental and laboratory-based research usually demands expensive, sophisticated equipment and highly-skilled manpower.

A rational strategy is to strengthen national research capability to enable each national health authority to analyse its own health problems and choose the best options for applying its available health care resources. The required developmental and more fundamental research would be promoted through national, regional or global efforts in a network of collaborating centres.

(b) Identification of potential collaborating research institutions

It is necessary to retain and regularly update information on the research institutions of tropical countries. Potential collaborating institutions may be identified in a variety of ways, as for example, through Scientific Working Groups, following a direct approach to the Programme Secretariat by the institution, through governments, through Regional Offices or country representatives of WHO, or through association with WHO in other research activities. Candidate institutions (Principal Centres and Special Centres) will be assessed through documentation of the institutions' existing and required resources and through a site visit. This assessment will be a collaborative effort between consultant scientists and WHO staff from the region and from headquarters.

Assessment will include:

- the quality of the research carried out by the institution

- the current national and international scientific status of the institution

- the manpower and other resources available

- the potential for development of the institution, including assessment of existing and future support in manpower and other resources from sources other than the Special Programme

- commitment to the research and training activities which are specifically proposed

- an estimate of the probable effect of additional support upon the institution itself and on the research capabilities of the country.

2. Principles of Selecting the Designated Centres

Institutions will be recommended for designation as collaborating centres in the Special Programme on the basis of the report of a site visit plus an evaluation of:

- the proposals made by the institution for collaborative research and training within the Special Programme
- the level and stability of existing national and international support to the institution
- the potential to obtain increased national support for manpower (career posts) and other required resources
- national commitment to the objectives of the Special Programme
- constraints which limit the research capability of the potential centre.

Limiting factors may include:

- personnel (scientists, technologists, etc.) - certain key personnel may not be available or may have important commitments for teaching or service in other areas
- physical facilities - laboratory space, capital equipment, consumable laboratory materials, maintenance and repair facilities, etc.
- support services - library, purchasing, computer, transport and travel, etc.

3. Organization of the Institution Strengthening Activities

The overall organization and the management of the Special Programme are described in detail in the documents Administrative and Technical Bodies and Operational Programme Management (Documents TDR/WP/76.28 and TDR/WP/76.29 in this volume). A Scientific and Technical Advisory Committee (STAC) will review the content, scope and dimensions of the Special Programme, including the technical approaches to be adopted. The planning, implementation and evaluation of specific research activities will be under the direction of Scientific Working Groups which are comprised of independent scientists from various complementary disciplines.

The organization of the Special Programme's institution strengthening and training component includes:

(a) The Central Group responsible for the planning and coordination of all aspects of research and training in the Special Programme including institutional support. The central group activities are carried out by the Secretariat of WHO, both in headquarters and in the Regional Offices. This includes all relevant divisions and units of WHO, including the Divisions of Malaria and the Parasitic Diseases, Communicable Diseases, Vector Biology, and Health Manpower Development, in addition to the Tropical Disease Research group which has the responsibility for planning and development of the Special Programme. The responsibility for research, training and institution strengthening activities will be allocated so as to achieve the maximum efficiency. The central group will:

- establish the Scientific Working Groups (SWG) on the basis of recommendations by the STAC. SWGs will plan, implement and evaluate the research activities of the Programme. In addition to this function, the SWGs will advise the central group on aspects of the training programme and institution strengthening relevant to their particular projects. They will also assist in identification of potential Centres, and in creating opportunities and facilities for training and institution strengthening.
- coordinate the activities of the collaborating centres within the scientific and administrative guidelines of the Special Programme.
- coordinate the Special Programme with related activities of WHO and other organizations.

(b) Designated centres, which will include:

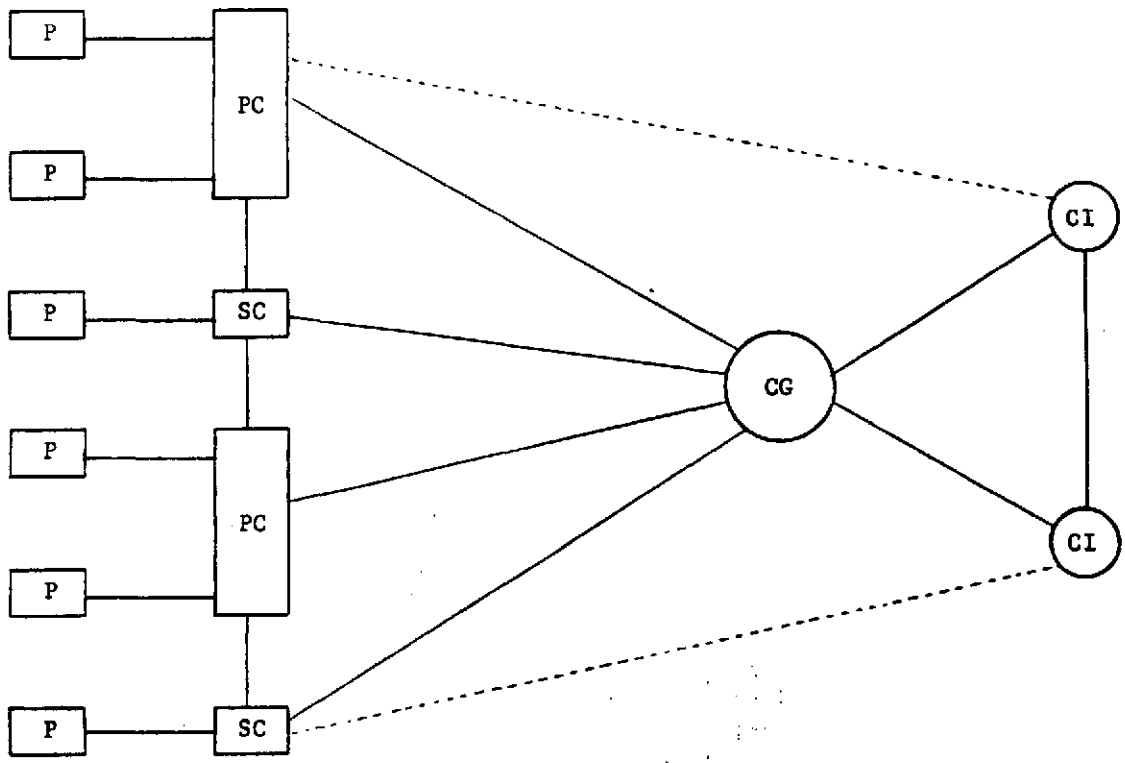
- Principal Centres engaged in multidisciplinary research and training within the Special Programme. These Centres will form the foundation of the research and training activities of the Special Programme within the endemic countries. They will function as resource centres for their regions and become focal points of health research within the countries where they are located.

- Special Centres having particular characteristics, facilities and skills to undertake specific research and training tasks in the Special Programme of a more limited nature than those of the Principal Centres. Special Centres will play a significant part in increasing national research capabilities. They may often require support to permit them to carry out the specific research and training activities assigned to them by the Special Programme.

- Peripheral Units linking research and training in the Special Programme to community health services of tropical countries.

The activities of these Centres and Units in the tropical developing countries will be complementary to the work of research and development in Collaborating Institutions in the non-tropical countries.

(c) Schema of network of Centres in the Special Programme



CG indicates the Central Group of the Special Programme, comprising all programme planning, implementation and evaluation. It includes WHO secretariat, the Scientific Working Groups, and the Scientific and Technical Advisory Committee.

PC indicates Principal Centres)
SC indicates Special Centres) in tropical countries
P indicates Peripheral Units)

CI indicates Collaborating Institutions in non-tropical countries

The discontinuous line indicates specific collaborative programmes which may develop between Principal Centres or Special Centres and Collaborating Institutions.

(d) Functions and operations of the Centres and Units

(i) Principal Centres - A number of Principal Centres will be established in tropical countries. These centres will carry out multidisciplinary research and training, and will often be concerned with more than one disease.

- Functions: the Principal Centres will:

  • plan and execute research projects outlined by the Scientific Working Groups

  • establish training programmes based on: the recommendations of the Scientific Working Groups; regional and national requirements; the need for multidisciplinary training of research workers, e.g. epidemiologists may require training in parasitology or immunology.

  • provide a regional and national consultant function

  • plan, implement and evaluate the activities of Peripheral Units.

- Operations

  • Activities of Principal Centres will be carried out within the scientific and administrative framework of the Special Programme and its review and evaluation mechanisms.

  • The Special Programme research and training activities carried out by Principal Centres will be planned and operated by a Centre Coordinating Committee. This Committee will be responsible for the preparation of the Centre's programme budget and could include representatives from the Centre, government, universities or other research and training institutions and councils.

- Criteria for the assessment of the suitability of institutions to become Principal Centres. There are a number of specific attributes which characterize a Principal Centre. It is, however, unlikely that any one centre will possess all of them.

  • human resources: a Principal Centre will require

  - scientific and technical staff
  - teaching staff capable of planning and executing an educational programme in research
  - management and administrative staff

  • physical plant and facilities. a Principal Centre will require

  - laboratories
  - lecture rooms
  - equipment (scientific instrumentation and teaching aids)
  - a library
  - laboratory animal colonies and associated facilities
  - accommodation for trainees and visiting scientists
  - an equipment maintenance workshop
  - access to data processing services

  • location: a Principal Centre should be:

  - located in an endemic area and close to an infected community (for epidemiological surveys and clinical trials)

- readily accessible by various means of communication

- in proximity to a medical school with hospital facilities, and to other scientific centres.

In the overall plan for the development of Principal Centres, the question of language must be considered. In Africa, for example, Principal Centres should be set up to operate in the main languages of the continent, i.e., Arabic, English, French and Portuguese.

