

WORLD HEALTH
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PROGRESS REPORT ON WHO GLOBAL RESEARCH PROGRAMME
SPECIAL PROGRAMME FOR
RESEARCH AND TRAINING IN TROPICAL DISEASES

The Special Programme for Research and Training in Tropical Diseases (TDR) deals with six main disease groups, namely malaria, schistosomiasis, leishmaniasis, trypanosomiasis, filariasis (including onchocerciasis) and leprosy. In order of priority, malaria and schistosomiasis are the main subjects of relevance for the whole Region, although onchocerciasis and leprosy do constitute an important area of research for some countries in the EMR. In addition to the six diseases for which Scientific Working Groups (SWG) have been established by the Special Programme, other trans-disease Scientific Working Groups have also been created namely in biomedical sciences, epidemiology, vector biology and control, and social and economic research related to the six diseases.

A substantial amount of funds available to the TDR are also devoted to research capability strengthening, which includes training of research workers and strengthening of facilities in research and training institutions.

Few details of each SWG priorities are given in the attached note (Annex I) divided by subject. For more details, interested research workers may refer to the Third Annual Report of the TDR, which outlines the activities of the Special Programme from 1 July 1978 to 30 June 1979. The Fourth Annual Report, covering the subsequent period, from 1 July 1979 to 30 June 1980, will become available in the very near future.

The total number of research projects assisted by the TDR in the EMR, since the inception of the programme in 1975 is 35. The areas of research which have been supported are malaria, schistosomiasis, filariasis, leishmaniasis, leprosy, social and economic research, training, institution strengthening and miscellaneous small one-time grants from the Director's Initiative Fund (DIF).

The countries assisted by the TDR are the following :

<u>Country</u>	<u>No of projects</u>
Egypt	6
Iran	1
Iraq	3
Israel	9
Pakistan	1
Somalia	1
Sudan	14
	<hr/>
	35

The following eighteen institutions are or have been involved in research related to the TDR :

- Biomedical Research Centre for Infectious Diseases, Cairo, Egypt
- Institute of National Planning, Cairo, Egypt
- Faculty of Medicine, Tanta University, Tanta, Egypt
- University of Alexandria Research Centre (UNARC), Alexandria, Egypt
- Faculty of Medicine, University of Cairo, Cairo, Egypt
- School of Public Health, University of Teheran, Teheran, Iran
- Endemic Diseases Institute, Baghdad, Iraq
- College of Medicine, University of Baghdad, Baghdad, Iraq
- Hadassah Medical School, Hebrew University, Jerusalem, Israel
- School of Pharmacy, Hebrew University, Jerusalem, Israel
- National Health Laboratories, Islamabad, Pakistan

- Malaria Control Services, Mogadishu, Somalia
- Onchocerciasis Control Project, Khartoum, Sudan
- Institute for Tropical Medicine, Khartoum, Sudan
- Medical Research Council, Khartoum, Sudan
- Faculty of Medicine, University of Khartoum, Khartoum, Sudan
- Faculty of Veterinary Sciences, Khartoum, Sudan
- Khartoum Eye Hospital, University of Khartoum, Khartoum, Sudan

The decision-making bodies or the SWGs (the Steering Committees) normally decide on the opportunity or otherwise to finance research proposals on the basis of :

- Relevance to the Special Programme objectives as indicated by the Scientific Working Groups.
- Scientific quality and feasibility of success.
- Reasonableness of budget and time-phasing.

A total of sixteen projects are still pending approval while forty-two projects have been rejected or withdrawn as at 30 June 1980. The reason for such rejection are various. The most common is the fact that the topics for research do not correspond to the priorities established by Scientific Working Groups. Such rejection does not diminish the value of the proposed research that may still find support or financing from other sources within WHO or elsewhere.

Another reason for rejection has been the level of excellence of the proposed research which could not stand competition of similar research proposals by other groups working in more equipped or more sophisticated establishments.

A third reason for rejection has been insufficient details of the design of the proposed trial or experiment, and of the methodology of implementation or analysis of data.

From the above, it is clear that strengthening of the research capability in the Region largely depends on three corrective measures : (1) the uplifting of the institutional research capability; (2) the training of research workers in experimental design and advanced research methodologies; (3) the establishment of regional research priorities which fit within those established by the global SWGs, or their inclusion in the global priorities.

