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special programme for research and training in tropical diseases

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AFRICAN TRYPANOSOMIASSES COMPONENT REVIEW FILE - 1986

This file has been assembled to assist STAC-8 in their review of the African trypanosomiasis component.

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1. CURRENT WORKPLANS (Excerpts from SC In-depth Report - 1981)

3.2 The overall workplan is shown in Fig. 3.2.

3.2.1 EPIAF

The plan of research is depicted in Figs. 3.2.1.1, 3.2.1.2 and 3.2.1.3.

3.2.2 CHEMAF

The workplan is shown in Fig. 6.2.

3.2.2.1 Pharmacokinetics and pharmacodynamics of existing drugs (See A, in Fig. 3.2.2).

3.2.2.2 Fundamental biological research (See B, in Fig. 3.2.2)

3.2.2.3 Systematic chemical research (See C, in Fig. 3.2.2,

3.2.2.4 Screening of compounds (See D and E, in Fig. 3.2.2)

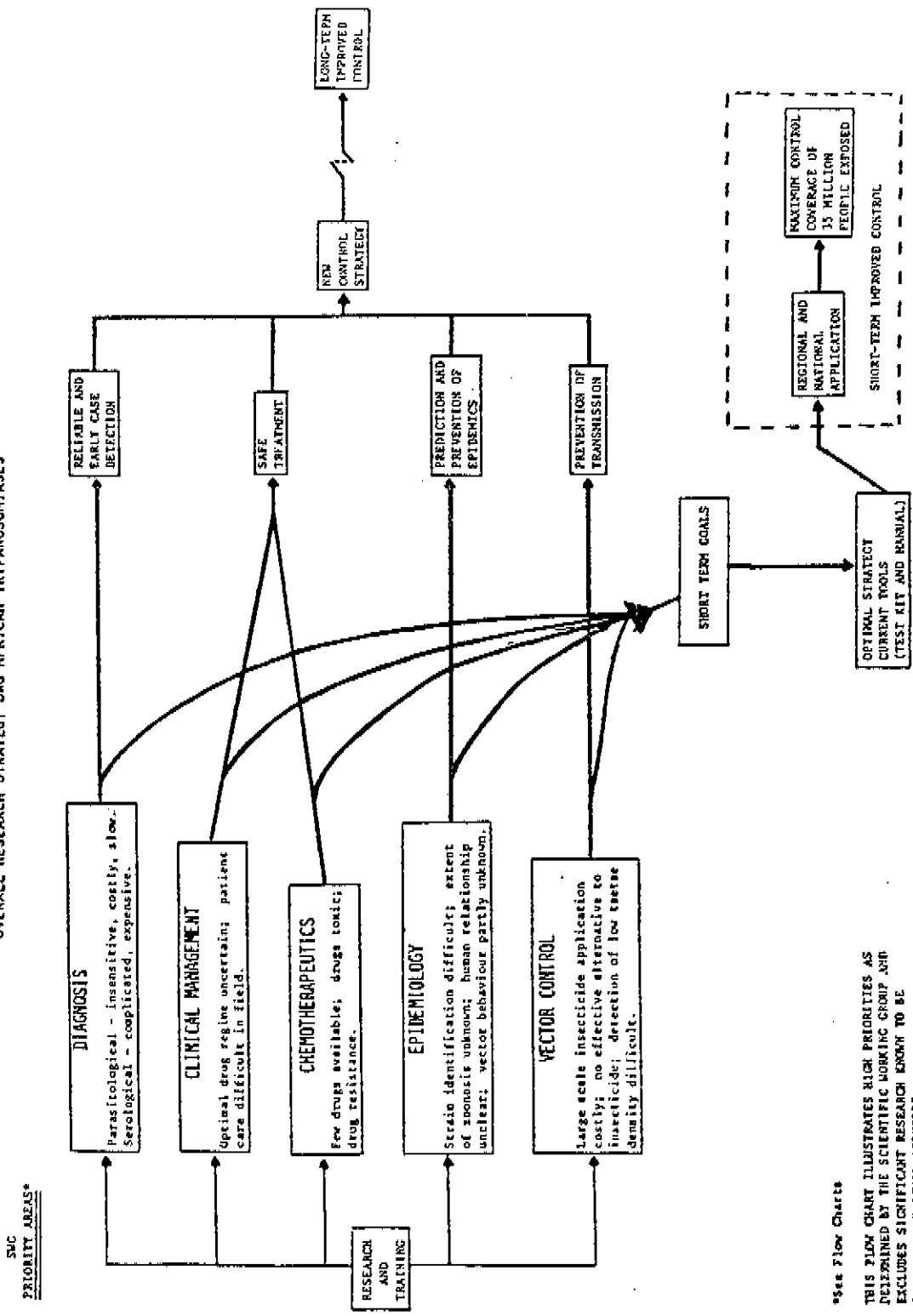
3.2.2.5 Secondary and tertiary screening (See F, in Fig. 3.2.2)

3.2.3 IMMAF

The broad workplan is shown in Fig. 3.2.3.

