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PLAN FOR THE SECOND DECADE

INTERNATIONAL LABORATORY FOR RESEARCH ON ANIMAL DISEASES
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FOREWORD

The International Laboratory for Research on Animal Diseases (ILRAD) was established in 1973 with a mandate to develop improved control measures for livestock diseases which seriously limit world food production. A virulent form of theileriosis - East Coast fever (ECF) - and African animal trypanosomiasis were chosen as ILRAD's first disease targets. During the first 10 years, a modern laboratory complex was constructed on the outskirts of Nairobi, scientific and support staff were recruited, research and training programs were established and substantial research results were achieved. This plan for the second decade was prepared as a basis for continuing the programs and measuring progress towards ILRAD's disease-control objectives. It should also serve as a basis on which to anticipate the resources which will be needed to support ILRAD's research and training programs in the future. The plan has been formulated by senior members of staff with participation by the Board of Directors.

This document begins with a brief description of constraints on livestock production in Africa and other developing regions, including the impact of trypanosomiasis and theileriosis. Next the history of ILRAD's establishment and development is outlined, and ILRAD's research strategy is described and compared with the approach of other organizations working towards improved control of theileriosis and trypanosomiasis. Current research strategies and achievements are presented and future strategies developed. ILRAD's training and outreach programs are also described. Consideration is then given to the resources which will be needed to support ILRAD's future research, training and outreach activities. In conclusion, possible new research areas on other diseases are considered in the event of success in present research efforts.

It is notoriously difficult to predict the outcome of any basic research program. When research is concerned with the development of immunological methods for the control of refractory haemoprotozoan diseases, the task is doubly difficult. Success cannot be guaranteed by prolonged effort and hard work, but depends also on scientific acumen, improvements in basic knowledge, developments in related fields and good fortune!

Theileriosis and trypanosomiasis are intractable animal diseases which have been studied for over 80 years, and still no overall solutions are available. Substantial progress has been recorded in the search for improved immunological control of theileriosis, but in the case of trypanosomiasis no fully satisfactory solution is yet in sight. Many years of research may still be required before satisfactory immunological control measures can be developed and put into practice.

Meanwhile, substantial scientific results are being obtained, many of which will contribute to eventual solutions, and can also be applied to improve existing theileriosis and trypanosomiasis control measures. Given the magnitude of the problems caused by these two important diseases, any improvement, no matter how slight, will have a significant impact on livestock productivity and agriculture in general in the regions where they occur.

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It is worth remembering the extent of the areas in Africa where ECF and tsetse-transmitted trypanosomiasis are endemic, and the benefit that would accrue from the availability of effective disease prevention measures. The elimination of ECF would prevent the loss of an estimated 500,000 cattle a year, while vaccines for trypanosomiasis would allow an increase of approximately 120,000,000 cattle (or the equivalent numbers of sheep and goats) in an area of approximately 7 million square kilometres, with accompanying benefits to mixed agriculture and socio-economic development.

I would like to take this opportunity to thank the national and international donors who have provided the financial support necessary to carry out ILRAD's research and training programs. In 1983, core funds were provided by the World Bank (International Bank for Reconstruction and Development - IBRD), the United Nations Development Program (UNDP) and the governments of Australia, Belgium, Canada, the Federal Republic of Germany, France, Italy, the Netherlands, Norway, Saudi Arabia, Sweden, Switzerland, the United Kingdom and the United States of America. In previous years, the Rockefeller Foundation, the International Development Research Centre (IDRC) and the government of Ireland also contributed to ILRAD's core funds. Special research projects, conferences and training activities have been supported by ILRAD's regular donors, and in addition by the Food and Agriculture Organization (FAO), the World Health Organization (WHO), the Organization of African Unity (OAU), the International Atomic Energy Agency (IAEA), the Ford Foundation, the Commonwealth Foundation, the Australilan Centre for International Agricultural Research, the Deutche Stiftung für Internationale Enwicklung, the Wellcome Trust and the International Cell Research Organization.

A.R. Gray
Director General

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BACKGROUND

Domestic livestock play a fundamental role in agriculture throughout Africa and other developing regions of the world. In areas which support crops, animals are usually closely linked with household food production. They provide meat and milk, and also manure which is used as fertilizer and fuel. For 90% of the world's farmers who do not have access to tractors or other forms of mechanization, animals also provide the only alternative to hand cultivation. In these circumstances, it has been estimated that one draft ox can increase the productivity of a farm household sixfold. By raising animals for family consumption and sale, farmers can balance the risks of crop failure. Livestock also provide farmers an outlet for savings in areas where investment opportunities are rare.

Two-thirds of all the agricultural land in the world is unsuitable for crop production. Over vast areas where crops cannot be grown, domestic livestock support ranching enterprises and pastoral households. The contribution of ruminant livestock is particularly important because cattle, sheep, goats and camels can transform herbage which has no value for direct human consumption into high-quality foods and other products.

Food production is particularly critical in Africa, with over 400 million people, high population growth rates and a shrinking agricultural sector. It is no longer possible to increase food supplies substantially simply by bringing additional land under cultivation or by dramatic improvements in farming technology - new opportunities in both these areas are limited.

Improvements in livestock productivity represent a major opportunity for increasing food supplies. At present, protein consumed from animal sources is equivalent to over 50% of the protein provided by cereals, and FAO estimates that the effective demand for animal products in developing countries will have doubled by 1990 over 1976 levels. African farmers and herdsmen keep approximately 160 million cattle and 286 million sheep and goats, but productivity is low - 13% of the world's cattle are raised in Africa, but the continent produces only 5% of the world's beef. Developing countries as a whole account for 60% of all livestock in the world, but only 20% of all livestock products.

Several factors contribute to low animal production levels in Africa and other developing regions. These include poor animal nutrition, the limited production potential of many local breeds, inadequate marketing outlets, and management systems which are not geared towards maximum production.

Disease is also an important constraint on animal production - in many areas the major constraint. An estimated 50 million cattle and buffalo and 100 million sheep and goats die from disease each year. It has been estimated that a 6% reduction in these losses would result in food for an additional 250 million people. Furthermore, mortality figures alone do not reflect the full impact of livestock disease because many animals become diseased but eventually recover. In these cases, the expense of treatment and

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losses in growth and productivity add enormously to the overall cost of livestock disease.

Effective measures are available to control many of the most lethal bacterial and viral diseases which affect livestock. However, for many parasitic diseases, safe, effective and inexpensive control measures have not yet been developed. Among these, theileriosis and trypanosomiasis are particularly important.

In Africa alone, these parasitic disease complexes are believed to account for the deaths of 3 million cattle a year. These diseases also inhibit the use of cattle, and in the case of trypanosomiasis even human settlement, over a large area of the continent.

THEILERIOSIS

A number of theilerial diseases affect cattle, sheep and goats in Africa, the Middle East and Asia (see Figure 1).

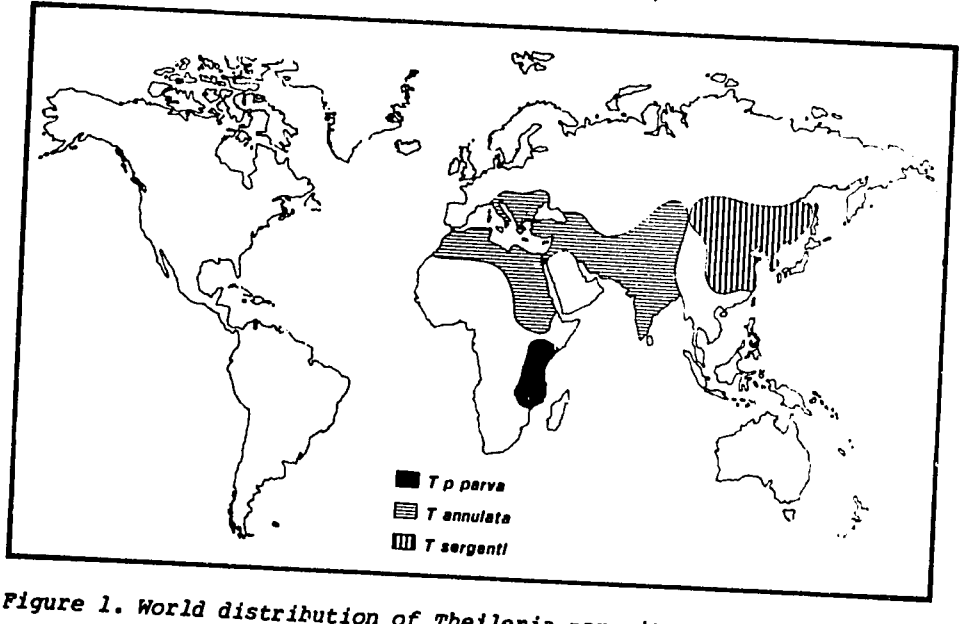

Figure 1. World distribution of Theileria parasites.