For this purpose, the policies of the various SWGs have been summarized in the attached document, so that the ACMR might verify the relevance for the Region of those priorities and point out those aspects which it is desirable to have included.

Attempts have been made to stimulate interest in few research institutions to expand their activities into TDR research priority areas, and if necessary formulate proposals which may be acceptable for institution strengthening, and for individual research workers' training.

Some of the research projects considered of particular importance for the countries of the Region have been partially financed by the WHO Regional regular budget. These are four onchocerciasis research projects in the Sudan, and one malaria research project in Somalia. This procedure is followed when the TDR financing is not sufficient to cover local costs as well as costs for expatriate services.

The WHO Regional Office assists in

- promotion of the activities of the TDR with interested institutions and scientists;
- dissemination of information,
- coordination of TDR priorities and objectives with those established by the regional ACMR;
- coordination of TDR activities with national disease control efforts;
- assistance to national scientists in the preparation of proposals;
- assistance to national institutions in the implementation of funded research projects;
- assistance in general to those interested in TDR activities in the preparation and forwarding of proposals.

While such assistance is offered by the Regional WHO staff and by the Programme staff, decisions made by bodies of the Special Programme, such as the Steering Committees (SC) of the Scientific Working Groups, and the Research Strengthening Group, are completely independent. Regional support/ assistance therefore does not necessarily mean approval of the proposals.

The members of the regional ACMR who are familiar with research institutions and scientists in their own respective countries would greatly contribute to the success of the programme in the Region by pointing out to the Secretariat names of individuals and institutions who may be conducting or have the capability of conducting studies within the priorities indicated in the attached document (Annex I).

It is the intention of the Region to complete a list of national institutions and individual research workers who are involved in research in the subjects covered by the TDR so that dissemination of information concerning the TDR may be possible.

Simple forms have been prepared for this purpose and are attached as Annexes II and III.

ANNEX I

MALARIA

The three SWGs in malaria, range from basic biology, through research directed to the development of vaccines and new drugs, to the field research to find the best way to use available control methods.

CHEMAL. The improvement of existing drugs and the development and application of new ones are the main priorities of the SWG on Chemotherapy of Malaria (CHEMAL). In cooperation with the Walter Reed Army Institute of Research (WRAIR), mefloquine, a new antimalarial drug, is now undergoing clinical trials in Brazil and Thailand. Promising leads in sustained release formulation of antimalarial drugs and studies on innovative ways of targeting drugs are also being pursued.

IMMAL Progress is being made in the complex task of developing a vaccine or vaccines against malaria under the SWG on Immunology of Malaria (IMMAL). Research ranges from identification of antigens on parasites and cell membranes to trials of potential vaccines in animal models. Through its SWG members the Programme keeps close contact with various other groups planning and funding research in this area. Advances have been made in the test systems for the detection of circulating antigens, and the remarkable new technique for the production of monoclonal antibodies is being exploited in an effort to isolate particular antigens and assess their role in the induction of protective immunity.

Joint Activities. The field of basic biology is being pursued jointly by the CHEMAL and IMMAL SWGs. The improved continuous in vitro cultivation of erythrocytic forms of Plasmodium falciparum is being used increasingly as a system for drug susceptibility testing and the screening of potential antimalarial drugs, as a source of antigen for immunological studies, and as a model for in vitro studies. Good progress has been made in the isolation of different stages of the parasite from infected erythrocytes, and of free parasites, an essential pre-requisite for immunological research towards vaccines. Studies on membrane structure and function, carbohydrate metabolism and protein synthesis have produced valuable leads for further immunological and chemotherapeutic research.

FIELDMAL The Scientific Working Group on Applied Field Research in Malaria (FIELDMAL) is concerned with the improvement of methods of malaria control in the field. Its work is strongly oriented towards solving technical, ecological, socio-economic and human problems facing malaria control and eradication programmes all over the world. A large project on the epidemiology and control of malaria in various ecological strata in West Africa continues to provide data which can directly be translated into malaria control strategies in corresponding ecological strata in tropical Africa.