Figure 3.2

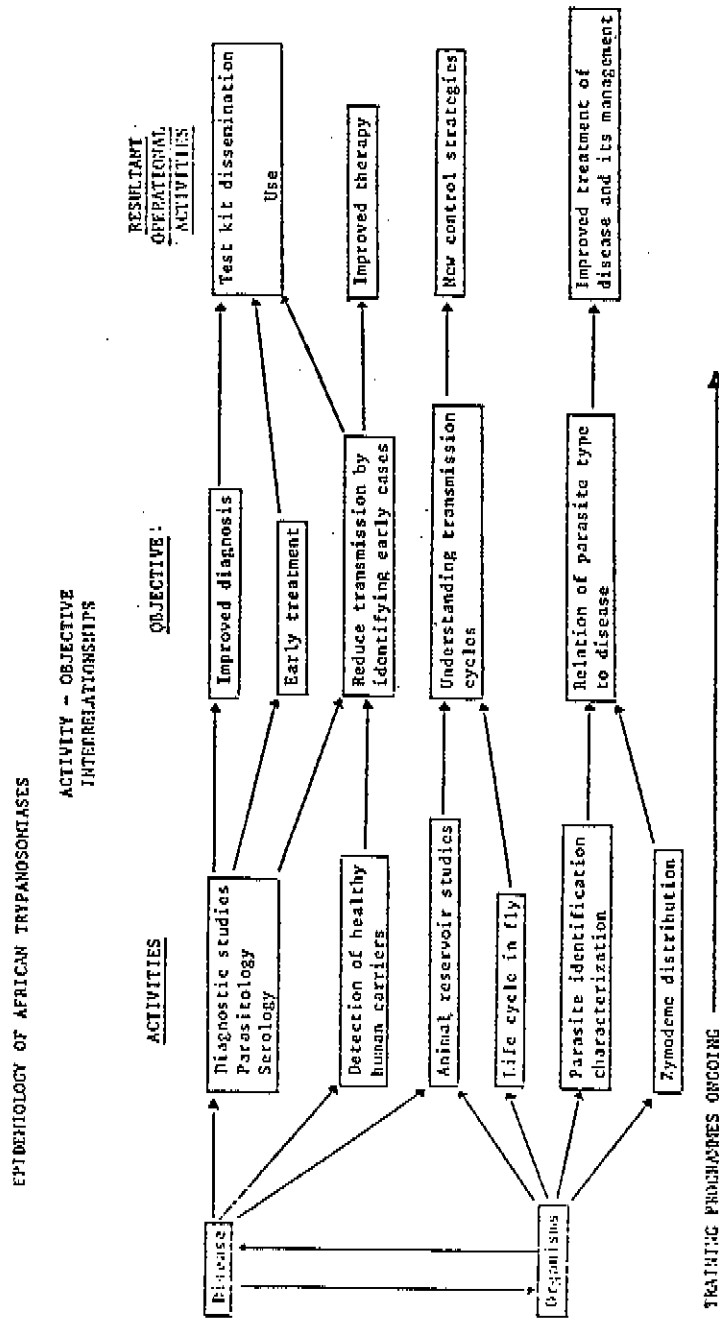
OVERALL RESEARCH STRATEGY SWG AFRICAN TRYPANOSOMIASIS



*See Flow Charts

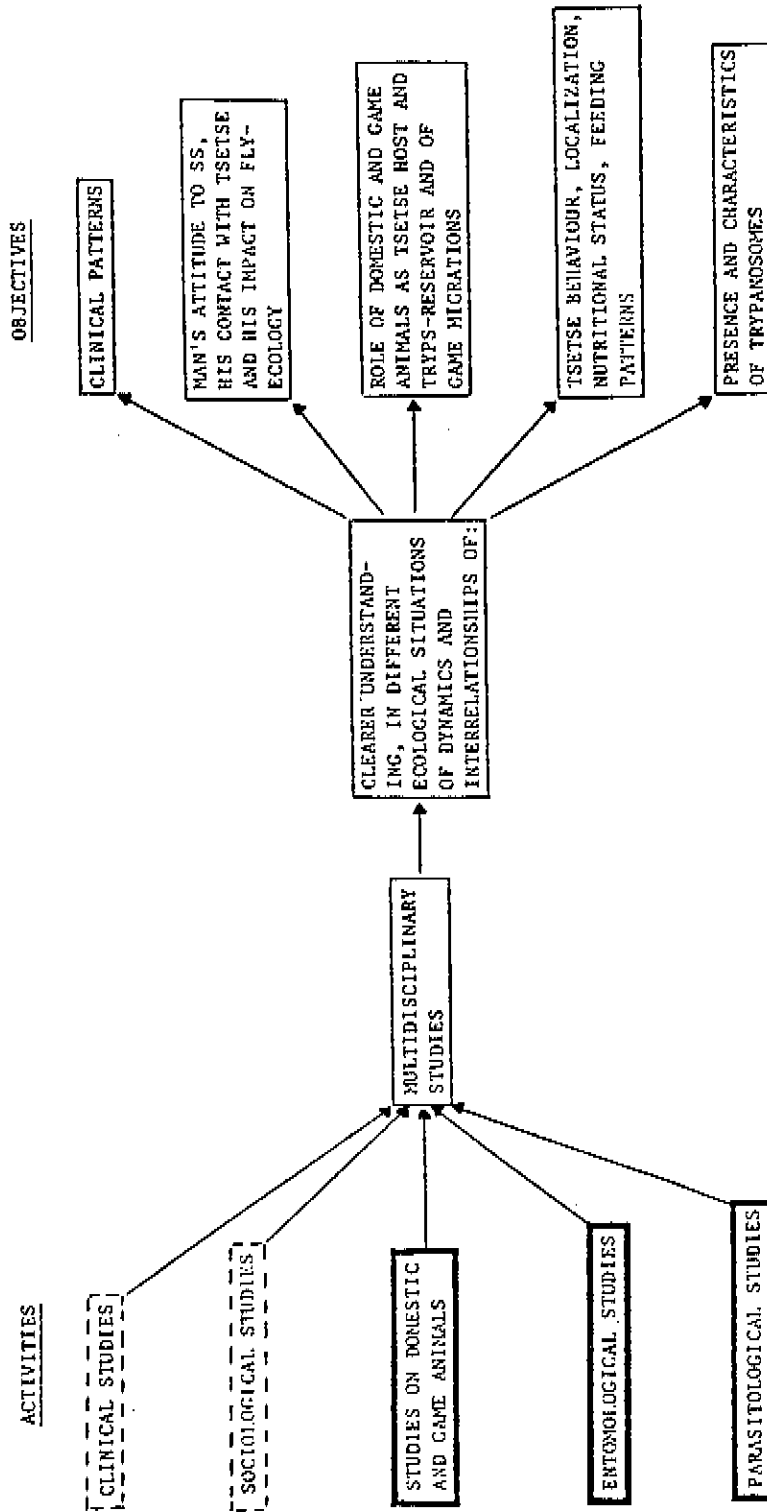
THIS FLOW CHART ILLUSTRATES HIGH PRIORITIES AS DETERMINED BY THE SCIENTIFIC WORKING GROUP AND EXCLUDES SIGNIFICANT RESEARCH KNOWN TO BE SUPPORTED BY OTHER AGENCIES

Figure 3.2.1.1



RESEARCH STRATEGY - EPIDEMIOLOGY - AFRICAN TRYPANOSOMIASIS

Figure 3.2.1.2



This figure illustrates the totality of activities appropriate for research on the epidemiology of African trypanosomiasis. Activities outlined by a continuous line are those carried out at present by EPLAF.