ECF is a form of theileriosis which affects cattle in Kenya, Uganda, Tanzania, Rwanda, Burundi, Zaire, Malawi and Mozambique. The disease is severe and frequently fatal. Cattle losses attributed directly to ECF are estimated to be as high as 500,000 a year from a total cattle population of 25 million in the endemic area.

ECF is caused by the protozoan parasite Theileria parva, which is transmitted by the brown ear tick, Rhipicephalus appendiculatus. Two subspecies of the parasite occur in Kenya, T. parva parva maintained in cattle and T.p. lawrencei maintained in buffalo. Three related species, T. taurotragi, T. velifera and T. mutans, also occur and may cause mild infections in cattle.

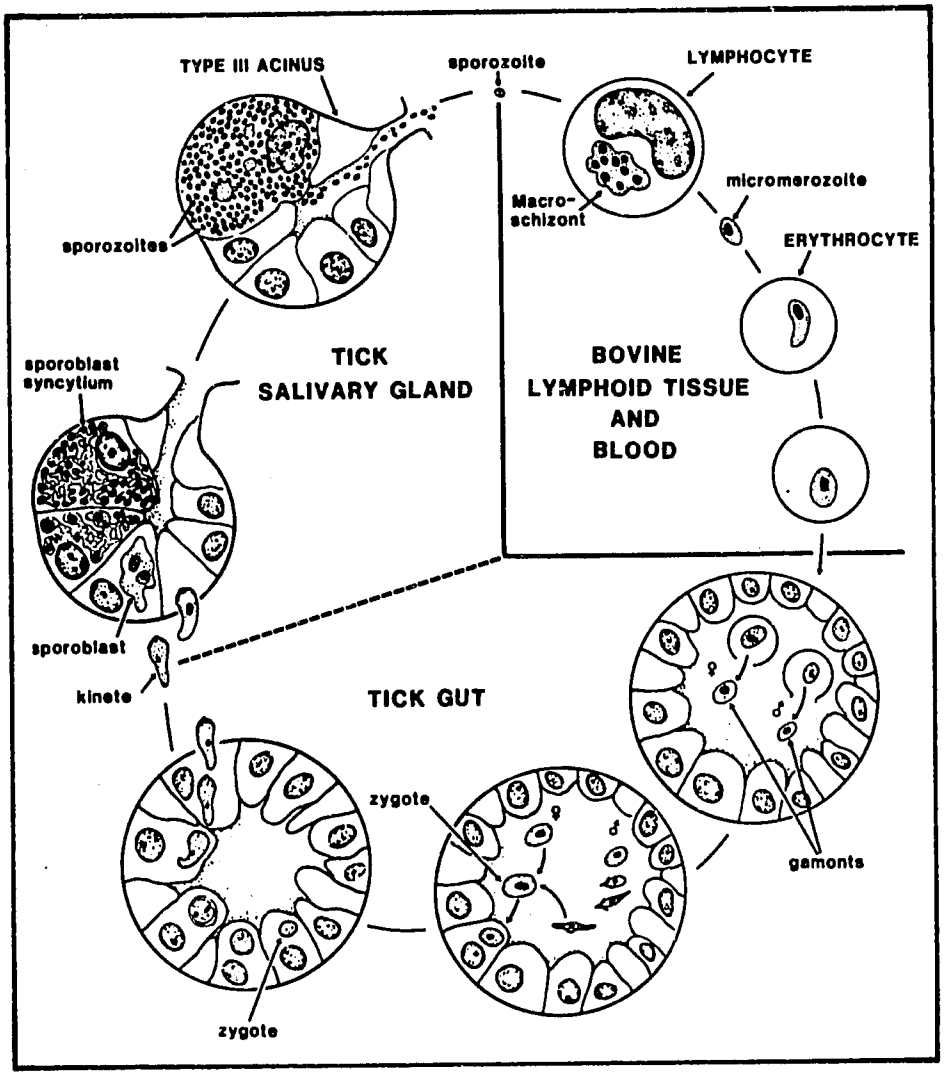

Figure 2. Lifecycle of T.p. parva. Sporozoites are transmitted to the bovine host in tick saliva. They enter the lymphocytes and develop into macroschizonts. After a period of nuclear divsion, these give rise to microschizonts which produce numerous micromerozoites. The micromerozoites escape from the lymphocytes and enter the erythrocytes where they are ingested by feeding ticks. In the tick gut, the parasites differentiate into male and female gametes which fuse to form zygotes. These enter the cell lining of the gut where they differentiate into kinetes. The kinetes traverse the gut wall and become free in the tick's body cavity. They move to a salivary gland and enter one cell type, the E-cell of the type III acinus. Here they form an elaborate intracellular sporoblast syncytium which undergoes segmental fission and gives rise to 30,000 to 50,000 sporozoites. These are introduced with the saliva into a new mammalian host, initiating a new cycle of parasite development.

The Theileria parasite undergoes a complex lifecycle in the tick vector and the bovine host (Figure 2). Ticks feed on cattle three times - as larvae, as nymphs and as adults. Transmission of ECF is thought to occur most commonly when ticks feed on infected cattle as nymphs and then on disease-free animals as adults. ECF sporozoites which develop in the salivary glands of infected ticks are transmitted to cattle when the ticks feed. These sporozoites invade bovine lymphocyte cells where they develop into macroschizonts which multiply rapidly. The infected lymphocytes are transformed into enlarged lymphoblast cells, and many of these are induced to multiply synchronously with the parasites. The number of parasitized cells increases rapidly and large-scale destruction of lymphoid cells occurs, often leading to death of the animal.

During the infection, some of the macroschizonts change to microschizonts. These give rise to micromerozoites which are released and infect red blood cells. The infection of further ticks occurs when the ticks ingest the infected red blood cells.

The first sign of ECF in cattle is enlarged lymph nodes. The temperature rises and the animal loses condition. Milk production declines and pregnant cows may abort. Acute cases occur in fully susceptible animals, particularly in valuable imported stock, and mortality rates may be as high as 100%.

Infections with a related Theileria species, T. annulata, are a major problem in North Africa, the Middle East and Asia, causing chronic anaemia, reduced productivity and often death. T. sergenti also occurs in Asia, causing an important cattle disease in affected areas, while T. hirci affects sheep in the Middle East.

TRYPANOSOMIASIS

Different forms of trypanosomiasis occur over large areas of Africa, Latin America, Asia and the Middle East, as shown in Figure 3. In tropical Africa, tsetse-transmitted trypanosomiasis is found over an area of about 10 million square kilometres, or roughly one-third of the continent. With information available at present, it is impossible to assess, even approximately, the direct losses caused by animal trypanosomiasis, but the fact that livestock in Africa are treated with more than 25 million doses of trypanocidal drugs a year gives some indication of the magnitude of the problem.

Trypanosomiasis is caused by protozoan parasites which infect cattle, sheep, goats, pigs, horses, donkeys, camels, many wildlife species and man. In Africa, the major pathogenic trypanosome species for domestic ruminants and wildlife are Trypanosoma congolense, T. vivax, T. simiae and T. brucei. Closely related subspecies of T. brucei, T.b. rhodesiense and T.b. gambiense, cause sleeping sickness in man. These trypanosomes are transmitted by tsetse flies (Glossina species) and very occasionally by other biting flies.