The resistance of P. falciparum to 4-amino-quinolines presents a serious and urgent problem with respect to malaria control. A global programme for the assessment and monitoring of drug susceptibility is now being implemented, it also includes studies on alternative drug regimes for individual and community use and on methods for limiting the spread and eliminating the foci of drug resistant malaria. Standard kits for in vitro sensitivity testing are produced in Manila,

and distributed to the collaborating institutions throughout the world. A new microtechnique, recently developed outside the Programme, has now been shown to offer several advantages. CHEMAL is continuing the development of this method which may lead to the large-scale production of simpler and more effective test kits.

SCHISTOSOMIASIS

The objectives of the SWG on Schistosomiasis are:

- To improve current methods of schistosomiasis control
- To develop or obtain better drugs than those currently available.
- To improve and standardize diagnostic techniques, and
- To study immune responses to lead towards vaccine development and an understanding of the mechanisms of pathological processes

The strategic plan in this SWG continues the research approaches previously adopted: epidemiology and snail control, chemotherapy and biochemistry, and immunology and basic sciences. The fourth, applied field research, will take advantage of recent advances in the chemotherapy of schistosomiasis to plan and implement the required field trials.

The pharmaceutical industry continues to show interest in the development of schistosomicidal drugs and the special Programme has maintained its role in support of this development effort, especially by clinical evaluation of new agents. Biochemical studies of the schistosome have revealed a number of interesting findings, especially on the tegument of the worm. The modes of action of various drugs and their metabolic pathways are being clarified and it appears that the effectiveness of some antischistosomal drugs is dependent upon the immune response of the host.

One of the priority areas for immunological research is the production and purification of antigenic materials for immunodiagnostic tests.

Studies are in progress on the metabolism of Biomphalaria snails, on their chemo-reception mechanisms, and on differences between strains that are highly susceptible and those that are refractory to miracidial infection.

During 1980-1981 the activities in the four research approaches will continue according to the strategic plan. These will include another workshop on Population Epidemiology, lead directed synthesis in drug development, the characterization of antigens and field research on control methodologies.

FILARIASIS

The overall objectives in this SWG area are:

- to improve the use of existing filaricides and to find new ones,
- to find means of reducing the inflammatory reactions to filarial parasites in man;
- to identify filarial antigens for both serodiagnostic tests, and possibly vaccine development, and
- to study the vector and human components of filarial infections in order to improve control of transmission in problem situations

The research approaches are divided into chemotherapy, immunology and pathology, and epidemiology, field and vector studies

The aims in chemotherapy are to improve the treatment of ocular onchocerciasis, to find and develop new macrofilaricides effective against O. volvulus, and to determine practical dosage schedules for large-scale treatment of lymphatic filariasis.

Clinical research has included the quantitative assessment of the Mazzotti reaction and means to alleviate it, the adverse effects of diethyl carbamazine (DEC) treatment on posterior segment eye lesions in onchocerciasis, an assessment of reactions to transepidermal DEC lotions, attempts to reduce the reactions to death of microfilariae in the cornea, and trials of metrifonate, amodiaquine, furazolidone and nitrofurantoin. The causes of low-grade persistent microfilaraemia after DEC treatment of W. bancrofti infections are also being investigated.

In the search for new filariacides, more than 970 compounds have been screened at the primary level, and a secondary Onchocerca screen in cattle has been developed. Mebendazole and flubendazole appear to be promising leads; these compounds may be macrofilaricidal and embryostatic, especially if preceded by treatment with levamisole

Investigations into the causes and prevention of inflammatory reactions to the death of microfilariae are in progress by using animal models and in man. Efforts are being made to develop in vitro and in vivo culture systems, especially as a source of parasite antigens. This is necessary for efforts to improve serodiagnostic tests, and for research towards the possible development of vaccines.

During the next two years this SWG will continue work already underway and expand the programme on the basis of results obtained.

AFRICAN TRYPANOSOMIASIS

The SWG on African Trypanosomiasis has three Steering Committees, each dealing with one subject area: epidemiology (EPIAF), chemotherapy (CHEMAF), and immunology/pathology (IMMAF). The overall objectives of this SWG are:

- better understanding of the epidemiology of African trypanosomiasis,
- development of simple diagnostic tests,
- development of new chemotherapeutic agents,
- improvement of clinical management of patients and definition of standard procedures of treatment, and
- improvement of tsetse fly control.