Figure 3.2.1.3

VECTOR BIOLOGY AND CONTROL OF AFRICAN TRYPANOSOMIASIS

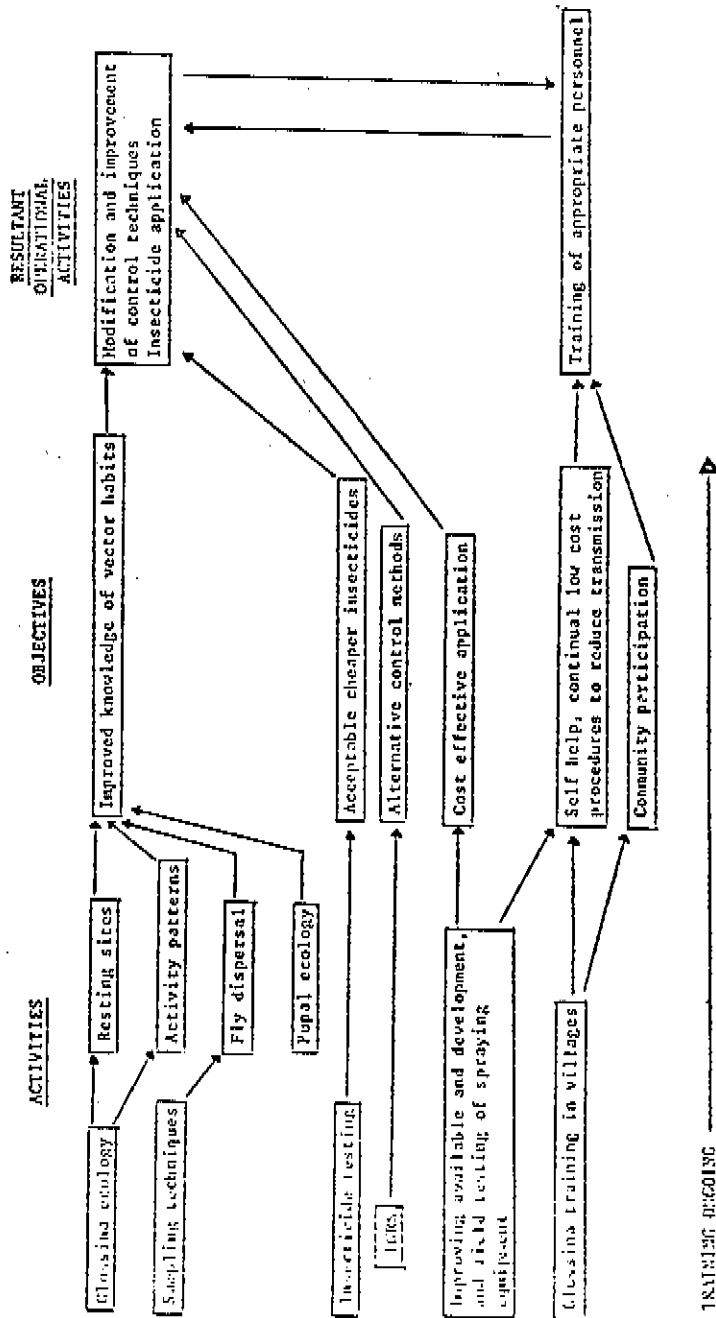


Figure 3.2.2

INTERRELATIONSHIPS BETWEEN MAJOR ACTIVITIES IN THE SEARCH FOR NEW ANTITRYPANOSOMAL AGENTS

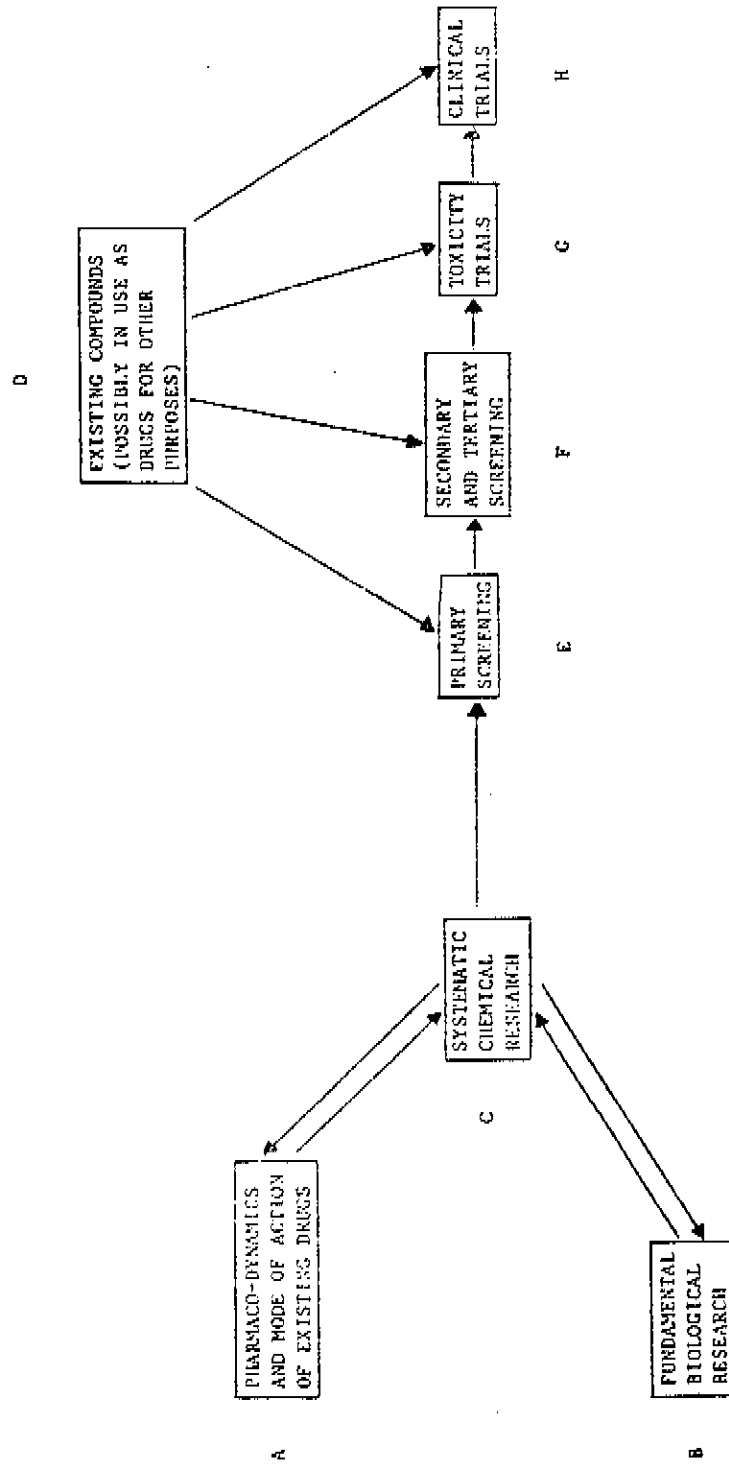
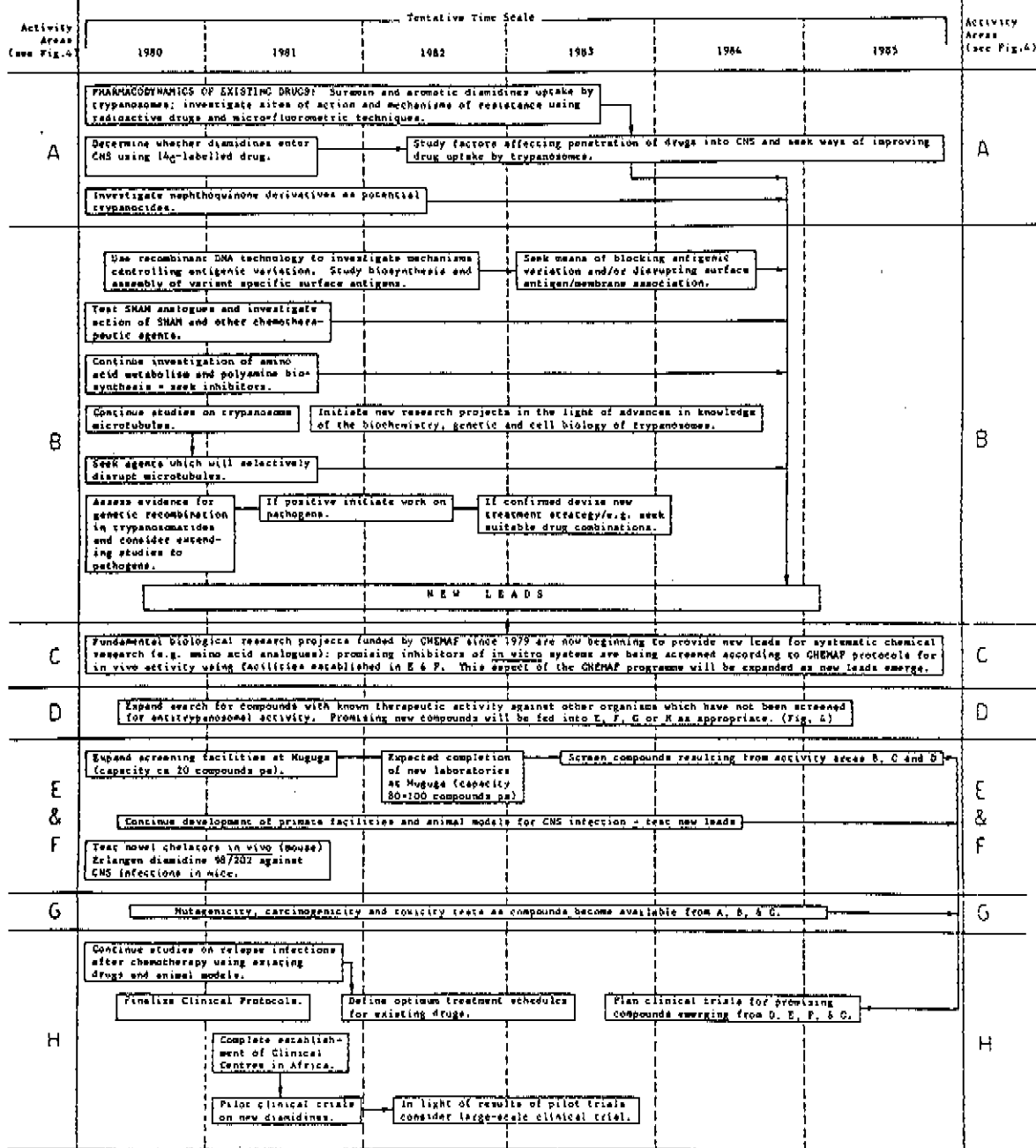