The components of a Principal Centre may not necessarily all be located in a single building or institution. A Principal Centre could be constituted by several institutions or laboratories located in reasonable proximity to each other.

(ii) Special Centres - These Centres will be identified on the basis of their existing skills, facilities and interests to carry out specific research and training tasks within the Special Programme. They could be established in University Departments, for example in pharmacology and immunology; in Research Units and Institutions, such as those of the East African Medical Research Council; and in field research projects, such as the current WHO malaria field research project in Nigeria. Special Centres will be identified and assessed in a way similar to that outlined above for Principal Centres.

(iii) Peripheral Units - These Units are important points of contact between the Special Programme and the health services of the community. They will be based in existing health care facilities, such as rural health centres and clinics.

- Functions - Peripheral Units will be concerned with identification of practical problems of disease control and identification of the types and specifications of tools necessary to improve control. Such units will usually be identified by and associated with Principal or Special Centres. Designation will be based on the need to carry out specific tasks, and the designation may terminate when the tasks are completed. The health care facility forming the base of the Peripheral Unit may require strengthening in aspects such as manpower training and equipment to carry out the Special Programme's tasks, which will be additional to their health service activities. Such strengthening, for example by training in diagnostic methods for parasitic diseases, will be of long-term benefit to the health service itself.

4. Support for Institution Strengthening

Centres will be supported in the following ways:

(a) Principal Centres. Principal Centres will receive "institutional programme support". This is relatively large-scale support for renewable five-year periods to cover institutional research and operating costs and minor capital expenditures. This will enable the Centres to carry out research projects outlined by the Scientific Working Groups and participate extensively in the Special Programme's training activities. Principal Centres may require additional "project support" for particular research projects and "training support" for special training activities.

(b) Special Centres. Special Centres may receive "project support", "training support" or "core support".

- project support, to carry out specific research projects requested by the Scientific Working Groups.

- support for research training, on the basis of the type and number of training activities they undertake.

- core support, to create in these Centres the stable base of manpower and other resources necessary for effective collaborative research within the Special Programme. Such support will usually be for renewable three-year periods, with the specific level of support reviewed annually. It is anticipated that core support will be used for a variety of purposes including salaries and the purchase and maintenance of equipment. The three-year continuity

of core support gives the countries in which these Centres are located an opportunity to plan and build up their research establishments, and thus strengthen their national research capability.

(c) Peripheral Units - These Units will receive project support and training support for specific research projects and training activities. Peripheral Units may require strengthening in terms of manpower and equipment to carry out these research and training tasks which are in addition to their health service activities. The duration of support would relate to the duration of specific research and training activities carried out by the unit, but would normally be considered in two-year periods.

5. Proposed programme of Institution Strengthening

The strengthening of research institutions will progress as a phased operation beginning in Africa, and followed by a steady expansion into other endemic areas of the tropics. The immediate plans therefore include a review of institutions and training programmes in Africa: the identification of potential collaborating institutions; and assessment of their possible role in the programme and their requirements to fulfil this role.

(a) The African Network

This is based upon the African continent, as defined geographically. This includes the WHO African Region (AFRO) and parts of two other WHO Regions, the Eastern Mediterranean Region (EMRO) and the European Region (EURO). Two or three Principal Centres, in English-speaking and in French-speaking Africa, will be designated in Africa by 1977. These centres, along with associated Peripheral Units, should be fully operational by 1980. The Programme expects ultimately to designate some 10 Special Centres in Africa. The strengthening of institutions in other tropical areas will begin parallel with the efforts in Africa: planning for this has already begun, especially through the work of the Regional Advisory Committees on Medical Research which have recently been established (see Time-Table for Institution Strengthening, Appendix).

(b) The Ndola Multidisciplinary Research Centre

The Government of Zambia contributed the physical facilities of this research centre to the Special Programme and has carried out alterations to provide laboratories and other facilities required for carrying out research and training. The facilities are located in a well-equipped, modern hospital in an area in which at least four of the priority diseases of the Special Programme are endemic. A number of potential peripheral units are in the immediate vicinity and pilot projects have been designed and are being implemented in the Ndola Centre:

- Clinical pharmacology and drug trials for anti-malarial and anti-schistosomal drugs. (Clinical trials to assess efficacy and tolerance to a new schistosomocidal drug have already taken place, including full biochemical and haematological monitoring. Parasitological follow-up over a three-month period is very promising.)

- Epidemiological research. This will be designed and conducted in collaboration with the Ministry of Health of Zambia. The objective is to develop and refine epidemiological methods, especially techniques required for analysing health problems posed by multiple parasitic infections. A nutritional component of the study is also planned to define interactions between nutrition and parasitic infections, especially as they affect morbidity and the response to prophylactic and therapeutic agents. Particular attention will be placed on developing simplified field methods for collecting and processing materials.

- Applied immunology, and in particular serological epidemiology. The proposal includes building up serum and cell banks for immunological studies.

The potential of this centre as a Principal Centre will be assessed through these and other Special Programme research and training activities. It is foreseen that there will be an initial plan of development over a period of three to five years; the eventual scale of development of this Centre, as of others, will be determined by its potential for contribution to the objectives of the Programme, including regional and national requirements.

B. THE MANPOWER COMPONENT OF THE SPECIAL PROGRAMME

1. Guiding principles

The following principles guided the development of the strategy for the manpower component of the Special Programme:

- in order to meet the national manpower needs for research, countries should be assisted to attain self-reliance in research training in as short a time as possible

- the research and training programme must be developed in relation to national or regional health service planning, viewing research development and application (control) as integral parts of the overall health care system. The development of new tools will require a continuous interplay between research, training and service activities.

In order to provide the appropriate trained research workers, a research manpower plan must ensure that:

(a) the research and training programme is geared to the needs of the health services;

(b) there is an appropriate national career structure to attract and retain competent research workers;

(c) existing manpower resources are most effectively utilized and coordinated;

(d) potential leaders in research are identified and trained, so that in turn they can train others, thereby generating a multiplier effect;

(e) the training is relevant to the tasks to be performed;

(f) the training is appropriate to conditions and facilities which exist or are likely to exist in the near future in the national training and research centres;

(g) the training programme has a problem-solving or research orientation, best achieved by participation in research;

(h) research workers are trained on a broad base to enable them to develop the full potential of their specific disciplines towards the goals of the Special Programme;

(i) the Programme seeks to identify, coordinate and promote existing and planned research training activities; and

(j) research training programmes are planned on sound educational principles which:

- assign high priority to the training of teachers;
- specify the competencies to be attained by trainees of the programmes;
- ensure that learning materials are appropriate;
- ensure continuous feedback to learners; and
- ensure flexibility of training to suit varying needs.

2. Strategies in developing research manpower

A sequence of activities necessary to develop a manpower plan for the Programme is outlined below.

(a) Specification of manpower requirements. It is essential to specify the type and quantity of manpower well ahead of the time when it will be needed; item B.4(a) is a guide for a provisional specification. However, such specifications will need to be constantly updated in view of changing needs and feedback from evaluation.

(b) Identification of available manpower resources. It is necessary to identify different types of existing manpower:

those trained and working in the appropriate field

those trained but not working in their respective speciality

those who have some training but need further training to achieve the required competence.

(c) Identification of existing research and training institutions. A complete and up-to-date inventory is essential for identification of potential centres for the Special Programme (see Inventory of African Research Institutions, TDR/WP/76.33, in separate binder).

(d) Provision of resources. Though they will differ for each of the training activities, the resources required will include:

- fellowships, including travel and living expenses both within and outside the region;
- teaching staff, including visiting lecturers;
- the development and provision of learning materials; and
- the provision of material and supplies to institutions to support research by trainees.

(e) Development of an evaluation scheme. Since development of manpower resources is not a static process, but must change as needs change and as the result of feedback from evaluation, it is essential to design mechanisms for monitoring the training programme and effecting necessary changes.

A continuous evaluation process must ensure that the Programme functions efficiently, achieves its objectives and adapts to changing needs. Such a system requires continuous gathering and analysis of information on selected features of the Programme.

3. Types of Training

There will not be a unique stereotyped training programme. Training activities will be designed to be appropriate to the tasks for which people are being trained, the educational attainments of the trainee at the time of entry into training, the resources available, and the need to meet the overall purpose of training - that is, to equip every trainee to contribute to the attainment of the objectives of the programme, including the improvement of the health services in his own country. It is envisaged that training programmes will include the following:

	Type of trainee	Format	Typical duration
1.	Senior researchers (professionals with postgraduate qualification)	1. Research as part of a successful established group, which may be located either within or outside the country or region of the trainee.	1-3 years
		2. Courses in specialized techniques	4-6 weeks
		3. Participation in conferences	2-4 weeks
2.	Junior researchers (professionals with some postgraduate experience or graduates entering research work)	1. Supervised research activities plus formal instruction	1-2 years
		2. Formal course, e.g. M.P.H.	1-2 years
		3. Special courses (workshops, seminars) mainly within the region	
3.	Technologists (diplomats from recognized higher education institution)	1. Courses for development of specialized skills	3-6 weeks
		2. Supervised on the job training	6-12 months
4.	Technicians - technical assistants, field workers	Special courses	3-6 weeks

4. Recommendations for the implementation of Manpower Strategies in Tropical Countries

(a) Categories of manpower required for the Special Programme - based on specification of manpower requirements. While the programme will seek to influence the basic education of professional and technical personnel, its main responsibility is to upgrade and develop the competence of people who have already received their initial training.

The locale of the training will be predominantly in existing training and research centres in the endemic areas. The selection of sites for training will be influenced by the main scientific working languages of the region.