The Applied Research Programme in West Africa undertakes research on animal reservoirs, diagnostic methodology, and aerial spraying of insecticides. Some important advances have been made including the confirmation of an animal reservoir of T. B. gambiense, a field trial of a new and promising card flocculation test, a new technique for detecting low levels of parasitaemia and practical information about the effects of aerial spraying of insecticides in the control of the tse-tse fly. An in-depth review of this project was carried out early in 1979 (See Book 4 of the Annexes to the Third Annual Report, STRC Report No. TDR/308: Trypanosomiasis).

Activities in the forthcoming biennium will be a continuation of and logical extensions of present research.

Under EPIAF, activities will include new or expanded research on:

- further development of diagnostic tests, including improvement of the card flocculation test, field trials of improved tests,
- animal reservoirs,
- ecology of Glossina, and
- simple means of tsetse control.

Under CHEMAF:

- systematic chemotherapy with new leads and existing compounds including screening and clinical trials,
- Pharmacodynamics,
- identification of new potential chemotherapeutic targets such as enzymes,

AFRICAN TRYPANOSOMIASIS (cont'd)

- a study of the genetics of trypanosomes, including the genetics of antigenic variation and drug resistance

Under IMMAF:

- improved serodiagnosis,
- pathology and immunopathology using a network of collaborating centres now being established in Africa, and
- characterization of antigens

LEISHMANIASIS

The objectives of the SWG according to subcomponent are:

Epidemiology (EPH/ISH):

- obtain precise information on the geographical distribution, incidence, and prevalence of the human disease, the reservoirs of infection, and the zoonomids and taxonomy of sandfly vectors, including the design of improved methods for effective control, and

- improve methods for the identification of the parasite

Immunology (IM/ISH):

- develop better immunodiagnostic tests and a reference serum bank,
- develop a vaccine, and
- elucidate the macrophage/parasite relationship and the parasite biochemistry.

Chemotherapy (CH/ISH):

- define optimal treatment schedules using currently available drugs,
- develop new therapeutic compounds; and
- support research on the mode of action and targeting of chemotherapeutic agents.

A modest drug development programme has commenced and a protocol for the treatment of mucocutaneous leishmaniasis has been drawn up. Epidemiological projects and studies on phlebotomine sandflies have been initiated in several countries. Research on experimental immunization and the mechanisms of host resistance, and on certain leishmanial antigens, which are necessary steps towards the development of vaccines and improved serodiagnostic tests, is in progress

The work plan for the 1980-81 biennium calls for continuation of the projects underway and addition of :

- a training seminar on epidemiological methods for leishmaniasis,
- epidemiological projects in Brazil, Israel, and Honduras, and
- a biosystematics study on sandflies.

LEPROSY

Research in the leprosy component is carried out by two Scientific Working Groups: Immunology (IMMLEP), and Chemotherapy (THELEP). In early 1979 the entire programmes of both IMMLEP and THELEP were subject to an in-depth evaluation. Based on that review, specific recommendations were made on how best to exploit the considerable success to date.

The objectives of IMMLEP are:

- development of an antileprosy vaccine,
- development of leprosy-specific immunological methods for detection of immune responses to M leprae, and
- an increased understanding of immunopathological mechanisms involved in leprosy .

IMMLEP research has reached a stage where it appears that development of an effective vaccine is a real possibility. During the 1980/81 biennium the work will continue to be focused on this objective.

The objectives of THELEP are:

- better ways to use existing drugs,
- development of new drugs; and
- assessment of national needs for improved chemotherapeutic methods.

THELEP has initiated clinical trials of combinations of drugs in India and West Africa using a standardized protocol. Thirteen drug development projects are currently underway, including the study of the modes of action of compounds.

THELEP work in progress will continue in 1980-81 with the following additions:

- a study of the efficacy of some established drugs in normal mice,
- short-term clinical trials to evaluate new therapeutic regimes,
- new surveys of the prevalence of dapsone-resistance, and
- development of new drug screening systems and possibly some other field trials of new and combined drug therapy.

VECTORS OF DISEASES

Research on vector control is coordinated by the SIG for Vector Biology and Control and the individual diseases of the SWG.

This Component aims to: 1) develop techniques and methods for biological control of vectors, 2) promote research on model systems pertinent to control of the diseases, and 3) coordinate research in the field of vectors in the other SIGs.