It has been established that tsetse flies occur in 38 African countries. This includes approximately 7 million square kilometres of savannah and light woodland with good rainfall, considered suitable for livestock or mixed agricultural development. Today, out

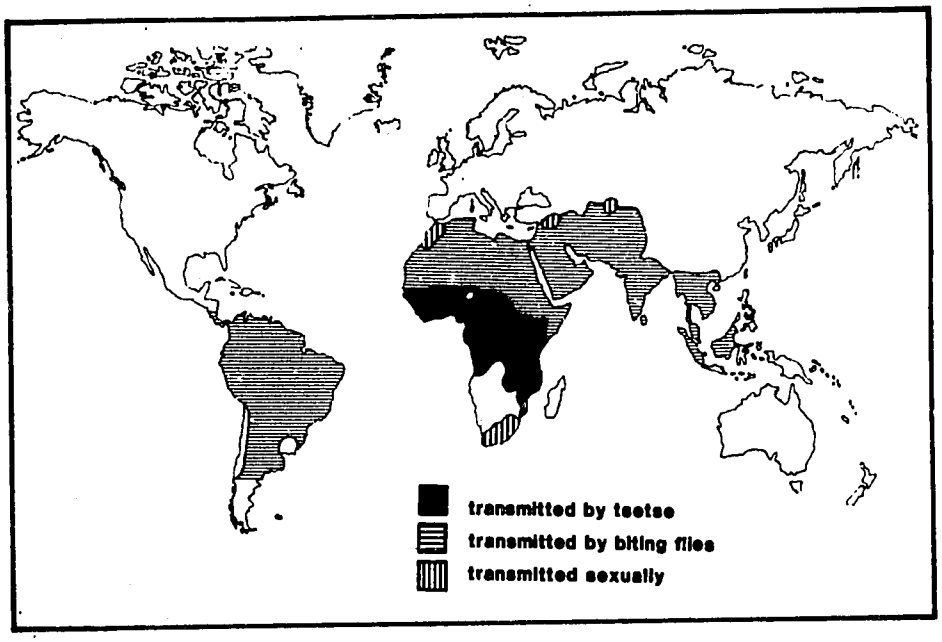

Figure 3. World distribution of animal trypanosomiasis.

of a total cattle population of about 160 million in Africa, only 20 million are located in the tsetse-infested zone. Effective control of trypanosomiasis would make it possible to raise a further 120 million cattle in this region without environmental stress. This increase in production could provide an additional 1.5 million tons of meat a year, as well as significant improvements in other forms of agriculture.

African trypanosomes are ingested by tsetse flies which feed on the blood of infected animals (see Figure 4). The parasites undergo a cycle of development within the fly. The three major African species finish this phase of development as metacyclic forms in the mouthparts or salivary glands of the tsetse. When infected tsetse feed, the metacyclic parasites are transmitted to mammals and initiate new infections which develop in the blood and tissues, causing anaemia, emaciation, reproductive disorders and death.

Livestock may also play a role in the epidemiology of human trypanosomiasis. T.b. rhodesiense has been isolated from cattle, sheep and goats, and T.b. gambiense has been found in sheep, pigs and dogs. WHO estimates that 45 million people are at risk from human trypanosomiasis, with 20,000 new cases occurring each year. The disease can destroy whole rural communities, and fear of trypanosomiasis can lead people to desert otherwise productive land, causing incalculable losses of food production.

Trypanosomiasis caused by T. evansi is transmitted mechanically by biting flies. This disease is a major problem in Africa, the Middle East, Asia and South America. It causes a severe disease in horses and camels and loss of productivity in cattle and buffalo. T. vivax infections have occurred in 12 South American countries, and

some outbreaks have been severe. The epidemiology and economic impact of T. vivax in South America have not yet been assessed, but it is clearly a significant threat to the cattle population of the continent.

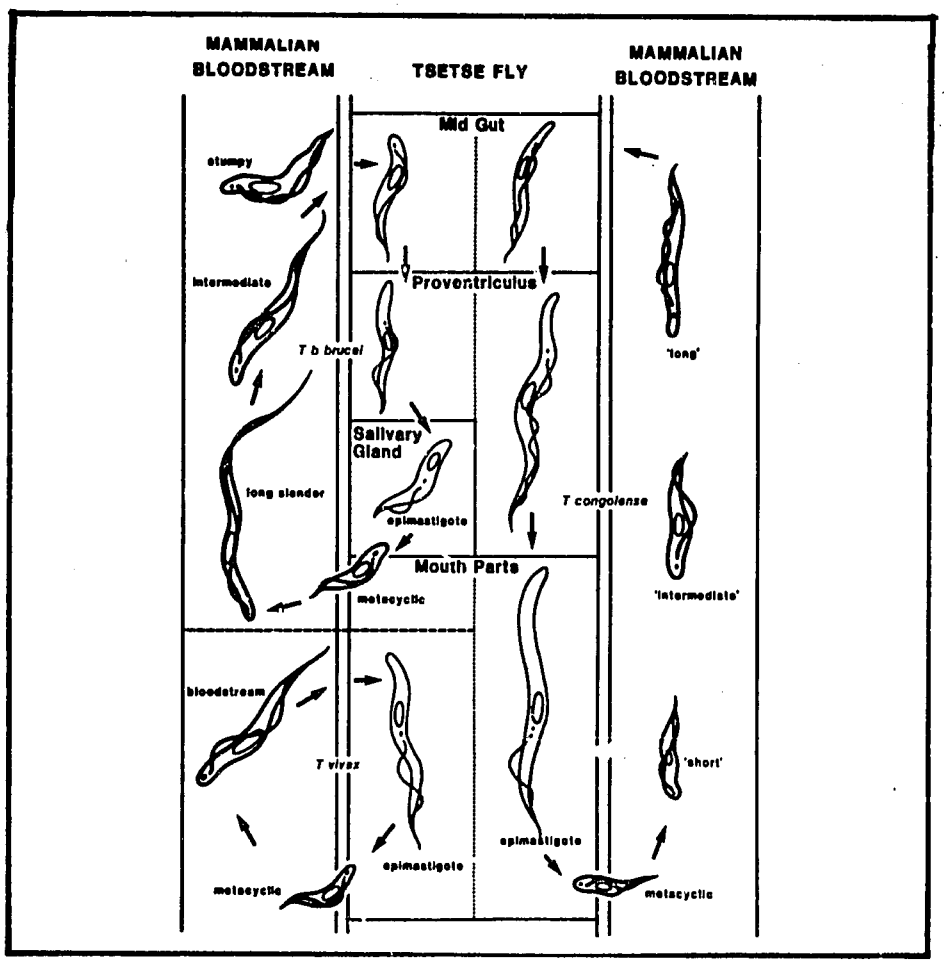

Figure 4. Lifecycle of T.b. brucei, T. congolense and T. vivax. Heavy outlines indicate parasite forms with surface coats consisting of variable glycoprotein antigens. Light outlines indicate uncoated forms which are not infective to mammals. T.b. brucei develops in the tsetse midgut, proventriculus and salivary glands, where metacyclic forms occur which are infective to mammals. T. congolense develops in the tsetse midgut, proventriculus and mouth parts, where infective metacyclic forms are produced. T. vivax develops in the tsetse mouthparts.

CURRENT METHODS OF THEILERIOSIS AND TRYPANOSOMIASIS CONTROL

The control or prevention of any infectious livestock disease can be approached in a number of different ways. Efforts may focus on breaking the pattern of disease transmission, in the case of theileriosis and trypanosomiasis by vector control, on eliminating the agent which causes the disease, i.e. by chemotherapy, or on increasing the level of innate or acquired immunity in the animals at risk.

Vector control as a means of breaking the transmission cycle

Only one major species of tick, R. appendiculatus, transmits ECF, and vector control by a high standard of management and regular application of acaricides can be effective. However, this approach requires a level of supervision and capital investment often beyond the reach of small farmers. The development of acaricide resistance presents an additional problem.

