UNITED NATIONS

DP

Governing Council of the United Nations Development Programme

Distr.
GENERAL

DP/PROJECTS/REC/23
22 April 1987

ORIGINAL: ENGLISH

Thirty-fourth session
26 May-19 June 1987, New York
Item 5 (b) of the provisional agenda

PROGRAMME PLANNING

COUNTRY AND INTERCOUNTRY PROGRAMMES AND PROJECTS

Assistance for a global project

International Laboratory for Research on Animal Diseases (ILRAD)

Improved Control of Animal Trypanosomiasis (GLO/87/004)

Recommendation of the Administrator

Estimated UNDP contribution	$2 600 000
Duration	Three years
Executing agency	UNDP

I. BACKGROUND

1. The International Laboratory for Research on Animal Diseases (ILRAD) was established in 1974 by the Consultative Group on International Agricultural Research (CGIAR) to assist in the development of effective controls for two major livestock diseases: trypanosomiasis and theileriosis. Together, these two diseases prevent livestock production in vast areas of some 50 developing countries in Africa, Central and South America, the Middle East, the Indian subcontinent, and the rest of Asia. The total loss in human and economic values - not only in milk and meat, but also in leather, wool, fertilizer, and other animal by-products, to say nothing of animal power, as well as in potential capital resources - is incalculable. These goods are produced by ruminant livestock from vegetation that man cannot eat, often on land that man cannot use for crops. Where the land is

arable, integrated livestock and cereal production may be desirable. The welfare of hundreds of millions of people, among them some of the world's poorest, is at stake.

2. Trypanosomiasis is a disease complex which affects both man and his livestock in Africa, Asia and South America. Especially in Africa, it is one of the major constraints of rural development and is also a serious disease of man. The disease in cattle is caused by three species of trypanosomes: Trypanosoma brucei, Trypanosoma vivax and Trypanosoma congolense. The transmission of these trypanosomes is done mainly by the tsetse fly. Trypanosoma evansi may be important in camels; the transmission of this species is achieved mainly by the bites of bloodsucking flies other than the tsetse. T. gambiense (West Africa) and T. rhodesiense (East Africa) are well-known human pathogens also transmitted by the tsetse fly. Most of the countries south of the Sahara are affected and large areas which are potentially capable of raising large and small domestic ruminants are not used or are only sparingly used for animal production. It is known that Africa harbours about 170 million head of cattle and even more sheep and goats; specialists estimate that these figures, especially those concerning cattle, could be doubled and, in some cases, even tripled, providing trypanosomiasis can be kept under permanent control or eradicated. Cattle, sheep and goats, as well as other domesticated and wild animals, may be infected by one, two or three trypanosome species. The animals develop an acute or chronic disease showing anaemia and weakness; death occurs very frequently. In any case, productivity is seriously affected and the economic losses are very heavy. This, in turn influences human welfare and health.

3. Some effective methods for control of both animal and human trypanosomiasis and their vectors are available and it is known that in some areas chemotherapy and insecticides have been successfully used. Nevertheless, except in rare areas where success has been obtained after great and expensive efforts, trypanosomiasis still constitutes a major hazard for man and his livestock: neither chemotherapy nor prophylaxis, nor the use of short-acting or residual insecticides can yet be considered economic, effective and environmentally safe methods against the disease or its vector. The use of the sterile male technique with tsetse flies is still uncertain and costly. For some years, both national and international authorities have become conscious of the potential importance of the phenomenon of trypanotolerance, which is known to be prevalent in some breeds of cattle and small ruminants and in many species of wild herbivores as well. Moreover, some trypanotolerant animals and, perhaps, human beings are capable of self-curing a trypanosome infection. Despite the fact that trypanotolerance has been known for nearly 80 years, very little is known of its mechanism; only recently have modern techniques provided some hope for the study of this phenomenon. Its understanding could provide an opportunity for the development of many areas of Africa.

4. In view of the constraints indicated above, the ILRAD research programme has focused predominantly on investigating host/parasite/vector relationships which may prove susceptible to immunological control techniques. Unlike other diseases for which effective vaccines have been produced, there was little evidence from the field to suggest that animals could develop a significant immunity to trypanosomiasis under natural conditions. The reason behind this failure to

develop a significant degree of acquired resistance was held to be the fact that the trypanosome has evolved a sophisticated process termed "antigenic variation". This allows its successful survival in, and onward transmission from, livestock which were inherently capable of mounting protective immune responses to the parasite. The process of antigenic variation is simply a means by which the parasite, throughout its life in the animal, continuously changes its surface molecules so as to avoid the lethal effects of the host's immune response to molecules previously manifested.

5. ILRAD has therefore developed an institutional framework which provides a multidisciplinary approach to investigate the problems involved in analysing the major areas in host/parasite/vector relationships which could be relevant to the possible development of practical immunological control measures for this disease. This approach involved the following disciplines: parasitology cell biology, biochemistry, molecular biology, immunology, pathology and entomology.