The table below shows some of the types of skills required to fulfil certain functions. Thus, for example, essential skills for identifying health problems with respect to tropical diseases are epidemiology, clinical medicine, pathology and parasitology. These skills may need to be supplemented with expertise in entomology and malacology. An additional set of skills is required for operational research for testing, applying and adapting control methods to local needs. Other skills in basic biological sciences are required for developing new tools. Managerial skills, although not included in the table, are essential for coordination and optimal utilization of limited research resources.

Functions / Fields of Competence	Problem Identification	Development of New Tools	Testing of Tools and Study of Feasibility
I. MEDICAL SCIENCES			
(a) Epidemiology	X		X
(b) Clinical Medicine	X		X
(c) Pathology	X		
II. BASIC BIOLOGICAL SCIENCES			
(a) Entomology	X	X	X
(b) Malacology	X	X	X
(c) Pharmacology (basic and clinical)		X	X
(d) Biochemistry		X	
(e) Immunology		X	X
(f) Molecular and cell biology		X	
(g) Genetics		X	
(h) Laboratory animal science		X	X
III. OTHER			
(a) Statistics (including data processing)	X	X	X
(b) Behavioural sciences	X		X
(c) Economics			X
(d) Information systems including library facilities	X	X	X

(b) Identification of available manpower resources. Manpower in Africa is being identified by means of questionnaires from WHO, and by briefs from Medical Research Councils in East and West Africa. Information has also been received on facilities in East and West Africa for training technologists, technicians and technical assistants.

Although the available information is at present incomplete, it is already clear that there are major manpower shortages. As an example of the staffing position, the East African Medical Research Council's Institutes can be cited. In 1975 in an establishment of 113 scientists in 7 selected Institutions of the East African Community there were 50 vacancies.

Shortages in the following disciplines are especially pertinent to the Programme:

- Epidemiologists. The few epidemiologists in Africa are fully committed in teaching and service.

- Pharmacologists. There are only a small number of pharmacologists in teaching institutions. Some do research mainly on chronic noninfectious diseases and endocrinology, and virtually none is working in research on tropical diseases.

- Related Disciplines. There is a pronounced shortage, e.g., in medical entomology, medical parasitology and malacology. It has been difficult to attract people to these fields.

- Laboratory Sciences. Some facilities for basic training of technologists, technicians, and technical assistants exist in Africa. For the purposes of the programme, it will be necessary to extend and complement this training. Of particular importance will be training in biochemistry, immunology, laboratory animal technology and instrumentation.

It is realized that, for various reasons, a number of well-trained scientists from Africa and other tropical areas are working in developed countries. A means of locating and encouraging some of them to return is desirable.

5. Completion of the Inventory

An inventory of the existing research and training institutions and projects dealing with tropical diseases in Africa has been prepared and is distributed as part of the documentation of the Special Programme. Similar inventories of other regions will be prepared.

THE ROLE OF RESEARCH INSTITUTES AND SCIENTISTS IN NON-TROPICAL COUNTRIES

To ensure that the objectives of the Special Programme are quickly and efficiently achieved, institutions anywhere in the world may be drawn into the network according to need. The contributions of institutions in non-endemic temperate zones are required, as well as those of the endemic areas, and many of the initial steps in the biomedical research necessary to obtain new tools will take place in these institutions. The Special Programme will encourage a systematic transfer of this advanced technology to institutes of the tropical endemic areas.

Research workers and institutions in non-tropical countries have made, and continue to make, major contributions to knowledge about tropical diseases. In this paper there has been much emphasis on the training of manpower in endemic areas and the strengthening of local institutions, but it is recognized that research in non-endemic areas will continue to play an important role. As the scientists and institutions in tropical countries become increasingly more self-reliant, there should be appropriate and complementary changes in the activities of scientists from non-endemic areas. If the continuing interest of scientists in the non-tropical countries is to be sustained, it is important to identify ways to secure their participation.

1. Career Prospects for Scientists

An adequate career structure is essential if capable young scientists from non-tropical countries are to be attracted to research on tropical diseases. Formerly service in institutions in dependant territories offered a life-time career prospect. Now there are few such opportunities, and this may account for the difficulty in attracting scientists in non-tropical regions into this field.

One solution to this problem would be for the non-tropical countries, through governmental and other means, to set up a number of career positions in tropical diseases. These could enable scientists to work as most appropriate, in tropical countries or in their home base, within an established career framework.

For the governments of developed countries and their institutions, this scheme would ensure a continuous flow of scientists, including clinicians with knowledge and experience of tropical diseases. In these days of increasing and rapid travel, there is a significant problem of imported diseases. There are many tragic examples of avoidable morbidity and mortality in people who have become ill on return from the tropics, sometimes due to lack of experienced clinical care. As long as malaria, schistosomiasis and similar infections remain endemic in the tropics, it will be necessary for non-tropical countries to maintain medical expertise in their diagnosis and treatment.

From the point of view of the tropical countries, the involvement of scientists from abroad would provide additional strength and expertise which might not be available locally. The concept of self-reliance, for any country, includes both the competence to tackle significant national problems and the ability to work to best advantage with scientists from outside the country on their solution.

2. Institutions of Tropical Medicine in Non-Endemic Areas

Much of the present knowledge about parasitic and other communicable diseases has been generated from studies based in institutions of tropical medicine outside endemic areas. These institutions should continue to play an important role in research, especially in the more fundamental aspects of the basic biology of parasites and of the host-parasite relationships. The accumulated experience and highly specialized expertise of such institutions can assist the development of research centres in the tropical regions in mutually beneficial collaborative ventures. These institutions should also play a major role in developing new aspects of biomedical research in relation to tropical diseases, as outlined in The Role of Biomedical Research, TDR/WP/76.20, in Volume II of these papers.

The resources of the Special Programme will be used to support the global network of collaborating institutions both in the tropical countries as well as in the developed countries in the non-endemic areas. Whereas institutions in the developing countries would require substantial support as Principal and Special Centres, it is hoped that the research institutions in the more developed countries would obtain most of their support from national and other sources. Thus, the Special Programme may provide funding to initiate an essential activity in a research laboratory in a developed country and hopefully, this would generate more substantial support from the appropriate national research council or health authority. Similarly it is hoped that the national authorities in the developed countries would endorse and support relevant training in their institutions.

3. Proposals

National authorities of non-tropical countries should be encouraged to:

(a) Create and maintain career structures for scientists to work on problems of tropical diseases in their own national institutions or on secondment abroad.

(b) Support research in tropical diseases in their most appropriate institutions. Research related to Scientific Working Group programmes could receive priority for support, but it would also be of value if those non-tropical countries having major research facilities were to develop their own programmes in tropical medicine research, to complement the goal-oriented programmes of the Scientific Working Groups.

(c) Develop research as described under (2) in such a way as to assist in the training and institution strengthening activities of the Special Programme.

4. Mechanisms

Various mechanisms will be explored:

(a) Visiting senior scientists in both directions - from the institutes in tropical countries to those in non-tropical areas and vice versa.

(b) Institution-to-institution relationship. Long-term programmes linking institutions in tropical countries to those of the non-tropical countries can be highly beneficial. Joint activities can include both research and training.

(c) Special training activities. At present, scientists from tropical countries often receive their basic training in tropical institutes situated in non-tropical areas, such as Western Europe. Teachers from such institutes can assist the establishment of similar courses in the tropical areas where the diseases are endemic. The institutions of the non-tropical zones could then more usefully concentrate on providing the more specialized advanced courses which cannot at present easily be conducted in the tropical developing countries. This dynamic approach should lead to the orderly transfer of technology, with each type of institution identifying and fulfilling its most appropriate role.

(d) Contacts have been made with relevant organizations such as the Council for the European Schools of Tropical Medicine and relevant scientific societies such as the Royal Society for Tropical Medicine and Hygiene and the American Society of Tropical Medicine. Since it is desirable to recruit into this field scientists who have not previously been engaged in research on parasitic and other tropical diseases, contact will also be made with scientific associations of epidemiologists, immunologists, molecular biologists and other basic disciplines.

(e) On the recommendations of the appropriate Scientific Working Groups, grants will be made to institutions in the developed countries to support their participation in specific research and training activities. Such grants are intended to initiate and extend relevant work in this area, but would not normally cover all or even most of the expenses involved. The hope is that the "seed-money" provided from the Special Programme would be supplemented by more substantial support from the national authorities.

APPENDIX

PROJECTED TIME-TABLE FOR INSTITUTION STRENGTHENING

	1976		1977		1978		1979		1980	
	Africa	Other	Africa	Other	Africa	Other	Africa	Other	Africa	Other
Principal Centres	1*	0	1	1	2	2	3	2	3	3
Special Centres	5	0	8	2	10	5	10	10	10	15
Peripheral Units	5	0	7	3	15	10	20	15	20	20
TOTAL	11	0	16	6	27	17	33	27	33	38

* The Principal Centre established at the Central Hospital, Ndola, Zambia.

WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

TDR/WP/76.28

ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND
TRAINING IN TROPICAL DISEASES

ADMINISTRATIVE AND TECHNICAL BODIES OF THE SPECIAL PROGRAMME

Contents

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INTRODUCTION

This document describes the functions, composition and operation of three technical and administrative bodies: the Joint Coordinating Committee, the Steering Committee, and the Scientific and Technical Advisory Committee. These bodies ensure adequate representation of all governments and agencies* participating in the Special Programme, and provide technical and administrative support to the World Health Organization in its role as Executing Agency for the Programme. The organizational structure is described below and outlined graphically in the organization chart in Appendix I. (For detailed description of the functions of the Executing Agency, see the papers Operational Programme Management, TDR/WP/76.29 and The Strengthening of Research Institutions and Research Training, TDR/WP/76.24.