Trypanosomiasis may be transmitted cyclically by about 30 species and sub-species of tsetse fly, or mechanically by other biting insects. Both types of vector are highly mobile. Furthermore, different tsetse species occupy a variety of habitats, ranging from arid bush to dense rain forest. Early methods of tsetse control involved vegetation clearing and wildlife elimination. This approach has been abandoned except in special cases due to ecological drawbacks, high costs and technical problems stemming from rapid regeneration of tropical vegetation. Most current tsetse-control programs are based on insecticide spraying, but this method is not entirely effective in areas of dense vegetation or high rainfall.

A number of international and national organizations are conducting research into the development of new methods of trypanosomiasis vector control. The International Centre of Insect Physiology and Ecology (ICIPE) has concentrated on basic ecological studies of tsetse species in efforts to find vulnerable habits for attack. The Centre for Overseas Pest Research (COPR), WHO and FAO have undertaken operational research in tsetse-infested areas to find better methods of applying existing insecticides, in some instances in association with tsetse traps, and to evaluate more biodegradable insecticidal compounds. IAEA and various national bodies are exploring tsetse control methods based on the release of male flies sterilized by irradiation.

Control by chemotherapy or chemoprophylaxis

Efforts to find effective drugs for the treatment of ECF were fruitless until theilericidal activity was identified in menoctone and the coccidiostat halofuginone. An analogue of menoctone, 'Clexon', was first marketed in Kenya in 1983. However, successful treatment requires early diagnosis, and the drug is expensive for small farmers.

Treatment with trypanocidal drugs on an individual or herd basis has been an important method of trypanosomiasis control since the

1920s, in the case of T. evansi, and since the early 1950s for tsetse-transmitted infections. However, drug-resistant trypanosome strains are being encountered with increasing frequency. The cost of developing new drugs has escalated out of all proportion to the potential return from drug sales - no new trypanocidal drugs have been introduced for general use for the last 20 years. Furthermore, new drugs are likely to meet the same problems of drug resistance as their predecessors, and the existence of an extensive reservoir of infection in the wildlife population - beyond the reach of normal methods of drug application - militates against chemotherapy as a longterm solution to the trypanosomiasis problem.

Measures to increase levels of innate or acquired resistance

It has been known for some time that cattle which recover from ECF show high levels of immunity against subsequent attack. This finding was exploited many years ago by farmers who used Theileria-experienced livestock as draught animals in East and Central Africa. In the years preceding the establishment of ILRAD, a method of immunizing cattle by infection with Theileria sporozoites and simultaneous oxytetracycline therapy was developed in Kenya, but it was not exploited on a practical scale.

Several workers have shown that it is possible to immunize cattle against T. annulata using schizont-infected lymphoblastoid cell lines. Similar cell lines of T. parva were established in tissue culture in 1970, providing another potential immunizing material. These developments point to the very real possibility of developing a safe and effective ECF vaccine.

Early efforts to induce immunity against trypanosomiasis met with little success but clearly demonstrated the variability and multiplicity of protective trypanosome antigens. During the years just before ILRAD was founded, major advances were achieved in the understanding of human and murine immunology which could be applicable to problems associated with trypanosomiasis in domestic livestock. Furthermore, certain species of wildlife and some varieties of domestic livestock are able to develop a high degree of resistance to the pathogenic effects of trypanosomes. These factors led to the belief that a sustained attack on the immunology of trypanosomiasis could yield useful results.

ESTABLISHMENT OF ILRAD

ILRAD was established on the 13th September 1973 under a Memorandum of Agreement between the Government of Kenya and the Rockefeller Foundation, acting as executive agent for the Consultative Group on International Agricultural Research (CGIAR).

This document states

The purpose of the Laboratory will be to serve as a world centre for research on ways and means of conquering, as quickly as possible, major animal diseases which seriously limit livestock industries in Africa and in many other parts of the world. The Laboratory will concentrate initially on intensive research concerning the immunological and related aspects of controlling trypanosomiasis and theileriosis (mainly East Coast fever). It may, however, eventually extend its research to other serious animal disease problems for which its facilities and expertise are appropriate, provided such extension is approved by its Board of Directors and the Government of Kenya does not object from a disease safety standpoint. In carrying forward its programme, the Laboratory will develop close linkages with governmental and regional organizations undertaking research on the same or related disease problems.

The following activities were foreseen

1. Basic research, applied research, experimentation and field testing of results. These activities may be undertaken by the Laboratory on its own premises or in association with appropriate national or regional organizations, but field testing shall in all cases be carried out in accordance with appropriate disease safety regulations of the government in whose territory it is conducted

2. Publication and dissemination of research results

3. Strengthening and creating appropriate links with national and regional institutions dealing with the control of animal diseases and related problems of animal production, particularly in Africa

4. Organization of discussion groups, seminars, workshops and conferences on topics related to the work of the Laboratory

5. In cooperation with universities and other research institutes, provision of opportunities for advanced professional training and experience in animal disease research within the scope of the Laboratory

6. Training of scientists who will be involved in research, education and action programmes in cooperating countries in

which the Laboratory's programme will be applicable

7. Assistance to cooperating countries in using and applying the research results of the Laboratory

8. Such other activities as may be found necessary or desirable to further the objectives of the Laboratory.

FACILITIES

The Kenya Government provided a 70-hectare site at Kabete, on the outskirts of Nairobi, and construction of a modern complex of laboratories and support facilities began in May 1976. The complex was inaugurated on 5 April 1978 by President Daniel arap Moi, then Vice-President of Kenya.

ILRAD's facilities at Kabete comprise an administration block, six large research laboratories, electron microscopy, radioisotope and irradiation facilities, a library, conference rooms, breeding units for laboratory animals, tsetse flies and ticks, accommodation for cattle, sheep and goats, media preparation rooms, electronic and engineering workshops, a transport yard and stores. Screened isolation units are available for cattle, sheep and goats used for research on trypanosomiasis. Staff housing is provided for 28 families and hostel accommodation for 20 students. Catering and staff recreation facilities are also available. ILRAD's facilities now meet most of the requirements of the research program, and no major expansion is envisaged in the foreseeable future.

At the end of 1981, ILRAD acquired a 13,000-hectare ranch on the Kapiti plains about 40 kilometres from Nairobi. The ranch has a breeding herd of Boran (Bos indicus) cattle which provides nearly all the cattle required for ILRAD's research program. About 100 Bos taurus cattle are also used every year for experimental work. At present, these animals are purchased from local breeders.

STAFF

Staff development has advanced steadily at ILRAD, starting from a small nucleus of scientists who assembled in Nairobi in 1975 to initiate the research programs. The CGIAR guidelines for the longterm development of ILRAD envisage 51 senior positions recruited on an international basis. In 1983, ILRAD's senior staff positions consisted of 46 manyears, including 42.5 manyears funded by ILRAD and 3.5 manyears funded from outside sources. The Technical Advisory Committee (TAC) of the CGIAR has approved a staffing level of 48 to 50 manyears for 1984. The current allocation of senior staff positions is given in Table 1.

Specialized technical support is provided by Research Associates who are recruited on an international basis. Research Associates work in such areas as molecular biology, electron microscopy, tissue culture, radioisotope manipulation and the operation and maintenance of advanced equipment. They also train and supervise technical support staff. The number of staff members in this category is likely to remain fairly constant at about 20.

Table 1. Senior scientific and administrative staff (manyears).

	1983 Actual	1984 Approved
Research		
Scientists and Visiting Scientists	25	24-26
Post-doctoral Fellows	11	14
Research Support		
Director of Research	1	1
Clinical Veterinarian	1	1
Training and Information		
Training and Outreach Officer	1	1
Scientific Editor	1	1
Administration		
Director General	1	1
Director of Administration	1	1
Financial Controller	1	1
Animal Production Manager	1	1
General Operations		
Chief Engineer	1	1
Food and Housing Officer	1	1
Total	46	48-50

The technical support needs of the laboratories are met by Kenyans with university degrees or equivalent technical college qualifications. General support staff are also Kenyans, filling positions in areas such as secretarial and library services, building maintenance, animal production and transport. In 1983, 310 Kenyans were employed in these categories.

RESEARCH EQUIPMENT AND MATERIAL

The laboratories are equipped to high standards, and current budget procedures ensure that each scientist is provided with adequate materials and technical support. As the scientific staff has expanded through the years, new major items of equipment have been purchased. Further additions of equipment will be required until ILRAD reaches full staffing levels.