Biological Control of Vectors

The objectives of the SWG are:

- to identify, evaluate and develop biological control agents for the safe and effective control of invertebrate vectors and intermediate hosts of diseases, and
- to identify national and institutional needs for strengthening research and educational capacity and to participate in this strengthening.

A strategic plan has been developed, including an initial priority list of organisms to be evaluated.

Studies of individual control agents include:

- bacteria (B. sphaericus and B. thuringiensis),
- fungi (Cochliomyces, C. clavosporus, L. giganteum, M. anisopliae and others),
- nematodes (R. culicivora, C. da pratti and others)

The search for new biological control agents has high priority, with emphasis on spore-forming bacteria.

The most significant development thus far has been the promising results obtained with Bacillus thuringiensis israelensis.

The activities in 1980-81 will be a continuation and expansion of work underway, exploiting progress already made and expanding into new areas, such as predaceous invertebrates and larvivorous, such as **vector** control agent.

VECTOR BIOLOGY AND CONTROL (Cont'd)

Vector Ecology and Behaviour

To start activity in this area, a preliminary Scientific Working Group (Pre-SWG) met and considered two main series of objectives : (1) those involving the development and/or application of trans-disease tools, methods and approaches, and (2) those involving detailed investigations on a specific topic as a model with trans-disease relevance. Following a review of the proposed SWG plans the STAC recommended that the establishment of this SWG be postponed, and that relevant priority activities on vector ecology and behaviour be included in the SWG on Biological Control of Vectors.

EPIDEMIOLOGY

This multi-disciplinary trans-disease component relates closely to activities in the disease SWGs and is concerned with identifying and understanding the factors which influence the prevalence and severity of the six diseases. The objectives of this SWG are :

- to provide a basis for the design of measures to improve disease control,
- to promote locally relevant multidisciplinary field research projects in areas where several of the six diseases are endemic;
- to promote the development and dissemination of epidemiological methodology adapted to the study of the six diseases and related health problems; and,
- to promote training in epidemiology as it relates to tropical public health.

The SWG encompasses a wide range of disciplines, e.g. clinical medicine, laboratory sciences, pathology statistics, behavioural sciences and economics. The major activity at present is the long-term epidemiological study based in Zambia. In the development of research in epidemiology throughout the Programme, the disease-oriented SWGs relate closely to the SWG on epidemiology.

The epidemiological field studies and field trials of disease control at the TDRC, Ndola are now nearly completely staffed and equipped, and plans to conduct longitudinal broad-spectrum epidemiological studies have been started. A pilot survey has been conducted leading to the finalization of the study protocols and the mapping, census-taking and baseline surveys were started for the first multidisease long-term study in one area of the country.

In addition to work underway, the following activities are planned in 1980 :

- the proposals of the TDRC for training in epidemiology are to be consolidated into concrete training programmes;
- the longitudinal studies should become operational and new areas will be added, and,
- studies on transmission and control should be underway, in co-operation with the disease-specific SWGs (especially schistosomiasis, trypanosomiasis and malaria).

It should be noted that the disease-specific SWGs devote a significant proportion of their resources to epidemiological research, e.g. FIELDMAL, Schistosomiasis, African Trypanosomiasis, Chagas' Disease and Leishmaniasis

BIOMEDICAL SCIENCES

The aim of the Biomedical Sciences Scientific Working Group (BIOS) is to promote fundamental research on the diseases of interest to the Special Programme and on their pathogens, and through these efforts to develop new approaches to tools for diagnosis, therapy, prevention and control. BIOS functions through promoting information exchange and research training, and stimulating tropical disease research, including its funding. Workshops have been held on membrane pathobiology and cultivation technology and their proceedings will be published. Courses on hybridoma technology with applicability to parasitic diseases are planned, as is a course on micromethods applicable to research on tropical diseases.

SOCIAL AND ECONOMIC RESEARCH

This important trans-disease component is just reaching operational status. Activities to date involve the planning of an effective programme of activities.

The overall objective of this SWG is to improve the implementation of control measures and programmes for the diseases covered by the Special Programme.

To assist in reaching this objective, three main research categories have been developed with ten specific objectives. These are still tentative as the SWG has not yet met to draw up the Strategic Plan:

Social Research

- understanding of human perception or awareness of disease and how it affects the success of disease control activities;
- understanding of the role of human behaviour in disease transmission and control; and,
- definition and determination of the role of the community in disease control activities.