DEFINITIONS

(a) The Special Programme for Research and Training in Tropical Diseases is a global programme of technical cooperation with, and service to, governments which has been developed in response to a demand for coordinated research on control of tropical diseases, as expressed in the World Health Assembly resolution WHA 27.52 of 1974. The Special Programme has two interdependent objectives: the development of improved tools needed to control tropical diseases, and the strengthening of biomedical research capability in tropical countries.

(b) The Tropical Diseases Research Fund (hereinafter called the TDR Fund) is an international fund which the World Bank Group (hereinafter called the Bank) has been invited to consider establishing for the support of the Special Programme.

(c) Contributing Parties are those governments and organizations which have acceded to the Tropical Diseases Research Fund Agreement.

(d) Participating Countries are those countries directly affected by the diseases dealt with by the Special Programme.

(e) Sponsoring Agencies are the UNDP, WHO,(and the Bank)*. WHO also acts as the Executing Agency.

(f) Scientific Working Groups are groups of leading experts from throughout the world, including WHO staff, chosen for their competence in the relevant diseases and disciplines. A Scientific Working Group (SWG) is responsible for planning, implementing and evaluating a goal-oriented research programme to achieve the objective(s) for which it is established. SWGs will be established whenever significant gaps in the knowledge required to control the target diseases appear appropriate for intensified and focused research.

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* This document makes reference to the possible role of the World Bank Group in the Special Programme for Research and Training in Tropical Diseases. The role of the World Bank as described is one unanimously advocated by the Working Group on the Organization and Financing of the Special Programme for Research and Training in Tropical Diseases, meeting in Geneva 7-8 July 1976. The World Bank, of course, has the final decision on accepting or rejecting the role proposed in this document.

THE JOINT COORDINATING BOARD (JCB)

1. Functions

The JCB shall have the following functions:

- review and endorse the policies to be adopted in the planning and execution of the Special Programme. For that purpose it will keep itself informed of all aspects of the development of the Special Programme, and consider reports and recommendations submitted to it by the Steering Committee, the Executing Agency, and the Scientific and Technical Advisory Committee (STAC).
- review and endorse the proposed plan of action and the budget for the coming year on the basis of material presented by the Steering Committee.
- review and endorse the estimate of contributions and disbursements to be made to and from the TDR Fund in that year, prepared by the Executing Agency.
- review proposed longer-term plans of action and their financial implications.
- consider such other matters relating to the implementation and the financing of the Special Programme as may be referred to the Chairman of the JCB by any member thereof.

2. Composition

The JCB shall comprise the Sponsoring Agencies, representatives of the Participating Countries as designated by the relevant WHO Regional Committees, and the Contributing Parties. The membership of the JCB shall constitute a reasonable balance between Participating Countries and Contributing Parties. Other interested parties shall, at their request and at the invitation of the Executing Agency, be represented as observers.

3. Operation

(a) The JCB shall elect a Chairman from among its members who shall:

- convene the JCB annually at WHO headquarters in Geneva, and in extraordinary session as required.
- preside over the meetings of the JCB.
- undertake such additional duties as may be assigned by the JCB.

(b) The JCB shall reach its conclusions by consensus.

(c) The Executing Agency shall provide the secretariat to the JCB.

(d) Members of the JCB representing Sponsoring Agencies and Contributing Parties shall make their own arrangements to cover the expenses incurred in attending sessions of the JCB. Special arrangements shall be made to cover these expenses for the representatives of Participating Countries. Other expenses of the JCB shall, subject to the recommendation of the Steering Committee, be borne by the TDR Fund.

THE STEERING COMMITTEE

1. Functions

The Steering Committee shall be responsible for handling JCB business between sessions of the JCB and shall, inter alia, have the following functions:

- review the plan of action and budget for the coming year as prepared by the Executing Agency for presentation to the JCB.
- take cognizance of the reports submitted to the Executing Agency by the Scientific and Technical Advisory Committee (STAC) and of the Executing Agency's comments; make the necessary observations thereon; and transmit these with comments as appropriate to the JCB.
- review particular aspects of the Special Programme which may be referred to it by the JCB or any of the Steering Committee members, and present findings in the form of reports to the JCB.

2. Composition

The Steering Committee shall be composed of representatives of the membership of the JCB. Participating Countries and Contributing Parties shall each as a group designate two representatives to act as members of the Steering Committee for three-year terms. In addition, representatives of the Sponsoring Agencies shall be permanent members of the Steering Committee. To maintain continuity of membership, the initial terms of office of representatives of the Participating Countries and Contributing Parties will be staggered.

3. Operation

(a) The Sponsoring Agencies shall designate one person from among their Steering Committee representatives to carry out the following functions:

- convene the Steering Committee.
- assist with co-ordinating the work of the Steering Committee.
- carry out such other tasks as may be requested by the Steering Committee.
- report to the JCB on the activities of the Steering Committee.

(b) The Steering Committee shall usually meet at least twice a year: once at the time of the JCB meeting, and additionally between sessions of the JCB, at WHO headquarters in Geneva.

(c) The Steering Committee shall reach its conclusions by consensus.

(d) The Executing Agency shall provide the secretariat of the Steering Committee.

(e) Members of the Steering Committee representing Sponsoring Agencies and Contributing Parties shall make their own arrangements to cover the expenses incurred in attending sessions of the Steering Committee. Special arrangements shall be made to cover these expenses for representatives of Participating Countries.

THE SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC)

1. Functions

The STAC shall have the following functions:

- provide the JCB and the Executing Agency with a continuous independent evaluation of the scientific and technical aspects of the Special Programme.
- review the content, scope and dimensions of the Special Programme, including the technical approaches to be adopted.
- recommend priorities within the Special Programme including the establishment and disestablishment of Scientific Working Groups.

2. Composition

The STAC shall comprise 12-15 scientists and other technical personnel who will serve in their personal capacities to represent the broad range of biomedical and other disciplines required for Special Programme activities. Members of STAC will be selected on the basis of scientific or technical competence by the Executing Agency in consultation with the Steering Committee and with the endorsement of the JCB.

- members of the STAC shall be appointed to serve for a period of three years, and will be eligible for reappointment. To maintain continuity of membership, the expiration of the initial terms of office of members of STAC will be staggered.

3. Operation

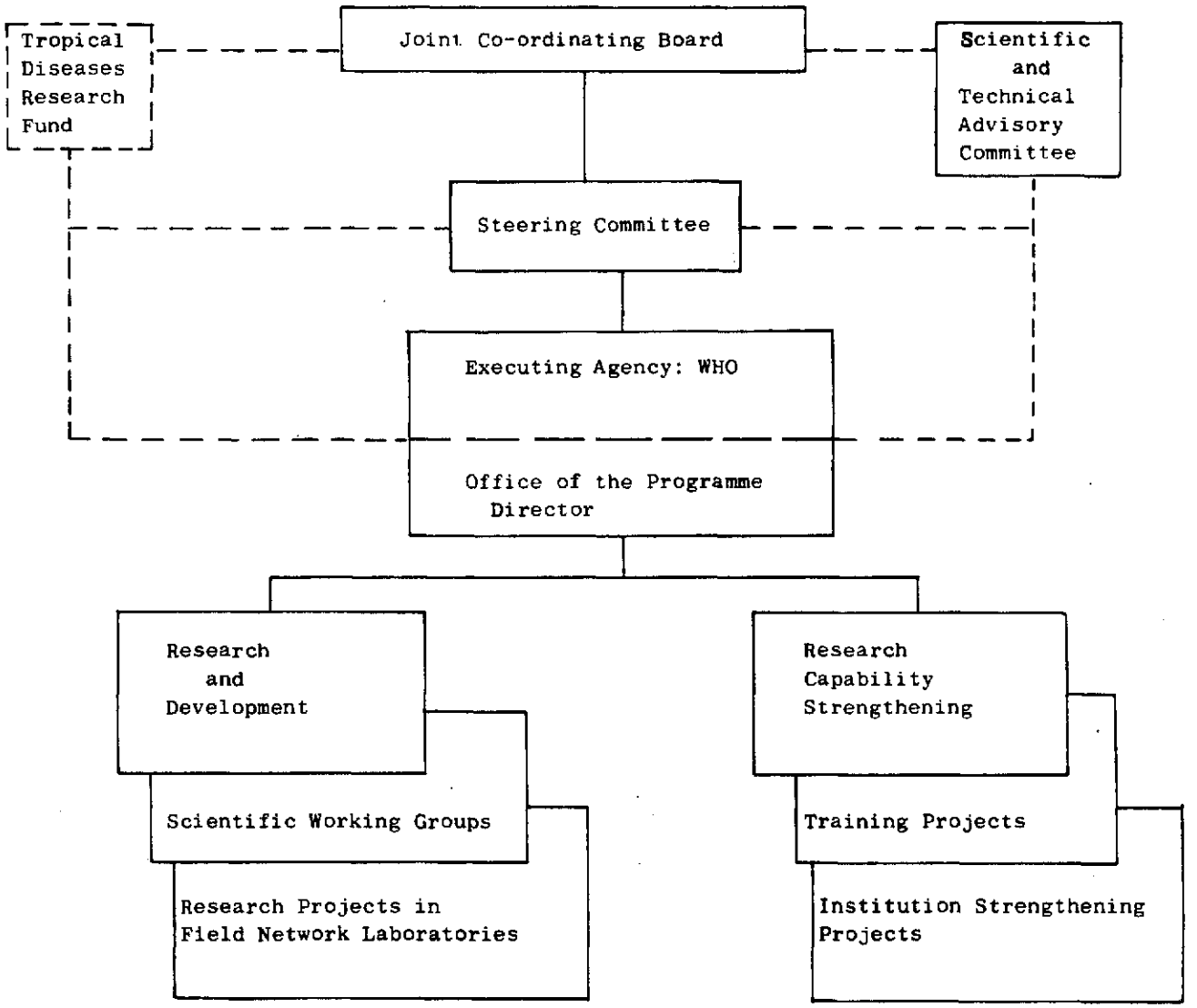
- The STAC shall elect a Chairman from its members who shall be eligible for re-election.
- The STAC shall meet twice a year. Additional meetings may be called by the Executing Agency in consultation with the Chairman of the STAC.
- The Executing Agency shall provide the secretariat to STAC.
- Costs of the STAC shall be borne by the TDR Fund.
- The STAC shall prepare an annual report on the basis of a full review of all technical and scientific aspects of the Special Programme. This report, containing its findings and recommendations, shall be submitted to the Executing Agency and to the Steering Committee. The Executing Agency shall submit its comments on the report to the Steering Committee. The Steering Committee shall transmit the report, together with its own observations, to the JCB not less than forty-five days before the JCB's annual session. The Chairman of the STAC, or in his absence a member of the STAC deputed to act for him, shall attend all sessions of the JCB.