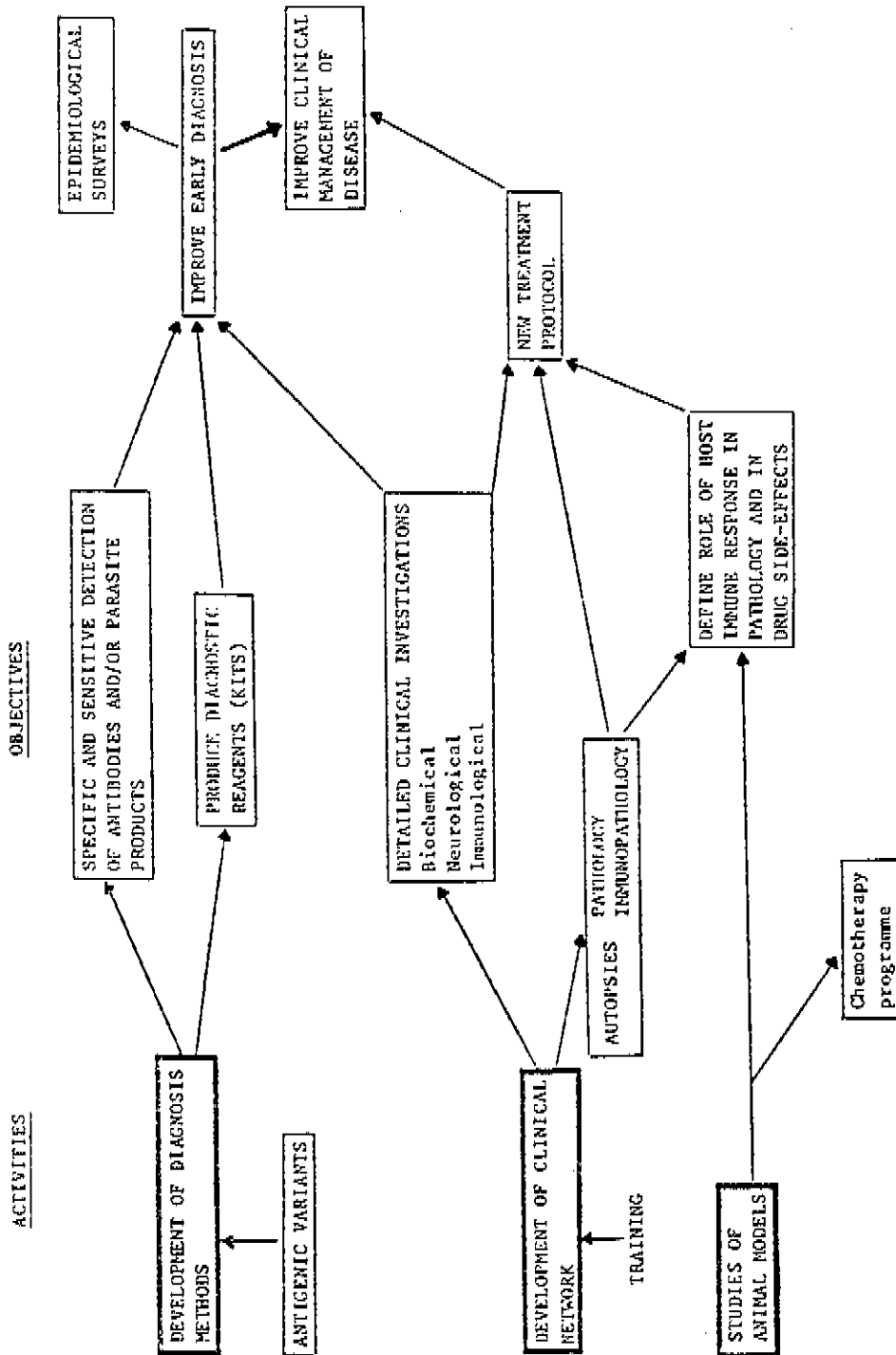
Figure 6.2

C N E M A F - PLAN OF ACTION FOR 1981-1982 AND PROJECTIONS TO 1985



RESEARCH STRATEGY - CLINICAL MANAGEMENT AND DIAGNOSIS - AFRICAN TRYPANOSOMIASIS

Figure 3.2.3



6. Projected Activities for the Next Four-Year Period (Excerpt from 2nd SWG Meeting, 1981)

6.1 EPIAF Workplan, 1982-85

<u>Subject</u>	<u>Approach</u>	<u>Target date</u>
Long-term multidisciplinary studies	Continuation of the two <u>T. b. gambiense</u> projects and one <u>T. b. rhodesiense</u> in East Africa	Beyond 1985
<u>Diagnosis:</u>		
- Serodiagnosis	Parallel evaluation of field tests to compare indirect haemagglutination and direct agglutination tests with IFAT in several foci	Mid-1982
- CSF	Evaluation of double centrifugation technique of CSF and studies on the significance of the presence of trypanosomes in otherwise unaltered CSF	End 1983
- Parasite detection	Further simplification of the anion exchange column technique and exploration of <u>in vitro</u> culture systems as a means of diagnosis	End 1985
- Parasite isolation	Search for better laboratory animals and <u>in vitro</u> systems	Beyond 1985
Parasite identification	Comparison of the DNA probing technique with isoenzyme characterization and BIIT as a means of differentiating <u>T. (T) brucei</u>	Mid-1983
	General application ?	1983-beyond
<u>Reservoirs:</u>		
- Animal reservoir	To expand surveys to other endemic areas (e.g., Congo, Gabon) and to undertake long-term studies using marked animals and following up their behaviour and exposure	1982-late 1983
- Human reservoir	To improve knowledge on possible "trypanotolerance" in man	Beyond 1985