Economic and Management Research

- development of methods of cost effectiveness analysis of disease control measures;
- analysis of manpower implications when shifting from vertical to horizontal disease programmes; and,
- improvement of the management of disease control programmes.

Social and Economic Conditions

- development of socio-economic indicators of the efficacy of disease control programmes;
- identification of the role of social and economic conditions in designing disease control programmes;
- improvement of the planning of economic development projects to minimize adverse disease impacts; and,
- evaluation of the role of population movements in disease transmission and control programmes.

SOCIAL AND ECONOMIC RESEARCH (Cont'd)

The pre-SWG meetings identified a number of pilot projects which have been supported, including :

- Socio-Economic Aspects of the Feasibility of Malaria Control Programmes
- Workshop on the Role of Human/Water Contact in Schistosomiasis Transmission
- Use of Engineering Control Measures to Prevent Schistosomiasis and Malaria Transmission

The first meeting of the SWG will be held late in 1979 to continue the development of the Strategic Plan and to review projects in priority areas for support in 1980.

RESEARCH CAPABILITY STRENGTHENING

The basic objective of this critical part of the Programme is to assist tropical endemic countries to assume their appropriate roles in the research needed to solve their health problems, in particular those related to the six diseases included in the Programme.

In 1978/1979, a draft Strategic Plan was reviewed by the Research Strengthening Group. The main objective of the plan is to establish a network of collaborating institutions in tropical endemic countries, which will initiate and conduct research and research training relevant to the prevention, treatment and control of the six diseases. The two main strategies reflected in the plan are : (1) institutional support, and, (2) a programme of research training as a component to the former.

All activities are being developed in close collaboration with national authorities, in the context of national needs and resources. Between 1 July 1978 and 30 June 1979, 59 training grants and 5 re-entry grants were awarded, and 19 institutions received various types of support ranging from a single capital grant to long-time support for periods up to five years.

Considerable importance is attached to the difficult question of the evaluation of progress in this area. One important step was a meeting of representatives of some of the institutions receiving long-term support, to lay the foundations for institutional self-evaluation. These efforts are continuing.

There are already some tangible indicators of success. For example, through the courses on continuous in-vitro culture of P. falciparum, a number of scientists in developing countries have now established this technique in their own laboratories, and have demonstrated their ability to teach others. Already one of the participants has made remarkable progress in his attempt to culture other plasmodia species. Thus there is ready evidence of successful transfer of technology.

One feature of major importance is the interaction between the RSG and the SWGs. Many research grants approved by SWGs provide useful training opportunities for scientists and technicians from tropical endemic countries. In a complementary way, group training in the working environment of an affected country, visiting scientists' grants and institutional grants enhance the opportunities for SWG-supported research, particularly in epidemiology and clinical and field trials. In the initial documents setting out the aims and attributes of the Programme the mutual reinforcement of these two Programme Areas was deliberately devised. Early experience of this interaction shows that the original concepts are feasible and effective.

In 1980 and 1981 ongoing activities will be continued, special emphasis will be placed upon making the RSG activities known to scientists and administrators in affected countries, identifying institutions which merit strengthening and assisting them as appropriate in preparing proposals.

ANNEX II

FORM A

No......

RESEARCH INSTITUTION SURVEY

Name of Institution

Address

Governing body

Financing bodies

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Premises (description)

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Staff

Professional

.....

Sub-professional

.....

Administrative

.....

Ancillary

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Facilities

Routine

Research

Laboratory

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Clinical

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Training

.....

Field areas

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COMPILED BY

ANNEX III

FORM C

No

RESEARCH WORKERS SURVEY

NAME SEX

AGE NATIONALITY

ADDRESS

PRESENT TITLE

.....

STAFF SUPERVISED

QUALIFICATIONS

ACADEMIC

.....

NON-ACADEMIC

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EXPERIENCE GENERAL

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CONTACTS WITH OTHER RESEARCH WORKERS AND INSTITUTIONS

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RESEARCH EXPERIENCE BY SUBJECT

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PUBLICATIONS IF ANY

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AREAS OF INTEREST

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COMPILED BY:

RESEARCH WORKERS SURVEY

NOTES AND REMARKS

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COMPILED BY :