THE EXECUTING AGENCY

The Executing Agency for the Special Programme is the World Health Organization. The Director-General of WHO, after such consultations as he may deem appropriate, shall appoint the Director of the Special Programme and appoint or assign all other personnel to the Special Programme as specified in the plans of work. Within the overall duties of the Executing Agency, the Director of the Special Programme shall be responsible for the development of the plan of action and budget, and also for the technical and administrative conduct of Special Programme operations. The Executing Agency shall also provide the Special Programme with appropriate technical and administrative support at WHO Headquarters, and at regional and country levels.

APPENDIX 1

MANAGEMENT STRUCTURE OF THE SPECIAL PROGRAMME



WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

TDR/WP/76.32
ORIGINAL: ENGLISH

SPECIAL PROGRAMME FOR RESEARCH AND
TRAINING IN TROPICAL DISEASES

PROGRAMME BUDGET

CONTENTS

The issue of this document does not constitute formal publication. It should not be reviewed, abstracted or quoted without the agreement of the World Health Organization. Authors alone are responsible for views expressed in signed articles.

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INTRODUCTION

1. The budget presentation in the Special Programme documentation is arranged so that an overview of the Programme is in this document, whereas the supporting budget details comprise separate documents and immediately follow each of their respective technical papers elsewhere in this documentation (e.g. Malaria Position Paper - TDR/WP/76.6, Malaria Budget Details - TDR/WP/76.7).

2. The budget is structured into four Programme Areas as follows:

I Research and Development - comprises the costs of the development of improved preventive, diagnostic, therapeutic and vector control methods specially suited to prevent, treat and control the selected tropical diseases in the countries most affected by them.

II Strengthening of Biomedical Research Capability - comprises the costs of activities aimed at strengthening of research capability in the countries most affected by tropical diseases, through training in biomedical sciences and various forms of institutional support.

III Technical and Administrative Bodies - comprises the costs of operation of the three technical and administrative bodies (the Joint Coordinating Committee, the Steering Committee, and the Scientific and Technical Advisory Committee) which are required to provide guidance and to ensure adequate representation of all governments and agencies participating in the Special Programme.

IV Programme Management - comprises the staffing and other costs of the Programme Secretariat in the carrying out of its management functions.

3. It is important to note that the budget documentation for the Special Programme is provisional. A final budget will be presented after the meeting, in late September 1976, of a Technical Review Group composed of internationally eminent independent scientists. The purpose of that meeting is to review the proposals submitted in this document.

4. Each activity listed in the budget has been classified according to its relative priority for implementation on a scale of A through C, with A being the highest priority. This means that all Priority A activities would normally be initiated before any Priority B activities are begun, and so on from B to C. These priority rankings were reached on the basis of expert opinion. In assigning priority rankings to specific activities for each disease or "trans-disease" area, as well as for that of biomedical research capability strengthening, experts in each area were asked to consider the following:

- What are the principal constraints to achieving effective control over each disease, or to strengthening research capabilities in the tropical countries?

- What are the most important research and development, or training and institution strengthening, activities required to overcome each of these constraints?

Each group of experts had to consider such factors as:

- the scientific probability of overcoming the constraints identified;

- the logistic possibility of performing each activity;

- the balance between short-term improvements to existing control methods and long-term development of more effective new methods; and

- the need to avoid duplication with on-going activities outside the Special Programme.

The result of these separate priority reviews is presented in the Programme Budget included in this document.

It is the task of the Technical Review Group to advise on the overall balance of priorities within the Special Programme. This Group will:

- advise on the balance between research and development activities on the one hand and training and institution strengthening activities on the other

- advise on the priority ranking between diseases, as well as between training and institution strengthening activities

- review the priority rankings which have been proposed within each area

- review the cost estimates given for the activities proposed. This is important because, while some estimates are based on extensions of on-going activities and are therefore quite firm, others are based only on expert opinion.

Throughout the budget details for each research area, activities are classified according to their current status as follows:

C.A. = Continuation of Current Activities.

R.I. = Activities already considered by an SWG and Ready for Implementation.

N.S. = Preliminary consultations have taken place: ready for Next Stage of planning.

E.O. = Activities which have not yet been considered by a Special Programme SWG but which have been tentatively included on the basis of Expert Opinion.

The final budget priorities will be presented after the meeting of the Technical Review Group and will therefore emerge from a rigorous application of the best scientific judgement possible.

5. The budget covers five one-year periods (1977-1981) and is expressed throughout in thousands of US dollars at 1976 values. Accordingly, no provision has been made in the figures for inflation, nor has any provision been made for other future price changes or future currency rate changes in relation to the US dollar. As an example of the effect of such changes on the budget, the following table presents the total budget figures at 1976 values compared with revised budget figures assuming an increasing cost rate (all factors) of 8% per annum.

(Amounts in US$ 1000)

	1977	1978	1979	1980	1981	Total 1977-1981
Total Special Programme at 1976 values	12 562	27 322	31 668	34 100	34 707	140 359
Total Special Programme at assumed 8% per annum increase	13 567	31 868	39 893	46 393	50 996	182 717

6. All cost data used in the preparation of the budget are those currently applied by WHO as of August 1976. WHO uses averages for staff costs, fellowships and meetings which take into account all known costs, as well as variations in cost factors between different geographical locations. As the presentation is, for the most part in thousands of US dollars it has been necessary to round cost figures to the nearest one thousand dollars. This has been done by rounding up to the next thousand amounts of $500 or more.

Exhibit 1

OVERVIEW OF ENTIRE SPECIAL PROGRAMME BY PROGRAMME AREA

Summary of Expenditure Estimates

Programme Area	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
I Research and Development	10 052	22 032	24 799	25 738	25 517	108 138
II Strengthening of Biomedical Research Capability	1 827	4 580	6 159	7 679	8 507	28 752
III Technical and Administrative Bodies	85	85	85	85	85	425
IV Programme Management	598	625	625	598	598	3 044
TOTAL SPECIAL PROGRAMME	12 562	27 322	31 668	34 100	34 707	140 359

Summary of Programme Area Estimates by Percentage

Programme Area	Percentage of Total					
	1977	1978	1979	1980	1981	Total 1977-1981
I Research and Development	80.0%	80.6%	78.3%	75.5%	73.6%	77.0%
II Strengthening of Biomedical Research Capability	14.5%	16.8%	19.4%	22.5%	24.5%	20.5%
III Technical and Administrative Bodies	0.7%	0.3%	0.3%	0.2%	0.2%	0.3%
IV Programme Management	4.8%	2.3%	2.0%	1.8%	1.7%	2.2%
TOTAL SPECIAL PROGRAMME	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Exhibit 1A

OVERVIEW OF ENTIRE SPECIAL PROGRAMME BY PRIORITY AND PROGRAMME AREA

Total Expenditure Estimates

Priorities and Programme Areas	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A						
I Research and Development	7 283	13 728	15 860	16 756	16 467	70 094
II Strengthening of Biomedical Research Capability	981	2 308	3 039	3 792	4 206	14 326
TOTAL PRIORITY A	8 264	16 036	18 899	20 548	20 673	84 420
Priority B						
I Research and Development	1 791	4 562	5 055	5 092	5 160	21 660
II Strengthening of Biomedical Research Capability	446	1 151	1 565	1 948	2 155	7 265
TOTAL PRIORITY B	2 237	5 713	6 620	7 040	7 315	28 925
Priority C						
I Research and Development	978	3 742	3 884	3 890	3 890	16 384
II Strengthening of Biomedical Research Capability	400	1 121	1 555	1 939	2 146	7 161
TOTAL PRIORITY C	1 378	4 863	5 439	5 829	6 036	23 545
TOTAL PRIORITY I & II (A + B + C)	11 879	26 612	30 958	33 417	34 024	136 890
III Technical and Administrative Bodies	85	85	85	85	85	425
IV Programme Management	598	625	625	598	598	3 044
TOTAL SPECIAL PROGRAMME	12 562	27 322	31 668	34 100	34 707	140 359