Transmission cycle:

- | | | |
|--------------------------------|--|-------------|
| - Vector/parasite relationship | Experimental studies on possible genetic factors related to susceptibility and behavioural changes in the infected fly | Beyond 1985 |
| - Fly infection rates | To develop appropriate techniques and parameters to determine when flies contain infective parasites; comparison of salivary gland examination and DEAE column-filtered, macerated flies | Late 1984 |

Vector Biology and Control:

- | | | |
|--|--|-------------|
| - Identification of vectors (e.g., cuticular hydrocarbons) | To evaluate as taxonomic tools | Late 1984 |
| - Sampling techniques | To compare different techniques primarily olfactory and visual attractants | Late 1984 |
| - Tsetse ecology in relation to control | Determination of vectorial capacity involving studies on population dynamics, feeding habits, nutritional state, infection rates, resting sites, larviposition sites and fly movements | Beyond 1985 |
| - Simple and inexpensive means of tsetse control | Evaluation of traps and other devices and appropriate ground spraying techniques to control epidemic sleeping sickness (including evaluation of transmission) | Late 1984 |

6.2 CHEMAF Workplan, 1982-85

<u>Subject</u>	<u>Approach</u>	<u>Target date</u>
Pharmacokinetics/ pharmacodynamics	Synthesis of radio-labelled pentamidine and suramin.	1983
	<u>In vitro</u> uptake of labelled trypanocides.	1983-85
	<u>In vivo</u> distribution of labelled trypanocides.	1983-85
Drug resistance/ drug combinations	Mechanisms of acquired resistance.	Long-term
	Trypanosomes in "privileged sites".	1986
	Blood brain barrier.	1986
	Test of drug combinations	1983
Inflammatory mediators	<u>In vivo</u> anti-inflammatory drugs.	1984
	<u>In vitro</u> inflammatory mediator effects on trypanosomes.	1984

Basic biology/ host parasite differences	Inhibition of glycosome function. Selective disruption of microtubules. Programme synthesis inhibition. Threonine dehydrogenase inhibitor. Endocytosis and drug targeting.	Long-term 1985 1984 1983 1983-88
<u>In vitro</u> culture	Culture system improvement. Stage/variant differences in drug sensitivity.	Long-term 1983-88
Genetic	Genetic material exchange and role in drug resistance.	Long-term
Antigenic variation	Genetic control factors of variant antigen synthesis. Post-translational changes. Structure and assembly of surface antigens.	Long-term 1985 1985
Systematic chemical research	List of individuals as source of compounds. List of available compound sources.	1982 1982
Screening	Development of reference clones. Determination of drug sensitivities of clones. Directory of clones. Evaluation of monkey and other later stage models. Recruitment of senior investigator.	1984 1984 1984 1985 1982
Toxicity trials	Dependent on development of new leads.	
Chemical trials	Pharmacokinetics of melarsoprol in man.	1984

6.3 IMMAF Workplan 1982-85

<u>Subject</u>	<u>Approach</u>	<u>Target date</u>
<u>Diagnosis:</u>		
- Detection of antibody for epidemiological studies.	Field test CATT for <u>T. b. gambiense.</u>	1982
	Development of CATT test for <u>T. b. rhodesiense.</u>	by 1985
	Continued research on antigenic repertoires for both <u>T. b. gambiense</u> and <u>T. b. rhodesiense</u> , with a view to developing more sensitive tests.	by 1985

- Confirmation of active infections	Improved parasitological techniques.	1985
	Immunoassays for detecting antigens.	1983
	Detection of parasite metabolic products.	1983
- Improved diagnostic techniques	Creation of serum banks.	Established by 1982
	Monoclonal directory.	Established by 1982
	Workshops.	Annually as recommended

Clinical Centres:

- Research	Evaluation of diagnostic tests & studies on the pathogenesis of the disease in man.	<u>T. b. gambiense</u> in progress by 1982
	Studies are required on <u>T. b. gambiense</u> and <u>T. b. rhodesiense</u> .	<u>T. b. rhodesiense</u> to be initiated by 1985
	Improved pathology and immunology facilities in Research Centre at Daloa.	1982
- Network	Visits by consultants. Provisions of protocols and kits for the collection of serum and stabilized pathology specimens.	1982

Pathogenesis for improved clinical management in man:

a) Human pathology	Study of the pathology of the disease in man.	1983
b) Mechanisms of Inflammation	Identify the main inflammatory agents and attempt to block their activity.	1985
c) Relapsing infections	Evaluate the possibility that privileged physical sites exist that are inaccessible to drugs or antibody.	1985

d) Immune response in man	Study the nature of the immune response in man and evaluate the contribution made to the disease by immunosuppression, immunopathology and trypano-tolerance.	1985
e) Pathophysiology	Amino acid metabolism.	1985
	Endocrine function.	1985
	Toxic factors generated by trypanosomes.	1985
f) Mixed infections	Influence of the disease on diagnosis, the disease process and on management and therapy.	1985

7. Workplan 1986-89 (1 January 1986)

<u>OBJECTIVES</u>	<u>PLANS</u>	<u>ACTIVITIES</u>
To gain a better understanding of epidemiology as a basis for improved disease control.	To conduct long-term multidisciplinary studies.	Studies of <u>T. b. gambiense</u> infection in Central Africa and <u>T. b. rhodesiense</u> in Ethiopia and Zambia.
	To improve diagnostic tests.	Development of improved parasitological and serological tests for blood and CSF for epidemiological and clinical use; development of serological tests for <u>rhodesiense</u> infection; establishment of serum banks.
	To improve methods for parasite identification.	Exploitation of the blood incubation infectivity test (BIIT) and isoenzyme marker; development of DNA probes.
	To assess significance of animal reservoirs and asymptomatic infection in man.	Surveys in Burkina Faso, the Congo, the Ivory Coast and Zambia.
	To assess vector/parasite relationships.	Studies of factors related to vector susceptibility of infection and behavioural changes, and methods for detecting infection in vectors.