THE GLOBAL EFFORT TO CONTROL THEILERIOSIS AND TRYPANOSOMIASIS - ILRAD'S ROLE

In undertaking research on theileriosis and trypanosomiasis, scientists at ILRAD are tackling two of the most intractable animal health problems in the world. Both diseases have been recognized since the last century as major constraints on livestock production, and scientists from many countries have worked for decades to develop effective control measures. These scientists have contributed a great deal to the understanding of the diseases and have provided a basis for current research efforts. Their work has also led to a number of improvements in control and treatment, but no fully satisfactory vaccine or other control method is yet in sight for either disease. Major problems remain to be solved which may require continuing research for many years.

Several national, regional and international agencies are involved in theileriosis and trypanosomiasis research projects and are carrying out field programs designed to improve disease control. The approach of these agencies is essentially practical, field oriented and related to immediate needs. Generally speaking, they do not have the mandate or the capacity to carry out substantial basic research, but they are in a position to benefit directly from results achieved in the laboratory.

ILRAD is the only major international institution concerned with theileriosis and trypanosomiasis which devotes the greatest part of its resources to basic research. Collaboration with international, regional and national programs ensures the efficient transfer of ILRAD's research findings and expertise to organizations directly involved in disease control in the field.

Among international agencies, FAO coordinates the largest disease control programs. The FAO Worldwide Program for the Control of Animal Trypanosomiasis was initiated in 1974, and FAO activities aimed at the control of ticks and tick-borne diseases began even earlier. Since ILRAD was founded, cooperation with FAO research and field programs has been close. ILRAD scientists have served on the FAO Panel of Experts on the Ecology and Technical Aspects of the Program for the Control of Animal Trypanosomiasis and Related Development and on the FAO Expert Panel on Ticks and Tick-borne Diseases.

WHO includes African trypanosomiasis as one of the six refractory diseases covered under its Special Program for Research and Training in Tropical Diseases. ILRAD collaborates closely with WHO, particularly in research on immunological aspects of African trypanosomiasis and in training. ILRAD scientists contribute to the Scientific Working Group on Trypanosomiasis and one scientist serves on the Steering Committee on Immunology and Pathology of African Trypanosomiasis. ILRAD staff members have also served on IAEA Expert Panels.

ILRAD is closely associated with OAU's Interafrican Bureau for Animal Resources (OAU/IBAR). The OAU/IBAR's International Scientific and Technical Research Commission (ISCTRC) is involved in the coordination of livestock disease control efforts on a regional

basis. The Director of OAU/IBAR is currently a member of ILRAD's Board of Directors, and the Director General of ILRAD is a member of ICSTRC's Executive Committee.

Several regional and international organizations concerned with agricultural development in Africa have become involved more recently in research and field programs aimed at improved control of livestock diseases. The seven principal bilateral donors to Africa formed an association called Cooperation for Development in Africa (CDA) in 1981 to coordinate activities and resources in close collaboration with African governments and regional organizations. The CDA is working to strengthen national research systems with the goal of increasing the productivity of smallscale farmers. This project will include an animal disease component to which ILRAD can contribute. ILRAD will also cooperate with regional disease control projects being introduced by FAO and the United Nations' Economic Commission for Africa (ECA) and with regional research on trypanosomiasis and ECF supported by the European Economic Community (EEC).

Several bilateral donors contribute to national livestock disease control programs in Africa. Support usually entails the contribution of material and specialized personnel, construction of facilities and training of national staff. For example, Denmark has provided major assistance for the construction of cattle dips in East Africa, Germany (Federal Republic) supports research on chemotherapy and tsetse control, Belgium and the Netherlands contribute to the development of national laboratory facilities for improved diagnosis of livestock diseases, the USA has made major contributions to several trypanosomiasis control projects, and France and Germany have initiated a joint research project in Upper Volta concentrating on immunity to trypanosomiasis. ILRAD is developing collaborative research activities with this joint project in areas of common interest.

ILRAD's research programs are designed to support the work of others and to follow promising avenues for disease control, particularly immunological approaches, which have not been fully pursued elsewhere. The needs of organizations involved in trypanosomiasis and theileriosis control were carefully considered in planning ILRAD's research strategy, and close collaboration on a continuous basis ensures that work does not overlap and that useful results are communicated as quickly as possible.

ILRAD'S RESEARCH PROGRAMS

ECF and trypanosomiasis research at ILRAD concentrates primarily on improved disease control by immunological means. However, this emphasis does not preclude research on other promising disease control methods, such as strategic use of chemotherapy or vector control.

Research at ILRAD is carried out on a multidisciplinary basis. Scientists in fields such as parasitology, entomology, biochemistry, molecular biology, immunology, cell biology, pathology and epidemiology work together on projects with defined disease-control objectives.

The organization of ILRAD's research programs into projects with defined objectives follows a recommendation made by TAC in its 1980 Quinquennial Review of ILRAD. Research on each disease is divided into three project areas. The project areas are interrelated, but they provide a framework for the efficient conduct of research towards well defined objectives. This structure allows flexibility to adjust research activities as needs and developments dictate.

The Program Committee of the ILRAD Board of Directors establishes research policies which are developed and implemented by the Director General and the Director of Research. ILRAD scientists with relevant research interests and expertise have been identified as project leaders to coordinate activities in each project area.

Given ILRAD's multidisciplinary approach, research in each area is often conducted in several laboratories, and collaborative studies are undertaken as appropriate with other organizations. Field studies are also carried out in collaboration with relevant national and international programs.

THE THEILERIOSIS PROGRAM

Epidemiological studies on ECF are providing basic information on the distribution and immunogenic characteristics of T. parva subspecies affecting cattle in East Africa. Trials, based on immunization by infection with sporozoites and treatment with a curative drug, have been successful and have validated the in vitro methods developed to characterize parasite stocks. Although this method of immunization against ECF is unlikely to be applicable on a large scale because of difficulties in providing sufficient parasite material and the cost of treatment, it can be used to protect small numbers of particularly valuable livestock.

Improved vaccines are still required for large-scale immunization. Such vaccines will, in all probability, be based on isolated antigenic components of Theileria parasites or of parasitized host cells. Current research concentrates on the identification and chemical characterization of immunogenic T. parva sporozoite antigen(s). The production of sufficient antigens for large-scale vaccination programs will involve the use of new technology to synthesize antigens artificially.

The development of a successful sporozoite-based vaccine will not preclude the necessity for developing, in parallel, a vaccine based on Theileria schizonts. Immunity to sporozoites could be stage specific and might not afford adequate protection against the schizont stage of the parasite, especially in cases where infected tick challenge is exceptionally high. Immunity to the schizont stages appears to be mediated by immune cells, rather than antibody. A major research effort will continue to elucidate the immune mechanisms and antigens involved. This research will also increase basic understanding of the bovine immune system and will thus be relevant to trypanosomiasis and other animal diseases.

Research on ECF has developed to a point at which potentially effective disease control methods can be identified. It is important to visualize the consequences of their application and to plan future activities which will meet the needs which are likely to arise.

Project area 1. Epidemiology and control of theileriosis

The objective of ILRAD's theileriosis epidemiology project is to increase knowledge of theileriosis epidemiology in Africa and other affected regions and to evaluate improved immunological control methods in endemic areas.

Research areas include

a. Study of the occurrence and importance of theileriosis caused by T.p. parva, T.p. lawrencei, and T. mutans in specified areas, giving consideration to vectors, parasites and hosts

b. Selection and evaluation of appropriate parasite strains and methods for immunization of livestock against T.p. parva and T. p lawrencei in different areas, based on infection with live sporozoites and chemotherapeutic treatment

c. Execution and evaluation of an integrated approach to the control of theileriosis, including various immunization methods, vector control and chemotherapy

d. Economic evaluation of the impact of methods to control theileriosis on cattle productivity under different epidemiological and management conditions, including assessment of the impact of other tick-borne diseases.

Strategies and achievements - 1973-83. Immunization by infection and treatment offers the best immediate possibility of improved ECF control while work continues on the development of a safe and effective vaccine based on antigens from sporozoites or schizont-infected cells.