Exhibit 2

OVERVIEW OF PROGRAMME AREA I: RESEARCH AND DEVELOPMENT

Description	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
A. Programme Planning and General Activities[1]						
1. Staff costs[2]	231	231	257	257	257	1 233
2. Consultants (12 months)	48	48	48	48	48	240
3. Duty Travel	30	30	30	30	30	150
4. Supplies and Equipment	5	5	5	5	5	25
5. Meetings[3]	36	36	36	36	36	180
Sub-total	350	350	376	376	376	1 828
B. Research and Development Planning and Evaluation[4]						
1. Malaria	285	216	216	216	216	1 149
2. Schistosomiasis	177	177	177	177	177	885
3. Filariasis	149	149	149	149	149	745
4. Trypanosomiasis						
- African Trypanosomiasis	135	135	135	135	135	675
- Chagas' Disease	88	88	88	88	88	440
5. Leprosy	164	180	236	180	164	924
6. Leishmaniasis	88	88	88	88	88	440
7. Epidemiological and Related Research						
- Epidemiology (Trans-Disease)	128	151	110	97	134	620
- Economic Research	91	96	96	135	135	553
8. Vector Biology (Trans-Disease)	26	37	40	37	73	213
9. Biomedical Research (Trans-Disease)	45	75	75	75	75	345
Sub-total	1 376	1 392	1 410	1 377	1 434	6 989
C. Research and Development Operations[4]						
1. Malaria	3 619	6 598	8 377	8 932	8 719	36 245
2. Schistosomiasis	1 724	5 816	5 828	5 846	5 843	25 057
3. Filariasis	649	1 581	1 656	1 896	1 898	7 680
4. Trypanosomiasis						
- African Trypanosomiasis	812	2 988	2 988	2 948	2 814	12 550
- Chagas' Disease	99	385	385	385	385	1 639
5. Leprosy	386	549	658	800	837	3 230
6. Leishmaniasis	68	362	625	625	625	2 305
7. Epidemiological and Related Research						
- Epidemiology (Trans-Disease)	232	431	421	456	575	2 115
- Economic Research	148	248	398	398	298	1 490
8. Vector Biology (Trans-Disease)	89	177	177	199	213	855
9. Biomedical Research (Trans-Disease)	500	1 155	1 500	1 500	1 500	6 155
Sub-total	8 326	20 290	23 013	23 985	23 707	99 321
Total Programme Area I	10 052	22 032	24 799	25 738	25 517	108 138

[1] The functions performed under the heading Programme Planning and General Activities are described in document TDR/WP/76.29.

[2] The staffing provisions are shown in detail in Table 2.1.

[3] The meeting provisions are shown in detail in Table 2.1.

[4] More detailed budgets for Research and Development Planning and Evaluation and for Research and Development Operations are presented in the attached Tables 2.2-2.12. For more specific information refer to the actual disease and trans-disease area research budgets

Exhibit 2
Table 2.1

SUMMARY OF EXPENDITURE ESTIMATES ON STAFF AND MEETINGS

Staffing Details

Function	MAN/YEARS				
	1977	1978	1979	1980	1981
Research Planning and Coordination	2	2	2.5	2.5	2.5
Pharmaceutical Development	1	1	1	1	1
Administrative Assistant	1	1	1	1	1
Secretary	2	2	2	2	2
TOTAL	6	6	6.5	6.5	6.5

Meeting Details

$35 800

Annual Meeting of Scientific Working Group
Steering Committee Chairmen, WHO, HQ, Geneva

- 16 non-WHO participants (from around the world)
- 6 WHO participants (4 professional and 2 general service)
- 3 days' duration

Costs included: meeting room; refreshments; pre- and post-meeting publications, communication expenses and all other expenses associated with planning for and convening the meeting, including interpretation and translation into French or Spanish.

Exhibit 2
Table 2.2

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	MALARIA					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	211	142	142	142	142	779
2. Professional/Operating Costs	74	74	74	74	74	370
Total Research and Development Planning and Evaluation	285	216	216	216	216	1 149
Research and Development OPERATIONS BY RESEARCH AREA						
1. Basic research in parasite biology and physiology	650	1 260	1 540	1 600	1 600	6 650
2. Chemotherapy						
2.1 Improvement of existing drugs already in clinical use	485	1 025	1 175	1 075	900	4 660
2.2 Development of new drugs	865	1 360	1 400	1 400	1 400	6 425
2.3 Clinical studies	500	750	1 000	1 000	1 000	4 250
3. Immunology	715	1 700	2 775	3 350	3 350	11 890
4. Field research strategies for the control of malaria in Africa	404	503	487	507	469	2 370
Total Research and Development Operations	3 619	6 598	8 377	8 932	8 719	36 245
TOTAL MALARIA	3 904	6 814	8 593	9 148	8 935	37 394

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	2 767	5 166	6 637	7 132	6 919	28 621
Priority B	832	1 410	1 695	1 750	1 750	7 437
Priority C	20	22	45	50	50	187
Total Research and Development Operations	3 619	6 598	8 377	8 932	8 719	36 245

[1] TDR/WP/76.7 in Volume 1.

Table 2.3

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	SCHISTOSOMIASIS					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	103	103	103	103	103	515
2. Professional/Operating Costs	74	74	74	74	74	370
Total Research and Development Planning and Evaluation	177	177	177	177	177	885
Research and Development OPERATIONS BY RESEARCH AREA						
1. Drug development	490	1 964	1 964	1 964	1 964	8 346
2. Epidemiology and control, including snail biology	504	932	944	962	959	4 301
3. Public health importance and socioeconomic effects	380	1 520	1 520	1 520	1 520	6 460
4. Immunology	250	1 000	1 000	1 000	1 000	4 250
5. Fundamental biological studies	100	400	400	400	400	1 700
Total Research and Development Operations	1 724	5 816	5 828	5 846	5 843	25 057
TOTAL SCHISTOSOMIASIS	1 901	5 993	6 005	6 023	6 020	25 942

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	734	1 785	1 797	1 815	1 812	7 943
Priority B	283	1 164	1 164	1 164	1 164	4 939
Priority C	707	2 867	2 867	2 867	2 867	12 175
Total Research and Development Operations	1 724	5 816	5 828	5 846	5 843	25 057

[1] For details see Document TDR/WP/76.9, in Volume I.

Exhibit 2
Table 2.4

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	FILARIASIS					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	103	103	103	103	103	515
2. Professional/Operating Costs	46	46	46	46	46	230
Total Research and Development Planning and Evaluation	149	149	149	149	149	745
Research and Development OPERATIONS BY RESEARCH AREA						
1. Chemotherapy	171	442	608	825	825	2 871
2. Immunology and pathology	114	428	420	438	440	1 840
3. In vitro culture of filarial parasites	28	105	105	105	105	448
4. Animal models	47	185	189	189	189	799
5. Clinical epidemiology and immunology	135	209	122	127	127	720
6. Disease ecology, environmental and other control method trials, and associated epidemiology	24	82	82	82	82	352
7. Epidemiological phenomena responsible for the spreading of filariasis in urban and semi-urban areas	130	130	130	130	130	650
Total Research and Development Operations	649	1 581	1 656	1 896	1 898	7 680
TOTAL FILARIASIS	798	1 730	1 805	2 045	2 047	8 425

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	276	422	438	655	455	2 246
Priority B	272	779	834	856	1 058	3 799
Priority C	101	380	384	385	385	1 635
Total Research and Development Operations	649	1 581	1 656	1 896	1 898	7 680

[1] For details see Document TDR/WP/76.11, in Volume I.

Exhibit 2
Table 2.5

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	AFRICAN TRYPANOSOMIASIS					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	71	71	71	71	71	355
2. Professional/Operating Costs	64	64	64	64	64	320
Total Research and Development Planning and Evaluation	135	135	135	135	135	675
Research and Development OPERATIONS BY RESEARCH AREA						
1. Chemotherapy	490	1 964	1 964	1 964	1 964	8 346
2. Pathogenesis and pathology	112	174	174	134	-	594
3. Experimental studies in immunopathology	75	300	300	300	300	1 275
4. Immunology	75	300	300	300	300	1 275
5. Epidemiology	60	250	250	250	250	1 060
Total Research and Development Operations	812	2 988	2 988	2 948	2 814	12 550
TOTAL AFRICAN TRYPANOSOMIASIS	937	3 123	3 123	3 083	2 949	13 210

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	540	2 164	2 164	2 164	2 164	9 196
Priority B	262	774	774	734	600	3 144
Priority C	10	50	50	50	50	210
Total Research and Development Operations	812	2 988	2 988	2 948	2 814	12 550

[1] For details see Document TDR/WP/76.13, in Volume I.

Exhibit 2
Table 2.6

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	CHAGAS' DISEASE					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	65	65	65	65	65	325
2. Professional/Operating Costs	23	23	23	23	23	115
Total Research and Development Planning and Evaluation	88	88	88	88	88	440
Research and Development OPERATIONS BY RESEARCH AREA						
1. Operational research	10	45	45	45	45	190
2. Chemotherapy	40	150	150	150	150	640
3. Diagnostic methods	20	75	75	75	75	320
4. Immune protection and immunopathology	10	35	35	35	35	150
5. Epidemiology	19	80	80	80	80	339
Total Research and Development Operations	99	385	385	385	385	1 639
TOTAL CHAGAS' DISEASE	187	473	473	473	473	2 079

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	40	150	150	150	150	640
Priority B	46	180	180	180	180	766
Priority C	13	55	55	55	55	233
Total Research and Development Operations	99	385	385	385	385	1 639

[1] For details see Document TDR/WP/76.13, in Volume I.

Exhibit 2
Table 2.7

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	LEPROSY					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	126	142	178	142	126	714
2. Professional/Operating Costs	38	38	58	38	38	210
Total Research and Development Planning and Evaluation	164	180	236	180	164	924
Research and Development OPERATIONS BY RESEARCH AREA						
1. Immunology (IMMLEP):						
1.1 Vaccine	197	250	275	375	385	1 482
1.2 Skin tests	80	125	130	85	90	510
1.3 Immunopathology	53	60	70	75	80	338
2. Chemotherapy (THELEP):						
2.1 Field studies	11	23	18	4	3	59
2.2 Laboratory studies	12	23	55	87	81	258
2.3 Clinical drug trials	25	50	85	135	150	445
2.4 Development of new drugs	8	18	25	39	48	138
Total Research and Development Operations	386	549	658	800	837	3 230
TOTAL LEPROSY	550	729	894	980	1 001	4 154

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	386	549	658	800	837	3 230
Priority B	-	-	-	-	-	-
Priority C	-	-	-	-	-	-
Total Research and Development Operations	386	549	658	800	837	3 230

[1] For details see Document TDR/WP/76.17, in Volume I.