6. At its January 1978 meetings, the UNDP Governing Council approved a five-year project at a cost of $3,605,200 to enable ILRAD to carry out intensive basic research concerning the immunological and related aspects of controlling animal trypanosomiasis. The overall objective of the ILRAD trypanosomiasis research programme is to develop economically effective means of controlling trypanosomiasis with a consequent increase in livestock production, improved human nutrition and better land use in affected countries. This will be achieved by possible development of new immunological control methods, utilization of resistant domestic livestock, improved use of available drugs and integrated programmes of vector control. The training of personnel involved in trypanosomiasis research and control in affected countries will be an essential component of ILRAD's trypanosomiasis programme.

7. ILRAD has, in a relatively short time, made significant progress in several important areas of trypanosomiasis research and identified new areas of importance for future studies. Significant progress has been made in elucidating the mechanisms underlying the phenomenon of antigenic variation and its relevance to the development of effective immunological control measures for trypanosomiasis. Studies in this area necessitated ILRAD the development of *in vitro* cultivation systems for the pathogenic bloodstream forms of the three trypanosome species important in animal disease. Long-term continuous cultivation was first achieved with *Trypanosoma brucei*, and similar culture systems for *T. congolense* and *T. vivax* are being established, the latter in collaboration with the Swiss Tropical Institute. Research in other laboratories and at ILRAD has also provided *in vitro* systems for cultivation of the animal infective trypanosome stage, which occurs in the tsetse (metacyclic trypanosome) of both *T. brucei* and *T. congolense*.

8. ILRAD research to date has thus helped to increase knowledge of the disease in the field, augment knowledge of the biology of the parasite and elucidate the host parasite relationships important to the manifestation of innate or acquired resistance to the disease. The research towards improved control of trypanosomiasis is being conducted in collaboration with national African institutions, international organizations including the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), the

International Atomic Energy Agency (IAEA), the International Trypanotolerance Centre, the Organization of African Unity (OAU) and the laboratories of developed countries.

9. Several conclusions that can be drawn from the research results obtained thus far can be summed up as follows:

(a) The available breeds of trypanotolerant livestock offer a very promising potential means for improving agricultural productivity in the tsetse-infested areas of Africa. It has been shown, both in the field and experimentally, that trypanotolerant cattle are capable, to varying extents, of resisting the pathogenic effects of trypanosomiasis and remaining productive. Elucidation of the mechanisms involved in this disease resistance pattern will offer important insights into: (i) the breeding of improved trypanotolerant livestock, and (ii) the possibility of developing new immunological control measures;

(b) The phenomenon of antigenic variation, especially in view of the recent demonstration that trypanosomes can exchange genetic material, still poses a major obstacle to the development of a widely applicable vaccine based on the variable antigens of either the bloodstream or tsetse-transmitted forms of these parasites. An understanding of the mechanisms of trypanotolerance may indicate potential non-variable trypanosome antigens which could serve as alternative immunogens against trypanosomiasis;

(c) It will be possible to sustain and also improve the current control of trypanosomiasis, based on the use of trypanocidal drugs and insecticides, by developing new techniques for the diagnosis of the disease and better assays for monitoring both drug levels in livestock and the development of drug resistance by the parasite; and

(d) In order to devise and support improved methods for control of trypanosomiasis, it is necessary to support sustained basic research to expand knowledge of the basic biology of the parasite, and the nature of its complex interactions with its hosts.

10. In order to help train national scientific personnel and disseminate information, ILRAD has been conducting an active programme. By the end of 1985, the Laboratory had trained over 300 personnel involved in trypanosomiasis research and control in affected countries. They included: (i) 143 participants in individual training programmes, 56 of whom were from African countries; (ii) 47 scientists and senior technicians who received specialized training for periods varying from one week to one year, 35 of whom were from Africa; (iii) 21 post-graduate students; and (iv) 25 post-doctoral fellows who gained experience in the application of modern technologies to animal disease problems.

ILRAD had also held 10 courses, seminars or workshops related to trypanosomiasis research. These have been attended by 549 participants, with 247 coming from 30 different African countries. In organizing these sessions, ILRAD has co-operated closely with FAO, WHO, IAEA and the International Cell Research Organization (ICRO).

ILRAD staff have also published over 100 scientific articles on trypanosomiasis.

11. ILRAD research programmes on trypanosomiasis and related activities were reviewed by an independent consultant appointed by UNDP in 1984. In October 1985, an external panel of independent specialists commissioned by the Technical Advisory Committee of the CGIAR also made a comprehensive review of the ILRAD programmes. This panel highly commended the work being carried out by ILRAD and strongly recommended continuation of further support from the international donor community.