Work is in progress to improve this experimental immunization method. Techniques have been developed to measure doses of parasite material more precisely, and experiments have been carried out to determine the earliest age at which calves can be immunized safely.

Cattle were immunized experimentally against parasite strains isolated at the Kenya coast and were exposed to field challenge at three sites in the ECF endemic area. The immunized animals withstood field challenge successfully, while non-vaccinated controls became infected with ECF and died. This has demonstrated that stocks of T.p. parva can be isolated in an area, characterized in the laboratory and used to immunize cattle against local strains. This program will now be expanded to other districts. Trials will include the combination of immunization with different methods of vector control, and several additional parameters will be considered, such as weight gains, comparative costs, economic benefits, and the impact of other tick-borne diseases.

The serological identification of T. parva strains which do and do not cross-protect is an important component of ILRAD's epidemiology program. A battery of 16 monoclonal antibodies has been produced which bind specifically to Theileria schizonts. Production of such monoclonal antibodies will continue. Based on profiles of monoclonal antibody responses, T. parva stocks isolated from widely separated areas of Kenya and from Uganda, Malawi and Zambia can be categorized into three distinct groups. When cattle are immunized by infection and treatment against a stock in one group, they resist reinfection by stocks of the same group, but may become infected by stocks of different groups. The results of these trials suggest that it may be possible to categorize Theileria stocks in the laboratory for local immunization programs and eventually develop hybrid strains as starting material for a vaccine which will protect animals over wide geographic areas.

Buffalo are often chronic carriers of ECF. The pattern of parasite strains is complex in areas where buffalo come into contact with cattle. Collaborative studies with the Kenya Agriculture Research Institute, the Ministry of Livestock Development and ICIPE are being carried out to define more precisely the immunological and parasitological relationship between T.p. lawrencei, carried by buffalo, and T.p. parva, which affects cattle.

Future strategies - 1984-93. Techniques developed at ILRAD will be applied to identify strains of T.p. parva and T.p. lawrencei which can be used to immunize cattle by infection and treatment on a trial basis. Areas for these trials will be identified in conjunction with FAO and other international organizations, regional agencies and national governments. ILRAD will produce, or help produce, the sporozoite stabilates needed for pilot immunization trials in each area and will act as a reference centre for characterization of T. parva strains.

Where necessary, ILRAD staff will supervise these projects in collaboration with the staff of national veterinary services. ILRAD will also train national personnel in the production of sporozoite material. Should any country wish to expand the pilot studies to a national program, ILRAD will provide technical advice and will help obtain the funds required for implementation.

It is anticipated that an improved ECF sporozoite vaccine based on isolated parasite components could become available in the next 5

to 7 years and would supercede the infection and treatment approach. The introduction of immunization schemes, initially based on infection and treatment and later on more refined vaccines, will require continual monitoring, investigation of any apparent failure and further improvement. This will be done for ILRAD's pilot studies, and national veterinary officers and technical staff will be trained to monitor their own field trials and immunization projects. ILRAD will assist national projects until affected countries have sufficient expertise and facilities to work independently.

Effective vaccines against T.p.parva and T.p.lawrencei will still leave cattle susceptible to a number of other tick-borne diseases, if expensive treatment with acaricides is discontinued. Three other tick-transmitted species of Theileria - T.mutans, T. velifera and T. taurotragi - also occur in ECF and trypanosomiasis endemic areas, but their importance is not known. Information obtained on the role of these parasites as disease agents will indicate the importance of developing vaccines against them.

Staffing requirements for ILRAD's theileriosis epidemiology project will increase from three to five senior scientific manyears in 1988 (see Table 3).

Project area 2. Development of an ECF vaccine using non-infective sporozoite antigens

The objective of ILRAD's second theileriosis project area is to identify, isolate and characterize sporozoite antigens which can induce protection against ECF and which could serve as the basis of a widely available, easily produced, safe and effective vaccine.

Research areas include

a. Evaluation of host responses to the sporozoite, including the role of antibody in immunity

b. Attenuation or chemical modification of Theileria sporozoites for immunization

c. Biochemical characterization and in vitro synthesis of sporozoite antigens to be used for immunization.

Strategies and achievements - 1973-83. It has been confirmed that cattle infected with ECF produce antibodies which are capable of neutralizing parasite sporozoites in vitro. It is important to determine whether only one antigen or a small number of antigens is sufficient to stimulate immunity under field conditions when animals are exposed to different parasite species and strains.

Research is in progress to isolate and characterize T.p. parva sporozoite antigens which are capable of stimulating an immune response. In one study, anti-sporozoite antibodies were taken from cattle infected with T.p. parva Muguga. When tested in vitro and in cattle, these antibodies were capable of neutralizing sporozoites of

other ECF strains isolated from different locations in East Africa. Sporozoites of all of the ECF strains tested appeared to produce either one common antigen or a mixture of antigens which stimulated an immune response. Monoclonal antibodies have been raised to identify these sporozoite antigen(s) more precisely. The antibodies all recognize one common sporozoite antigenic determinant and neutralize the infectivity of sporozoites of other Theileria strains, indicating that these sporozoites all share a common antigen. It has been demonstrated using immuno-electron microscopy that the relevant antigen(s) is located on the surface of the sporozoites.

Since the strains used in this work were isolated from widely separated locations, their common antigen may be found in other East African Theileria strains. This suggests that it might be possible to develop a vaccine based on this antigen which would protect cattle over a wide area. The antigen is now being characterized. Should it be a protein or a glycoprotein rather than a lipid, recombinant DNA technology might be used to provide large quantities of the antigen by synthesis in vitro.

ILRAD scientists are also investigating the use of chemically attenuated or killed sporozoite preparations, in combination with suitable adjuvants, as an alternative means of immunizing cattle with non-infective material.

Future strategies - 1984-93. Research will continue aimed at isolating and characterizing sporozoite antigens of T.p. parva and T.p. lawrencei which induce protection against theileriosis. This work will make it possible to assess the feasibility of producing these antigens on a large scale by genetic engineering or another synthetic process.

The Theileria genes coding for the protective antigens will be identified and systems developed for their expression in vitro. The antigenic material synthesized in vitro will be tested, in combination with various adjuvants, for its ability to stimulate protective immunity in cattle. Suitable immunization schedules for field application will then be developed.

Basic research required to develop a vaccine based on sporozoite antigens should be completed for T.p. parva by 1988 and for T.p. lawrencei by 1990. It is not anticipated that any increase in staff over 1984 levels will be required for this project (see Table 3).

Project area 3. Immunization against T. parva using schizont or schizont-associated antigens

The objective of ILRAD's schizont immunization project is to identify, isolate and characterize schizont or schizont-associated antigens which induce protective immune responses against the parasite and to evaluate their potential for use in a vaccine against ECF.

Research areas include

a. Selection and establishment of stocks and clones of T. parva in lymphoblastoid cell cultures suitable for all aspects of research in this area

b. Characterization of schizont-infected cells, the mechanism(s) by which they are maintained in a 'transformed' state, and the pathogenic effects they exert on the host

c. Elucidation of the mechanism of transfer of infection between cells of different histocompatibility types and investigation of ways to increase the rate of transfer to facilitate the use of cell lines for immunization

d. Definition of host protective immune responses and identification and isolation of antigens which might be used for immunization.

Strategies and achievements - 1973-83. In order to analyse the events involved in the invasion of bovine lymphoid cells, the proliferation of infected cells, and the consequent immune response, extensive basic research has been required to define cell types and subtypes of the bovine immune system and to analyse how such cell types interact to give protective responses. A number of bovine lymphoid cell types and subtypes have been defined using monoclonal antibodies. These include T cells which are fundamentally involved in all types of immune responses including direct cell-mediated cytotoxicity, B cells which produce antibody, and monocytes which process antigens and present them to T and B cells to induce immune responses.

Whereas markers for T and B cells and monocytes are generally stable throughout a species, each individual also carries antigens on its cell surfaces which are unique, termed histocompatibility antigens. Cattle will reject cells transferred from other cattle because different individuals are of different bovine histocompatibility antigen (BoLA) types. Sera to identify some common BoLA antigens are being prepared in collaboration with the Animal Breeding Research Organization (ABRO).