Exhibit 2
Table 2.8

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	LEISHMANIASIS					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	65	65	65	65	65	325
2. Professional/Operating Costs	23	23	23	23	23	115
Total Research and Development Planning and Evaluation	88	88	88	88	88	440
Research and Development OPERATIONS BY RESEARCH AREA						
1. Basic studies	6	37	75	75	75	268
2. Experimental studies	25	175	400	400	400	1 400
3. Epidemiology	37	150	150	150	150	637
Total Research and Development Operations	68	362	625	625	625	2 305
TOTAL LEISHMANIASIS	156	450	713	713	713	2 745

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	25	175	400	400	400	1 400
Priority B	6	37	75	75	75	268
Priority C	37	150	150	150	150	637
Total Research and Development Operations	68	362	625	625	625	2 305

[1] For details see Document TDR/WP/76.15, in Volume I.

Exhibit 2
Table 2.9

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	EPIDEMIOLOGY (TRANS-DISEASE)					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	54	41	54	41	54	244
2. Professional/Operating Costs	74	110	56	56	80	376
Total Research and Development Planning and Evaluation	128	151	110	97	134	620
Research and Development OPERATIONS BY RESEARCH AREA						
1. Epidemiological research	232	431	421	456	575	2 115
Total Research and Development Operations	232	431	421	456	575	2 115
TOTAL EPIDEMIOLOGY (TRANS-DISEASE)	360	582	521	553	709	2 735

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	232	431	421	456	575	2 115
Priority B	-	-	-	-	-	-
Priority C	-	-	-	-	-	-
Total Research and Development Operations	232	431	421	456	575	2 115

[1] [illegible]

Exhibit 2
Table 2.10

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]						ECONOMIC RESEARCH
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	29	29	29	58	58	203
2. Professional/Operating Costs	62	67	67	77	77	350
Total Research and Development Planning and Evaluation	91	96	96	135	135	553
Research and Development OPERATIONS BY RESEARCH AREA						
1. Economic Research	148	248	398	398	298	1 490
Total Research and Development Operations	148	248	398	398	298	1 490
TOTAL ECONOMIC RESEARCH	239	344	494	533	433	2 043

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	148	248	398	398	298	1 490
Priority B	-	-	-	-	-	-
Priority C	-	-	-	-	-	-
Total Research and Development Operations	148	248	398	398	298	1 490

1

Exhibit 2
Table 2.11

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	VECTOR BIOLOGY (TRANS-DISEASE)					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	5	16	19	16	52	108
2. Professional/Operating Costs	21	21	21	21	21	105
Total Research and Development Planning and Evaluation	26	37	40	37	73	213
Research and Development OPERATIONS BY RESEARCH AREA						
1. Safety testing	20	40	40	40	40	180
2. Field trials	56	110	106	121	128	521
3. Development of information systems	5	10	10	12	15	52
4. Collaborating centre for biological control	8	17	21	26	30	102
Total Research and Development Operations	89	177	177	199	213	855
TOTAL VECTOR BIOLOGY (TRANS-DISEASE)	115	214	217	236	286	1 068

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	89	177	177	199	213	855
Priority B	-	-	-	-	-	-
Priority C	-	-	-	-	-	-
Total Research and Development Operations	89	177	177	199	213	855

[1] For d[illegible] Page [illegible] TT/WP/7[illegible] 23 [illegible] Exhibit 1 [illegible] TT

Exhibit 2
Table 2.12

RESEARCH AND DEVELOPMENT:

BUDGET SUMMARY[1]	BIOMEDICAL RESEARCH (TRANS-DISEASE)					
Description of Activities	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Research and Development PLANNING AND EVALUATION						
1. Scientific Working Group Meetings	36	55	55	55	55	256
2. Professional/Operating Costs	9	20	20	20	20	89
Total Research and Development Planning and Evaluation	45	75	75	75	75	345
Research and Development OPERATIONS BY RESEARCH AREA						
1. Parasite culture	90	223	350	350	350	1 363
2. Lysosomotropic drugs	230	500	500	500	500	2 230
3. Surface membranes of parasites	90	216	325	325	325	1 281
4. Host-parasite interaction	90	216	325	325	325	1 281
Total Research and Development Operations	500	1 155	1 500	1 500	1 500	6 155
TOTAL BIOMEDICAL RESEARCH	545	1 230	1 575	1 575	1 575	6 500

SUMMARY OF RESEARCH AND DEVELOPMENT OPERATIONS BY PRIORITY

Priority Category	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A	320	719	834	834	834	3 541
Priority B	90	218	333	333	333	1 307
Priority C	90	218	333	333	333	1 307
Total Research and Development Operations	500	1 155	1 500	1 500	1 500	6 155

[1] For details see Doc t TT /WP/76 ?1 in ... TT

Exhibit 2A

OVERVIEW OF PROGRAMME AREA IC: EXPENDITURE ESTIMATES FOR 1977 BY PRIORITY AND BY CURRENT STATUS

Implementation Priority Category	Amounts given in US$ 1000 (1976)				Total for 1977
	Current Status[1]				
	CA	RI	NS	EO	
Priority A	1 373	2 113	635	1 436	5 557
Priority B	-	782	-	1 009	1 791
Priority C	-	20	-	958	978
TOTAL	1 373	2 915	635	3 403	8 326

[1] All activities included in Research and Development Operations (Programme Area IC) have been classified according to current status as follows:

CA = Continuation of Current Activities

RI = Activities already considered by an SWG and Ready for Implementation

NS = Preliminary consultations have taken place: ready for Next Stage of planning

EO = Activities which have not yet been considered by a Special Programme SWG but which have been tentatively included on the basis of Expert Opinion

The detailed research and development budgets which follow the individual technical papers in the Programme documentation show the current status of each research and development activity included in the totals above.

Exhibit 3

OVERVIEW OF PROGRAMME AREA II: STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY

Description	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
A. Programme Planning and General Activities[1]						
1. Staff costs[2]	165	280	386	373	373	1 577
2. Consultants (5 months at $4000 per month)	20	20	20	20	20	100
3. Duty travel	15	25	35	35	35	145
4. Supplies and Equipment	6	10	14	14	14	58
5. Meetings[3]	22	42	42	42	42	190
Total Programme Planning and General Activities	228	377	497	484	484	2 070
B. Training Activities[4]						
1. Medical Sciences						
(a) Scientists	43	97	179	260	260	839
(b) Technologists	36	80	129	244	244	733
(c) Field Assistants	32	64	64	128	128	416
2. Other Biological Sciences						
(a) Scientists	195	276	372	520	649	2 012
(b) Technologists	39	80	129	243	243	734
3. Other Sciences						
(a) Scientists	81	156	228	244	308	1 017
(b) Technologists	20	64	64	113	113	374
Total Training Activities	446	817	1 165	1 752	1 945	6 125
C. Institution Strengthening Activities[5]						
1. Principal centres	653	2 536	3 347	4 043	4 478	15 057
2. Peripheral units	100	250	350	400	400	1 500
3. Special centres	400	600	800	1 000	1 200	4 000
Total Institution Strengthening Activities	1 153	3 386	4 497	5 443	6 078	20 557
Total Programme Area II	1 827	4 580	6 159	7 679	8 507	28 752

[1] The functions performed under the heading Programme Planning and General Activities are described in document TDR/WP/76.29.

[2] The staffing provisions are shown in detail in Table 3.1.

[3] Meeting costs include meetings of the Research Training Committee and of Directors of Principal and Special Centres as described in document TDR/WP/76.29.

[4] Details of Training Activities are shown in Table 3.2.

[5] Details of Institution Strengthening Activities are shown in Table 3.3.

Exhibit 3
Table 3.1

STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY:

Staffing Summary - Programme Planning and General Activities

Location and Function	Man/Years					Priority
	1977	1978	1979	1980	1981	
WHO HQ						
- Professional Staff	1	1	1	1	1	A
- Support Staff	1	1	1	0.5	0.5	A
African Region						
- Professional Staff	1	1	1	1	1	A
- Support Staff	0.5	1	1	1	1	A
Eastern Mediterranean Region						
- Professional Staff	1	1	1	1	1	B
- Support Staff	0.5	1	1	1	1	B
South East Asian Region						
- Professional Staff	-	0.5	1	1	1	B
- Support Staff	-	0.5	1	1	1	B
Western Pacific Region						
- Professional Staff	-	0.5	1	1	1	B
- Support Staff	-	0.5	1	1	1	B
American Region						
- Professional Staff	-	0.5	1	1	1	C
- Support Staff	-	0.5	1	1	1	C
European Region						
- Professional Staff	-	0.5	1	1	1	C
- Support Staff	-	0.5	1	1	1	C
TOTAL STAFFING	5	10	14	13.5	13.5	

NOTE: The total amounts shown for staff costs on the summary table above have been obtained by calculating the US dollar sums from the above data.