	To assess aspects of vector biology and control.	Identification of vectors based on new taxonomic tools, and of vector attractants; studies of vectorial capacity and of vector control methods, including impregnated screens and traps.
	To evaluate role of community participation in disease control.	Studies in Central and West Africa.
To develop new and more effective drugs, and improve use of existing drugs.	To study basic biology of parasites and host/parasite differences.	Biochemical, genetic and cultivation studies, including studies of antigenic variation, and differentiation and growth regulation in trypanosomes.
	To identify potential new leads and compounds.	Screening of compounds for activity, assessment of toxicity and effectiveness.
	To assess pharmacokinetics and pharmacodynamics of drugs now in use.	Studies on <u>in vitro</u> uptake and <u>in vivo</u> distribution of trypanocides, using conventional methods, and development of simple methods for estimating drug concentration.
	To assess effectiveness of drug combinations and methods of combating drug resistance.	Studies on animal models, trials in man.
	To improve dosage and regimens of drugs now in use.	Studies on effectiveness of reduced doses of melarsoprol, and improved solvents for arsenicals.
To improve clinical management.	To assess pathogenesis of disease in man.	Studies on immunological, pathophysiological and biochemical features of infection in man.
	To assess effects of other concomitant infections on pathogenesis.	Studies in man.
To establish facilities for clinical research in endemic areas.	To establish a network of clinical centres in Africa.	Centres established in the Ivory Coast, Mozambique, Uganda, Zaire and Zambia.

2. TECHNICAL REVIEW GROUP I - SEPTEMBER 1976

1. Summary and Major Conclusions

e) The Group made a number of detailed recommendations in the report. These included reduction of the proposed budget for schistosomiasis, increase of the proposed budget for filariasis, changes in the distribution of the proposed budget for trypanosomiasis and a recommendation that increased attention be given to the question of vector biology and control.

4. The Selected Diseases

4.7 Trypanosomiasis (TDR/WP/76.12 and 76.13)

The two main categories of trypanosomiasis were considered separately.

4.7.1 African Trypanosomiasis

a) The TRG considered that establishment of chemotherapy as the first priority was valid, and that the research proposed in immunology and epidemiology was also justified on grounds of feasibility and present knowledge.

b) Studies of vector ecology and control, including operational feasibility studies (perhaps by small self-help campaigns) were considered of high priority in Gambian human trypanosomiasis, and should be added to the proposed programme. Operational research on measures to control the vector and in field diagnosis should so far as possible be carried out in the framework of existing control activities.

c) Immunopathology should be upgraded to priority A. The other priorities were considered valid. Vector control should be given priority B.

d) The TRG considered that the budget was unduly weighted towards chemotherapy, for which 60% of the total five-year budget was proposed. The total disease budget should remain unchanged; 10% of the allocation to chemotherapy should be transferred to immunopathology, and a new allocation of 10% of the total budget should be made for vector control.

5. The Balance of Priorities Between the Six Diseases

Trypanosomiasis was of less wide distribution. The African form appeared significant chiefly for the socio-economic effects which it causes and the present impossibility of eradicating infection due to T. rhodesiense. There was a great need for improved chemotherapy; research leads appeared good in the area of vector control and chemotherapy.

The TRG considered that:

The imbalance within the trypanosomiasis should be corrected. The budgets for the African and American forms should be more nearly comparable if the chemotherapy components were excluded. (These conclusions of the TRG have already been indicated under the specific disease headings). With these modifications, the TRG considered that the proposed balance of allocation of resources to the different diseases was reasonable, and reflected both their importance and the ability to mount effective research and development activities against them.

3. TECHNICAL REVIEW GROUP II - SEPTEMBER 1977

3. Progress Made in 1977

3.3 Research and Development

The SWGs on the chemotherapy and immunology of malaria, and on the chemotherapy of African trypanosomiasis began the funding of research projects according to plans which they had previously established. The SWGs on African trypanosomiasis, Chagas' disease, leishmaniasis, and trans-disease biomedical research will be convened within the next few months.

4. Recommendations

4.3 Operational Recommendations by Disease and Trans-Disease Components

4.3.4 African Trypanosomiasis

The Group noted that laboratories and institutions in East and West Africa had been grouped into operational "clusters" for the development of Special Programme research and training activities. They approved the development of activities in this way, and recommended that a third cluster be developed in the forest area of Central Africa.

Currently available drugs are either toxic to man or not sufficiently effective against trypanosomes. In view of the limited market for trypanocidal drugs, the Special Programme should support research and development of new chemotherapeutic agents. The Programme should also pay close attention to the veterinary aspects of the disease and collaborate with veterinary researchers as appropriate. Implementation of expanded research activities on African trypanosomiasis should take place mainly in the last half of 1978 when the SWG has become fully operational and the capacity to effectively utilize additional funds has been developed. Budget estimates for 1978 and activities for 1979 should reflect this time phasing.

4. TECHNICAL REVIEW GROUP III - AUGUST-SEPTEMBER 1978

3. Progress in 1977-78

3.2 Research and Development

Screening of new compounds for the chemotherapy of African trypanosomiasis began. Planning continued for research on Chagas' disease and the SWG will meet later in 1978 to consider specific proposals.

A start was made in collaboration with the pharmaceutical industry and academic institutions in the development and testing of drugs for the control of malaria, schistosomiasis, filariasis, African trypanosomiasis, leishmaniasis and leprosy. Such collaboration is essential for the success of this aspect of the Programme, in view of the unique capabilities of industry in drug synthesis and the capacity of the Special Programme to carry out both biological and clinical evaluations. In circumstances where industry is active in drug development, as in schistosomiasis, the objectives of the Programme may be met best by collaboration in the later stages of development, especially in clinical trials in endemic areas. If there is only limited industrial interest, as in drugs for filariasis, the Programme may initiate and support all stages of drug development, seeking to involve industry at any stage where it is appropriate.

4. Recommendations

4.4 Operational Recommendations

4.4.4 African Trypanosomiasis

Emphasis should continue to be given to chemotherapy. In order to provide the groundwork for rational development of new drugs, 70% of the total funds in the chemotherapy sub-component should go to research on biochemical and biological processes of the parasite. Facilities for testing, screening, clinical assays, drug trials and immunological studies should be arranged in an international network of centres.

As funds become available, epidemiological activities, including the WHO/UNDP applied research project in the moist savanna of West Africa, should be expanded to the tropical forest zone and to the dry savanna woodlands of Zambia.

Immunology research should be maintained at the same level as in 1978.

The level of funding for 1979 should be set at us \$1,985,000.

4.6 Programme Review and Evaluation

4.6.2 Large Projects

The Group noted that the following five large field research projects and their associated budgets were transferred from other WHO programmes to the Special Programme on 1 January 1978.

<u>1978 Budget - US \$</u>	Applied research on trypanosomiasis
669,000	epidemiology and control (Upper Volta)

(This was the project with the largest budget listed)

5. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-1)
AUGUST-SEPTEMBER 1979

3. Progress in 1978-79

3.2 Research and Development

Facilities to screen drugs against African trypanosomiasis are being developed in Kenya. A network of centres for clinical pathology of trypanosomiasis is being set up in Africa. A standard protocol for carrying out autopsies on trypanosomiasis victims was developed and incorporated into a manual for use by the clinical network. In applied field research in West Africa, further evidence for the existence of an animal reservoir for Trypanosoma brucei gambiense was obtained and field trials were conducted of a new and promising rapid diagnostic procedure. Practical information was obtained on the value of aerial spraying of insecticides in control of tsetse flies in moist and dry savannah and forest habitats.