Cattle can be immunized against T. parva by inoculation of approximately 100 million parasite-infected cells from lymphoblastoid cell lines originating from other individuals. It was suggested that parasite transfer from the inoculated cells to the host's own lymphoid cells was required for the induction of immunity. It has been shown that much lower numbers of infected cells will induce immunity if they are derived from another animal of the same histocompatibility type. Membrane preparations from such cells will also induce immunity. This strongly suggests that the infected animal responds to the schizont-infected cell by recognising not only parasite antigens, but rather parasite antigens in combination with its own histocompatibility antigens, or perhaps just its own modified antigens.

Research is in progress to define which antigen or antigen combination is required to induce a specific protective response. Infected cell lines are being characterized in terms of parasite antigens and histocompatibility. The aim is to identify a specific

cell type which will provide universally acceptable antigens for immunization of cattle of different histocompatibility types. This work is made difficult by a shortage of cattle of identical histocompatibility type, i.e. identical twins.

Future strategies - 1984-93. Research will continue aimed at identifying the factors which govern Theileria schizont proliferation and the accompanying proliferation of infected lymphoblastoid cells. Schizont-infected cells will be characterized and the nature of the protective immune response which they stimulate will be delineated. The antigens involved in inducing a protective immune response will also be characterized and the feasibility of developing vaccines based on these antigens will be assessed. This research will be facilitated by further definition of the BoLA antigens of cattle, and elucidation of their role in the generation of protective immune responses.

Bovine embryo-transfer technology and embryo-splitting techniques will be developed to provide cattle of identical histocompatibility types. These are needed to elucidate the mechanisms involved in induction of protective immune responses.

The feasibility of developing a vaccine based on schizont or schizont-associated antigens should be determined by 1989 to 1992. No increase in senior scientific manyears over the 1984 level is projected for the foreseeable future (see Table 3).

THE TRYPANOSOMIASIS PROGRAM

Research to date has not yielded any clear indication of how trypanosomiasis can be prevented on a large scale by immunological means. Research will therefore continue on a broad front until suitable means of control have been identified. Trypanosomiasis is a complex disease, involving a number of different parasite species, each containing many immunologically distinct populations, a large number of tsetse vector species and a large number of mammalian hosts. Despite years of research, the biology of the main groups of pathogenic trypanosomes and the responses of infected livestock are still not completely understood.

ILRAD's research program continues to elucidate the basic biological properties of the parasites, especially T. vivax and T. congolense. Special attention is given to identifying variable and non-variable protective antigens, parasite metabolic pathways which may be susceptible to chemotherapeutic or immunological attack, and mechanisms to control parasite differentiation which can alter the pathogenicity of the parasites in different hosts. The development of culture systems for both bloodstream and insect forms of T. brucei, T. congolense and T. vivax represents a major advance, making it possible to investigate parasite biology and differentiation in detail.

Immunological and non-immunological host responses to trypanosomiasis are being delineated, especially responses which lead to the pathogenic features of the disease. Much more basic

knowledge of bovine immune responses is required, and the responses of resistant livestock and wildlife must be investigated and compared with those of susceptible livestock to see if the responses of susceptible animals can be improved. The role of non-immunological factors in controlling parasite growth in susceptible and less susceptible animals must also be clarified. One objective is to find marker systems correlating with resistance to trypanosomiasis which could be used in livestock breeding programs.

The role of acquired immunity to trypanosome infections is being studied in one area of Kenya and will be extended to other sites in Africa. Studies also focus on the more efficient use of existing chemotherapeutic and chemoprophylactic compounds, especially the timing of drug administration and the role of chemotherapy in the acquisition of immunity. The analysis of mechanisms of resistance in certain wildlife species will be extended to include resistance in domestic livestock, especially N'Dama cattle, both at ILRAD and in collaborative projects in West and Central Africa.

Project area 1. Epidemiology and control of trypanosomiasis

The objective of ILRAD's trypanosomiasis epidemiology project is to apply existing knowledge and recent research findings in field situations to improve the control or prevention of trypanosomiasis in domestic livestock.

Research areas include

a. Elucidation of the epidemiology of bovine trypanosomiasis in defined areas

b. Identification and characterization of the serodemes (populations of closely related genetic background) of the major trypanosome species present in defined areas to determine the feasibility of immunization based on metacyclic trypanosome antigens

c. Investigation of factors affecting trypanosome infection rates in tsetse populations and development of methods for assessing tsetse and trypanosomiasis challenge in relation to different climatic zones and agricultural systems

d. Research in collaboration with the International Livestock Centre for Africa (ILCA) in Central and West Africa to determine the productivity of trypanotolerant cattle, sheep and goats under various levels of defined tsetse and trypanosomiasis challenge, possible utilizing chemotherapy. This work should also lead to the most effective use of trypanotolerant animals in projects sponsored by national and international organizations in tsetse-infested areas.

Strategies and achievements - 1973-83. Work has concentrated recently on the components of the trypanosomiasis complex at a field site in Kenya's Coast Province where there is a low level of trypanosomiasis risk and little movement of livestock or wild animals. A tsetse survey has been completed in the area and trypanosome isolates have been obtained from tsetse, bait cattle and

resident livestock. More than 5,000 sera have been collected from cattle exposed to infection. The parasites are now being examined for serodeme representation and bloodstream and metacyclic variable antigen type (VAT) composition. Examination of serum antibody levels will indicate past experience of infection with the parasites isolated from the area. The effect of routine chemotherapy on the development of protective immune responses will also be assessed. Should a limited number of trypanosome serodemes be present, consideration will be given to the merits of future immunization procedures, initially by the strategic use of chemotherapy.

Other work aims at improving the ability to assess trypanosome and tsetse challenge. This includes determination of tsetse host preferences, and infection rates with various trypanosome species in tsetse flies fed on wildlife. An improved serological system, based on the enzyme-linked immunosorbent assay (ELISA), has been developed for tsetse blood meal analysis. The ability of sterile male tsetse flies used in tsetse control schemes to transmit trypanosomiasis has also been studied. Sterile males of several different species were found to be capable of normal transmission of T. congolense, T. vivax and T. brucei. These investigations, supported by IAEA, will continue with different tsetse species.

Infection rates in tsetse were found to decrease dramatically when the flies were fed on ruminants treated with trypanocidal drugs. A similar effect has been observed in tsetse flies fed on animals experimentally immunized with uncoated forms of T. congolense, T. vivax or T. brucei. The antibodies concerned are species specific and have also been observed in livestock with longstanding infections. This may be a significant factor affecting the level of trypanosomiasis risk in areas where tsetse are heavily dependent on domestic livestock for blood meals.

Some of ILRAD's earliest research, carried out between 1976 and 1979, emphasized the importance of the resistance to trypanosomiasis exhibited by N'Dama cattle in The Gambia. ILRAD scientists are now collaborating with colleagues at ILCA in a research and training network focusing on the productivity and resistance to trypanosomiasis of livestock breeds under different management regimes and levels of trypanosomiasis challenge. The network covers sites in 13 African countries. ILRAD's role is to provide training and supervision for the animal health and tsetse survey components, to ensure uniformity of observations and maximum comparability of data. To date, 13 scientists from 8 countries have been trained at ILRAD. They have taken up positions in Ethiopia, The Gambia, Gabon, Ivory Coast, Kenya, Nigeria, Togo and Zaire. ILRAD scientists have visited sites in The Gambia, Gabon, Nigeria and Zaire.

Future strategies - 1984-93. Epidemiological studies of trypanosomiasis will continue for the next decade. Particular emphasis will be given to assessing tsetse and trypanosomiasis challenge and evaluating the role of chemotherapy in relation to the productivity of trypanotolerant cattle, sheep and goats in different climatic zones and agricultural systems in Africa. These studies will be carried out in collaboration with ILCA in Central and West Africa. The role of acquired immunity to metacyclic variable antigens will also be studied in suitably defined field situations.