Exhibit 3
Table 3.2

STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY:

Details of Training Requirements[1]

Type of Participant and Training	Number to be trained in each year						US$ (1976) Cost per participant per Course	Duration
	1977	1978	1979	1980	1981	Total 1977-1981		
MEDICAL SCIENCES[2]								
Scientists								
- Group Training	5	10	15	20	20	70	3 225	1 month
- Individual Training	2	5	10	15	15	47	13 000	18 months
Technologists								
- Group Training	5	10	10	15	15	55	3 225	1 month
- Individual Training	2	5	10	20	20	57	9 700	12 months
Field Assistants								
- Group Training	10	20	20	40	40	130	3 225	1 month
TOTAL MEDICAL SCIENCES	24	50	65	110	110	359		
OTHER BIOLOGICAL SCIENCES[3]								
Scientists								
- Group Training	20	25	35	40	40	160	3 225	1 month
- Individual Training	10	15	20	30	40	115	13 000	18 months
Technologists								
- Group Training	10	15	20	30	30	105	3 225	1 month
- Individual Training	5	10	15	20	30	80	9 700	12 months
TOTAL OTHER BIOLOGICAL SCIENCES	45	65	90	120	140	460		
OTHER SCIENCES[4]								
Scientists								
- Group Training	5	8	10	15	15	53	3 225	1 month
- Individual Training	5	10	15	15	20	65	13 000	18 months
Technologists								
- Group Training	0	5	5	5	5	20	3 225	1 month
- Individual Training	2	5	5	10	10	32	9 700	12 months
TOTAL OTHER SCIENCES	12	28	35	45	50	170		
Total Group Training	55	93	115	165	165	593		
Total Individual Training	26	50	75	110	135	396		
TOTAL ALL SCIENCES	81	143	190	275	300	989		

[1] To estimate yearly totals, multiply the "Number to be Trained Each Year" by the "Cost Per Participant Per Course".

[2] Medical Sciences include: epidemiology, clinical medicine, pathology.

[3] Other Biological Sciences include: pharmacology, immunology, molecular and cell biology, genetics, biochemistry, parasitology, microbiology, vector biology, entomology, malacology, laboratory animal science.

[4] Other Sciences in relation to tropical diseases research under this heading include: operational research, statistics, medical sociology, engineering, economics.

Exhibit 3
Table 3.3

STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY:

Details of Institution Strengthening Requirements

Type of Centre	Number being strengthened				
	1977	1978	1979	1980	1981
Principal Centre:					
- Full size[1]	1	1	1	1	1
- Half size	0	2	3	4	4
- Quarter size	1	1	1	1	1
Peripheral Unit[2]	10	25	35	40	40
Special Centre[3]	10	15	20	25	30
TOTAL	22	44	60	71	76

NOTES: [1] The cost of a full sized Principal Centre has been calculated as noted in the table below:

Item	Shown in US$ 1000 (1976)		
	Year I $	Year II $	Year III and beyond $
Staff	339	945	1 080
Supplies and equipment, running costs	137	221	170
Travel and per diem	10	20	25
TOTAL	522	1 300	1 392

[2] The average contribution to one Peripheral Unit is estimated at US$ 10 000 per year; the contribution is to assist in the cost of staff, supplies and equipment, transport, etc.

[3] The average contribution to one Special Centre is estimated at US$ 40 000 per year; the contribution is to assist in the cost of staff, supplies and equipment, transport, etc.

Exhibit 3A

OVERVIEW OF PROGRAMME AREA II: EXPENDITURE ESTIMATES BY PRIORITY[1]

Priorities and Type of Activity	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
Priority A						
- Programme Planning and General Activities	182	206	206	193	193	980
- Training Activities	222	409	583	876	973	3 063
- Institution Strengthening Activities	577	1 693	2 250	2 723	3 040	10 283
TOTAL PRIORITY A	981	2 308	3 039	3 792	4 206	14 326
Priority B						
- Programme Planning and General Activities	46	100	150	150	150	596
- Training Activities	112	204	291	438	486	1 531
- Institution Strengthening Activities	288	847	1 124	1 360	1 519	5 138
TOTAL PRIORITY B	446	1 151	1 565	1 948	2 155	7 265
Priority C						
- Programme Planning and General Activities	-	71	141	141	141	494
- Training Activities	112	204	291	438	486	1 531
- Institution Strengthening Activities	288	846	1 123	1 360	1 519	5 136
TOTAL PRIORITY C	400	1 121	1 555	1 939	2 146	7 170
TOTAL PROGRAMME AREA II	1 827	4 580	6 159	7 679	8 507	28 752

[1] For details see detailed budget in document TDR/WP/76.26.

The priorities for Training Activities and Institution Strengthening Activities were arrived at by applying 50% of total amounts to Priority A, 25% to B, and 25% to C.

Exhibit 4

SUMMARY OF PROGRAMME AREA III: TECHNICAL AND ADMINISTRATIVE BODIES[1]

Description	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
A. Joint Coordinating Board[2]						
Meeting costs[3] (assuming one meeting per year at WHO HQ, Geneva)	11	11	11	11	11	55
Sub-total	11	11	11	11	11	55
B. Steering Committee[2]						
Meeting costs[3] (assuming two meetings per year at WHO HQ, Geneva)	12	12	12	12	12	60
Sub-total	12	12	12	12	12	60
C. Scientific and Technical Advisory Committee (STAC)						
Meeting costs[3] (assuming two meetings per year at WHO HQ, Geneva)	62	62	62	62	62	310
Total STAC	62	62	62	62	62	310
Sub-total	85	85	85	85	85	425

Notes: [1] The functions performed by the Technical and Administrative Bodies are described in document TDR/WP/76.28. The World Health Organization will provide secretariat services for meetings of these bodies.

[2] Special arrangements which will be made to cover the expenses of representatives of Participating Countries incurred in attending meetings of the JCB and the Steering Committee may be an additional cost.

[3] The meeting costs included are listed on Table 4.1.

[4] The expenses of those responsible for coordinating the work of the Steering Committee between meetings will be covered by the sponsoring agencies.

Exhibit 4
Table 4.1

SUMMARY OF PROGRAMME AREA III: TECHNICAL AND ADMINISTRATIVE BODIES

Meeting Costs

Type of Meeting	Amounts shown in US$ (1976)
Joint Coordinating Board - 40 non-WHO participants - 10 WHO participants (7 professional and 3 general service) - 3 days' duration Costs included: meeting room, refreshments, pre- and post-meeting publications in both English and French, interpretation in English and French, communication expenses and all other expenses associated with planning for and convening the meeting	11 300
Steering Committee - 8 non-WHO participants - 3 WHO participants (2 professional and 1 general service) - 2 days' duration Costs included: same as for the Joint Coordinating Board	6 000
Scientific and Technical Advisory Committee - 15 non-WHO participants - 5 WHO participants (3 professional and 2 general service) - 3 days' duration Costs included: same as for the Joint Coordinating Board with the exception that travel and per diem expenses of all meeting participants are included	31 200

[1] All meetings to be held at WHO headquarters, Geneva.

Exhibit 5

SUMMARY OF PROGRAMME AREA IV: PROGRAMME MANAGEMENT[1]

Description	Amounts shown in US$ 1000 (1976)					
	1977	1978	1979	1980	1981	Total 1977-1981
A. Programme Secretariat:						
1. Staff costs[2]	231	231	231	231	231	1 155
2. Consultants (6 months)	24	24	24	24	24	120
3. Temporary staff (2 months)	4	4	4	4	4	20
4. Duty travel	35	35	35	35	35	175
5. Equipment, Supplies, data processing, etc.	40	40	40	40	40	200
6. Telephone, postage, etc.	10	10	10	10	10	50
Total Programme Secretariat	344	344	344	344	344	1 720
B. Supporting Services:						
1. Staff costs[2]	254	281	281	254	254	1 324
Total Supporting Services[3]	254	281	281	254	254	1 324
Total Programme Area IV	598	625	625	598	598	3 044

Notes: [1] The functions performed under the heading Programme Management are described in document TDR/WP/76.29.

[2] The staffing provisions are shown in detail in Table 5.1.

[3] Other supporting service costs such as office space, library, etc. will be provided at no charge to the Programme by the World Health Organization.

Exhibit 5
Table 5.1

SUMMARY OF PROGRAMME AREA IV: PROGRAMME MANAGEMENT

Staffing Details

A. Staff in Special Programme Secretariat

Function	MAN/YEARS				
	1977	1978	1979	1980	1981
Director	1	1	1	1	1
Programme Management	1	1	1	1	1
Administrative Management	1	1	1	1	1
Administrative Assistant	1	1	1	1	1
Secretary	2	2	2	2	2
TOTAL	6	6	6	6	6

B. Staff in other WHO Units

Function	MAN/YEARS				
	1977	1978	1979	1980	1981
Information Technical Writer	1	1	1	1	1
Programmer/Analyst	2	3	3	2	2
Clerical Services[1]	6	6	6	6	6
TOTAL	9	10	10	9	9

[1] Including budgetary, financial, supply, conference, personnel, and other administrative services.

Exhibit 6

SUMMARY OF WHO STAFF BY PROGRAMME AREA[1]

PROGRAMME AREA	MAN/YEARS									
	1977		1978		1979		1980		1981	
	P	GS	P	GS	P	GS	P	GS	P	GS
I. RESEARCH AND DEVELOPMENT										
A. Programme Planning and General Activities	3	3	3	3	3.5	3	3.5	3	3.5	3
B. Research and Development Planning and Evaluation	5	4	5	5	5	5	4	4	5	5
C. Research and Development Operations	27	3	50	3	50	3	51	3	51	3
II. STRENGTHENING OF BIOMEDICAL RESEARCH CAPABILITY										
A. Programme Planning and General Activities	3	2	5	5	7	7	7	6.5	7	6.5
B. Training Activities	-	-	-	-	-	-	-	-	-	-
C. Institution Strengthening Activities	10	-	39	-	64	-	79	-	90	-
III. TECHNICAL AND ADMINISTRATIVE BODIES	-	-	-	-	-	-	-	-	-	-
IV. PROGRAMME MANAGEMENT	6	9	7	9	7	9	6	9	6	9
TOTAL PROFESSIONAL STAFF	54		109		136.5		150.5		162.5	
TOTAL GENERAL SERVICES STAFF		21		25		27		25.5		26.5
TOTAL ALL STAFF	75		134		163.5		176		189	

[1] P = Professional Services
GS = General Services.

* * *