II. THE PROJECT

12. The purpose of the proposed project is to intensify research on trypanosomiasis with a view to developing and implementing improved control measures for trypanosomiasis. Specific objectives of the project are to:

(a) Determine the genetic basis and mechanisms involved in the enhanced natural resistance of certain breeds of domestic livestock to the pathogenic effects of trypanosomes;

(b) Develop and validate new techniques for the specific diagnosis of active disease in livestock, the accurate identification of trypanosome species in tsetse flies and surveys of the prevalence of trypanosomiasis in different locations;

(c) Develop new techniques to assay the levels of chemotherapeutic and chemoprophylactic compounds in the blood and tissue fluids of treated livestock and quantitative in vitro assays to accurately determine the development of resistance by trypanosomes to such compounds;

(d) Investigate the biological, biochemical and genetic properties of trypanosomes to identify suitable targets for immunological or chemotherapeutic attack; and

(e) Transfer information and technology developed at ILRAD and elsewhere to personnel involved in trypanosomiasis control at international, regional and national levels, by the issue of scientific publications, reports and newsletters, provision of technical training for both individual and course participants and by organizing scientific seminars and workshops.

13. The benefits of the proposed project will include:

(a) Provision of essential scientific information and data relating to the biology of pathogenic trypanosomes, the diseases they cause in man and animals and the nature of the host responses which contribute towards resistance to the trypanosomiases;

(b) Introduction of improved and more specific diagnostic tests for trypanosomes and more precise technologies for monitoring drug levels and the development of drug resistance, to help national organizations, both in Africa and

elsewhere, develop better trypanosomiasis control programmes using the currently available control measures and monitor them more effectively;

(c) The wider and more efficient use of trypanotolerant varieties of domestic livestock for food production and general agricultural purposes including traction in order to achieve better land use in the tsetse-infested areas of Africa;

(d) In the long term, the development of economically effective, environmentally sound, integrated measures for the control of trypanosomiasis. These may include the use of improved trypanotolerant livestock, vaccines, chemotherapy, tsetse control and alterations in land use; and

(e) Opportunities for the training of scientific and technical personnel concerned with trypanosomiasis research and control in countries infested by the tsetse fly and advanced scientific training and the transfer of new technology to staff of African universities and institutions of higher learning concerned with training future generations of scientists.

14. ILRAD will work closely with the International Livestock Centre for Africa (ILCA) in a large-scale study of the productivity of trypanotolerant livestock in Africa. ILRAD provides training in animal health procedures for ILCA field staff. ILRAD scientists will take an active part in defining the tsetse-trypanosomiasis levels affecting the rearing of livestock under different management systems. Close collaboration will also be maintained with the International Centre of Insect Physiology and Ecology (ICIPE) in Nairobi on various aspects of trypanosomiasis, the International Trypanotolerance Centre in the Gambia, and with national research institutions in African countries, as well as developed country laboratories. Project activities will also be co-ordinated with the WHO/Tropical Disease Research (TDR) Programme.

15. The Programme Committee of the ILRAD Board of Trustees annually reviews research progress and policy. Provision also exists for the formation of a Scientific Advisory Committee comprised of eminent scientists in disciplines related to the ILRAD research programme when the Programme Committee and the Director-General require specialized advice outside the expertise of Programme Committee members. Representatives of UNDP, FAO and WHO/TDR will be invited to join the annual ILRAD Programme Committees to review research progress and consider any project alterations required. In addition, representatives of major international organizations and donor countries are invited each year as observers at the Board of Trustees Meeting when the report of the Programme Committee is discussed. ILRAD staff also monitor the progress of each research project by twice yearly internal reviews. Towards the end of the project, UNDP, in consultation with ILRAD, will undertake an assessment of the research programme by a team of independent consultants. UNDP, however, will not field such a mission in the event the Technical Advisory Committee of the CGIAR schedules an independent review of ILRAD at that time.

16. UNDP funds will be used to provide the following: three senior scientific staff, one training officer; equipment and supplies; and training including

post-doctoral fellowships, in-service training, conferences and workshops which will receive approximately 30 per cent of the UNDP allocation.

17. UNDP direct costs will be used for financing a senior Administrative Secretary, mid and end-of-project evaluations and contingencies to be made available for special workshops related to animal trypanosomiasis and related activities to facilitate inter-institutional and intercountry co-operation. These will be considered strictly on merit on a case-by-case basis and subject to availability of funds.

18. The Administrator intends, through contractual arrangements between ILRAD and UNDP, to entrust the implementation of this project to ILRAD, with the clear understanding that the Director-General of ILRAD will seek the advice of FAO and WHO when needed. As in the past, UNDP will follow closely all the developments in this global project and, together with FAO and WHO, will participate in the Programme Advisory Committee referred to above.

19. The proposed UNDP contribution is $2,500,000, of which $2,230,000 will be for sub-contracts, while direct costs will account for the remaining $270,000. The expenditures under the project will be contained within the IPF available for global projects established by the Governing Council for the fourth cycle.

III. RECOMMENDATION BY THE ADMINISTRATOR

20. The Administrator recommends that the Governing Council approve this project.