4. Recommendations

4.2 Research Recommendations

4.2.4 African Trypanosomiasis

The Committee noted that approximately one-third of the total funds available for research on African trypanosomiasis is accounted for by a single large applied field research project in West Africa. An evaluation of and recommendations concerning this project (TDR 308) are summarized in Section 4.4.1 below. The present balance between the three components of the African trypanosomiasis programme (chemotherapy, immunology and applied field research) was considered reasonable. For next year, immunology research should not be provided a higher proportion of funds than in 1979. The Committee noted that major interest in the development of trypanocidal drugs relates to their potential veterinary use. Large amounts of research in trypanosomiasis are going on outside the Special Programme. The Committee recommended the expansion of links and collaboration with all national and international organizations working in research on human and animal trypanosomiasis, with the aim of maximizing the efficiency and effectiveness of resource utilization. The possibility of formalizing a coordinating procedure should be examined carefully, although the Committee was aware that extensive exchanges already are occurring. Closer links also should be forged with national trypanosomiasis control authorities in affected countries, perhaps by increasing utilization of the good offices of the Organization of African Unity (OAU).

It was recommended that funding for 1980 should be at the same level as for 1979.

4.4 Programme Evaluation

4.4.1 Evaluations by Scientific and Technical Review Committees (STRCs) in 1978-79

The Committee had before it a detailed review of all aspects of the leprosy component of the Special Programme and evaluations of two major applied projects - one on malaria control strategies, carried out in Nigeria; the other on trypanosomiasis epidemiology and control, located in Upper Volta and Ivory Coast. These evaluations were conducted in accordance with recommendations made by TRG III. The Committee made the following recommendations:

b) Applied Research on Trypanosomiasis Epidemiology and Control (TDR 0308)

The Committee concurred with the general findings of the STRC review, and noted that the project provides a valuable focus for African trypanosomiasis research and training in the field, but careful selection and planning of activities are needed. Training aspects of the project should continue to receive priority, perhaps through the RSG component of the Special Programme. Effects of aerial spraying on the ecosystem must be kept under continuous surveillance. New developments in spray application techniques, which will soon be available, may be applicable to inexpensive self-help vector control systems suitable for regular application by village populations. Such self-help programmes should be designed in consideration of their social and economic aspects.

The continued lack of written plans for work and training activities of the project made evaluation by STAC somewhat difficult to carry out. These must be made available to the Chairman of STAC prior to the meeting of the Steering Committee of the SWG on African trypanosomiasis in October 1979, and included in the next report to STAC.

The Committee concluded that for the next two years, i.e. until the end of 1981, the Special Programme should continue to fund the project completely. Before the end of 1981, alternate sources of funding for the application of research findings generated by the project should be sought, perhaps by appropriate bilateral arrangements. It would be appropriate to reduce Special Programme financial support to approximately one-third of 1979 levels by the end of 1981. However there will be a continued need for a field facility for applied research as new or improved control procedures become available.

6. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-2) - SEPTEMBER 1980

5. STAC Review and Conclusions

5.2 Review of SWG Activities

5.2.2 African Trypanosomiasis

STAC recommended no change in the direction of the research or substantial change in the level of funding. The applied field research project in West Africa, presently completely funded by the Special Programme, should be supported at the current (1980) level through 1981, after which the Special Programme support for 1982 should be decreased by two-thirds.

7. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-3) - SEPTEMBER 1981

4. Progress in 1980-81 and Recommendations, 1982-83

4.2 Research and Development

4.2.4 African Trypanosomiasis

As recommended by STAC-2, the applied field research project, TDR-308, (project 790637) is being reduced to one-third of its previous budget.

An STRC review on this component of the Special Programme will be considered by STAC-4.

Recommendations

Noting the progress being made and in order to maintain it, STAC recommended that financial support continue at the present level.

8. REPORT OF THE SCIENTIFIC AND TECHNICAL REVIEW COMMITTEE (STRC)
TO STAC ON THE ACTIVITIES OF THE SCIENTIFIC WORKING GROUP ON
AFRICAN TRYPANOSOMIASIS (1981)

1. Summary and General Recommendations

The STRC has made a number of recommendations throughout the report. The major ones are summarized as follows:

- a) It is recommended that STAC approve the budget shown in Table 1 (Page 14), the figures being based on the information given in this report.
- b) The STRC recommends that increased emphasis be given to developing and evaluating reliable, simple and inexpensive immunodiagnostic tests.
- c) Increased emphasis should be given to studies on the host-parasite relationship in man.
- d) Additional emphasis should be given to the development and testing of tsetse traps in various environments and against different fly species.
- e) There should be continued support of the integrated, longitudinal epidemiological studies now underway in the Congo, Ivory Coast and Zambia. These activities should be re-evaluated in two to three years time.
- f) The STRC recognizes the need to develop a sub-human primate drug-testing model to study central nervous system involvement.
- g) Resources should be made available so that the Steering Committees may approve training as an integral part of SC-sponsored research grants.
- h) The Daloa, Ivory Coast laboratory and clinical facility (TDR 308) should be considered by other TDR SWGs as a centre where research of interest to them could be conducted.

3.1.2 Recommendations (IMMAF)

- a) The STRC agrees that the present priorities established by IMMAF are realistic and within the overall priorities of the SWG and therefore recommends continuation of research along selected lines.
- b) Priority should be given both to testing the CATT in West Africa for effectiveness in T.b. gambiense diagnosis and to developing a CATT antigen suitable for detecting human T.b. rhodesiense cases.
- c) Reference banks for antigens, animal and human sera and mono-specific antibodies, including those produced by monoclonal techniques, should be established. Protocols for organization and operation, as well as a means for making the banked materials available to researchers worldwide, should be prepared by the IMMAF SC and the SWG.
- d) Continued attention should be given to the development of animal models for CNS-involvement studies.
- e) The STRC recognizes the efforts made to obtain human post-mortem material and recommends that the SC determine an appropriate means by which the autopsy kit recipients can now be urged to conduct these studies.

f) Cooperative efforts with national and international organizations should be continued and further workshops and conferences should be held, as appropriate, to ensure coordination and communication.

3.2.2 Recommendations (CHEMAF)

a) The STRC endorses and recommends continuation of the present CHEMAF priorities.

b) Encouragement should be given to studies on interactions between chemotherapy and immune response in human patients and in animal models.

c) Further research on the human clinical response to treatment is recommended.

d) Continued emphasis on clinical pharmacology and testing of existing and new drugs is recommended.

e) The pharmaceutical industry should be continually encouraged by CHEMAF to seek new anti-trypanocidal drugs.

f) STRC recommends that the CHEMAF SC seek funds to support the salaries of certain staff at KETRI to assure continuity of research on primate model development and drug testing. Furthermore, the SC should seek ways - perhaps through RSG - of providing primate facilities to KETRI.

g) STRC recommends that the CHEMAF SC seek ways - perhaps from the RSG - to give basic support to UTRO to ensure the survival of this important facility during the present period of severe economic constraint.

3.3.2 Recommendations (EPIAF)

a) The EPIAF priorities are within the goals of the SWG and the STRC recommends that, in general, research should be continued along the same lines.

b) The STRC was impressed with the integrated research efforts found during their site visits in the Ivory Coast, Congo and in Zambia and recommends that these efforts be continued; but the SWG is urged to solve the administrative problems in Zambia and budgetary and personnel problems in Daloa, in order to make these projects function optimally. The SWG is urged likewise to take steps to integrate epidemiological and entomological studies. These field projects should be evaluated again within the next two to three years to ensure that the present difficulties have been overcome and that satisfactory progress is being achieved. In the view of some members of the STRC, the fragmentation of the TDR programme into specific disease research areas and the transdisease areas of epidemiology and social and economic research, results in a false separation of efforts required to address the total disease in the field. This also emphasizes the desirability of a re-evaluation in two to three years.

c) Further development is recommended to produce inexpensive effective traps; they should then be field-tested under a variety of ecological situations.

d) The polluting effect of insecticides should be evaluated on a long-term basis.

e) Research on human and animal reservoirs should be intensified, including studies on "asymptomatic" human carriers.

f) STRC recognizes the past contributions of TDR 308 to the overall programme. It is recommended that this field station laboratory be considered as a centre in which TDR-sponsored research on other diseases could be carried out.

8. Recommended African Trypanosomiases Budget, 1982-84

TABLE 1

RECOMMENDED AFRICAN TRYPANOSOMIASES BUDGET: 1982-84

<u>IMMAF</u>	<u>1982</u>	<u>1983</u>	<u>1984</u>
	US\$	US\$	US\$
Isolation, antigen preparation field tests, diagnostic kits, VAT directory, ISOVAT Bank	85,000	85,000	90,000
Serum bank, monoclonal antigen development, monoclonal directory and bank	51,500	61,500	70,000
Human and experimental trypanosomiases pathology, pathogenesis, clinical pathology	240,000	240,000	240,000
Immunological mechanisms in <u>T. b. gambiense</u> infections and secondary effects of treatment	40,000	40,000	40,000
ISOVAT typing workshop	<u>10,000</u>	-----	<u>10,000</u>
<u>Sub Total IMMAF</u>	<u>426,500</u>	<u>426,500</u>	<u>450,000</u>
<u>CHEMAF</u>			
Fundamental research	400,000	450,000	500,000
Systematic clinical research	50,000	75,000	125,000
Studies on existing drugs	100,000	125,000	50,000
Preliminary screening in sub-human primate	25,000	30,000	35,000
Clinical studies	<u>100,000</u>	<u>125,000</u>	<u>150,000</u>
<u>Sub Total CHEMAF</u>	<u>675,000</u>	<u>805,000</u>	<u>860,000</u>

<u>EPIAF</u>	<u>1982</u>	<u>1983</u>	<u>1984</u>
Multidisciplinary long-term field studies	450,000	500,000	550,000
Research on tsetse control requirements	50,000	50,000	50,000
Experimental tsetse control including trapping, evaluation of self-help control cost effectiveness and socio-economic research	100,000	150,000	175,000
Parasitic characterization field testing	50,000	75,000	100,000
Life cycle studies and epidemiological models	<u>50,000</u>	<u>50,000</u>	<u>75,000</u>
<u>Sub Total EPIAF</u>	<u>700,000</u>	<u>825,000</u>	<u>950,000</u>
 TOTAL RECOMMENDED BUDGET	 <u>1,801,500</u>	 <u>2,056,500</u>	 <u>2,260,000</u>

9. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-4)
MARCH-APRIL 1982

1. Summary and Major Conclusions

The Committee:

- noted with pleasure findings indicating the efficacy of low-cost tsetse fly traps and the promise of the CATT test as a simple, efficient procedure for diagnosis of African sleeping sickness.

- commended plans for wide-scale testing of tsetse traps in rural areas.

- stressed the usefulness of monoclonal antibodies for the detection and isolation of protective antigens and for diagnostic purposes and commended the establishment of reference banks of these reagents.

2. Recommendations

STAC agreed in principle with the STRC reports on African Trypanosomiasis, Chagas' Disease, Biomedical Sciences and Research Capability Strengthening, but postponed decisions on budgetary forecasts until the meeting of STAC-5 in 1983. STAC made the following recommendations:

2.1.1 African Trypanosomiasis

a) Purification and characterization of antigens and antisera, and the establishment of reagent reference banks, as well as the development and testing of simple, sensitive and reliable immunodiagnostic procedures for T.b.gambiense and T.b. rhodesiense infections, should receive high priority.

b) The development and evaluation of animal models mimicking the human disease, the further delineation of the pathology and pathophysiology of human sleeping sickness and studies on the interaction of chemotherapy and the immune response, including the human clinical response to treatment, should receive prompt attention.

c) The pharmaceutical industry should continue to be encouraged to participate in TDR activities designed to identify, test and determine the effectiveness, clinical pharmacology, pharmacokinetics and related characteristics of existing and potential new drugs.

d) Further development and wide-scale testing of simple, inexpensive and effective tsetse traps under a variety of ecological situations as a potential tool for interrupting disease transmission should receive priority.

e) Integrated, longitudinal epidemiological studies should continue to be implemented and field research centres supported for this work.

f) The Daloa Centre should be strengthened as a base for clinical research, drug trials and immunological studies.

g) The Research Strengthening Group (RSG) should consider further support for the Kenya Trypanosomiasis Research Institute and the Uganda Trypanosomiasis Research Organization.

10. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-5) - MARCH 1983

2. Recommendations

2.1 Research and Development (Programme Area II)

d) African Trypanosomiasis

- Screening facilities for trypanocidal drugs should be made available for use by academic and industrial organizations to stimulate their participation in the development of new drugs; and

- funding for the 1984-1985 biennium should be maintained approximately at current levels.

10. Programme Activities Over the Next Four-Year Period, 1984-87

10.1 Priorities

10.1.13 Subject always to the appearance of new and promising research opportunities and leads, and changing disease patterns, STAC recommended that research on schistosomiasis, African trypanosomiasis, Chagas' disease, filariasis and leishmaniasis should be maintained at approximately the same resource levels as during the 1982-83 biennium.

11. SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEE (STAC-7) - MARCH 1985

1. Summary and Major Conclusions

1.5 African Trypanosomiasis

STAC approved the current workplan. In particular, STAC noted that the Clinical Research Centre, Projet de Recherches Cliniques sur la Trypanosomiase (PRCT), at Daloa, Ivory Coast, was playing an important role in clinical trials, in pharmacokinetic studies and in histopathological and immunopathological studies, and should continue to receive support.