The collection of basic data on trypanosomiasis and productivity should be completed by 1988. Improved methods of control will be introduced as they become available from ILRAD's basic research programs and their economic impact will be evaluated in different climatic zones and agricultural systems. Improvements made in diagnostic tests and tsetse-blood meal analyses will also be incorporated into the epidemiological studies. The application of these tests in field situations will allow more accurate disease surveys, better identification of reservoir hosts and improved understanding of trypanosomiasis epidemiology, leading to further opportunities for improved disease surveillance and control. ILRAD will also provide technology and expertise to national and international organizations who wish to initiate epidemiological studies of non-tsetse transmitted trypanosomiasis in Africa, the Middle East, India, Southeast Asia or South America.

Staff requirements will increase to reach a total of five senior scientific manyears in 1988 supported by ILRAD core funds. The additional manpower required for collaborative projects will be supported by specific non-core funding (see Table 3).

Project area 2. Trypanosome antigenicity, biochemistry and immunization

The aim of this project is to obtain knowledge of the major pathogenic species of trypanosome, especially relating to their antigenicity and biochemistry, which can be used to improve the control or prevention of African trypanosomiasis.

Research areas include

a. Development of methods to produce characterized trypanosome populations of the major pathogenic species, representing stages which occur in tsetse flies and vertebrate hosts

b. Establishment of methods for growing the important developmental stages of each trypanosome species in culture to facilitate research on biochemical, chemotherapeutic and immunological aspects of trypanosomiasis

c. Development and application of methods to characterize variable and constant trypanosome antigens for the identification of species and serodemes and the development of improved serodiagnostic tests

d. Elucidation of the genetic control of trypanosome antigen synthesis, with a view to manipulating antigen production

e. Study of trypanosome structure and metabolism to identify vulnerable areas for chemotherapeutic attack

f. Identification, production and testing of appropriate antigens for immunization against trypanosomiasis.

Strategies and achievements - 1973-83. Beginning with T.b. brucei, techniques have been developed at ILRAD to maintain

trypanosomes in tissue culture systems through all stages of their life cycle. Recent work has focused on extending this technology to the cultivation of T. congolense and T. vivax.

A simplified method has been developed for propagating T. congolense metacyclic forms in vitro. Much larger numbers of metacyclic forms can be obtained in this way than from infected tsetse flies. Host immunity to the variable surface antigens carried by cultured metacyclic trypanosomes is identical to the immunity induced by tsetse-transmitted metacyclic forms of the same serodeme.

Work with T. vivax concentrates on two stages of parasite development, the animal-infective bloodstream form and the tsetse-transmitted metacyclic form which is also animal infective. Present culture techniques allow multiplication of the bloodstream form and generate small numbers of metacyclic-like forms. Efforts are being made to increase the yield of metacyclic-like forms because T. vivax metacyclic forms are present in very low numbers in infected tsetse flies. Larger numbers of metacyclic parasites are required to analyse their variable antigen types as a basis for characterizing parasite populations.

Trypanosome culture systems are being developed and standardized so that field isolates of pathogenic trypanosomes can be maintained in vitro. The goal is to produce large numbers of trypanosomes of different species at different stages of their lifecycle for biological, biochemical, immunological and pharmacological research. Recently, T.b. brucei culture systems have been used to screen the effectiveness of trypanocidal drugs. Drugs will be screened using T. congolense and T. vivax cultures as they become available.

Improved techniques are being developed to identify species-specific trypanosome antigens. Monoclonal antibodies have been raised against T. congolense and T.b. brucei parasites and the antigens recognized by these antibodies have been isolated using immunoadsorbent columns. Purified T. vivax antigens are now being prepared using the same technique and antigens from all three species are being characterized biochemically.

An experimental system is being developed to identify trypanosome species and serodemes by analysing parasite DNA. This approach has been applied successfully to distinguish T.b. brucei from T.b. rhodesiense, one of the trypanosome species which cause human sleeping sickness. A simplified laboratory technique is now being developed for practical use and is being applied to T. congolense isolates.

Research also concentrates on the genetic basis of antigenic variation and on the structure and synthesis of the variable trypanosome antigens which comprise the parasite surface coat. The expression of different antigens forming the surface coat is associated with rearrangements in the parasite DNA. ILRAD scientists have observed two types of gene rearrangement in T.b. brucei, one based on expression-linked duplication and the other, more unusual, rearrangement involving the appearance of a minichromosome. Biochemists at ILRAD are investigating how the variable antigens are synthesized and moved to the cell surface. A full understanding of

this process could point to interventions which would disrupt the stability of the surface coat and render the trypanosome susceptible to host defences. Other metabolic pathways and enzyme constituents of trypanosomes are also being examined to identify areas of vulnerability to chemical and immunological attack.

Several studies are in progress on the changes which trypanosomes undergo at different stages in their lifecycle. These transitions might serve as points of intervention to disrupt the development of the parasites. Evidence has been obtained that all three major trypanosome species differentiate in the mammalian bloodstream from a rapidly-dividing to a non-dividing form. The nuclear and cytoplasmic proteins of the parasites responsible for this differentiation are being investigated.

It has now been established that some populations of all three pathogenic trypanosome species can, under certain conditions, penetrate the blood-brain barrier and invade the central nervous system of domestic ruminants. In this site they are protected from the effects of drugs normally used for treatment. Animals with central nervous system infections may show clinical signs of brain disease, and relapsing infections may occur in previously treated animals as parasites in the central nervous system re-invade the bloodstream. The importance of this phenomenon in the field has yet to be assessed.

The characteristics of trypanosomes which cross into the central nervous system will be investigated. Techniques have been developed to monitor such factors as antibody production and the timing of parasite appearance in the central nervous system by taking routine samples of tissue fluids from the brain during the course of infection. These technques could also be used to measure the rate of transfer of trypanocidal drugs into the central nervous system.

Future strategies - 1984-93. Research will continue to increase knowledge of the biological, biochemical and immunological characteristics of the major pathogenic trypanosome species and to identify ways to improve trypanosomiasis control. Research on T. congolense and T. vivax will be emphasized, as T. brucei received more attention in the past.

Studies on trypanosome biology will focus on identifying parasite characteristics which are involved in the establishment and maintenance of infections in both the mammalian host and insect vector. Biochemical studies will continue to delineate parasite metabolic pathways, including the synthesis of variable antigens, which may be susceptible to chemical or immunological attack. The nature of the genetic mechanisms controlling antigenic variation will be investigated and systems will be developed for the in vitro production of parasite antigens. The feasibility will be determined of developing assays to identify trypanosome species, sub-species and serodemes based on nucleic acid chemistry.

Immunological studies will focus on protective variable antigens, especially antigens produced by the metacyclic forms of the parasite. Other antigens will be investigated which may be involved in protection, and thus may provide a starting point for

diagnostic assays, or which may be relevant to the pathogenesis of the disease. The use of adjuvants to improve the immune response to trypanosome antigens will also be explored.

Results of present research should make it possible to focus more clearly on future research areas which are likely to lead to improved trypanosomiasis control. The development of diagnostic assays and techniques for in vitro drug screening and examining the products of parasite gene expression should be complete by 1987. Yet it is difficult to put a time-frame on all aspects of research in this area. It is anticipated that the number of senior manyears allocated to this area will decrease from 11 at the beginning of 1984 to 7 in 1988, as research becomes more focussed, as more work is conducted in collaboration with other institutes and as the development of diagnostic assays is largely completed (see Table 3).

Project area 3. Mechanisms of acquired and innate resistance to trypanosomiasis in different host species

The objective of research in this area is to identify immunological and non-immunological factors involved in resistance to trypanosomiasis and to develop measures to improve resistance in susceptible livestock.

Research areas include

a. Characterization of the immune systems of domestic livestock, particularly cattle, in order to improve protective immune responses against trypanosomiasis

b. Determination of mechanisms of innate and acquired resistance to trypanosomiasis in comparative studies with experimental rodents, trypanotolerant livestock and wild animals, in order to apply useful findings to the control of trypanosomiasis in susceptible livestock

c. Elucidation of the pathogenesis of trypanosomiasis in susceptible livestock to identify new approaches to the alleviation and prevention of the disease by both immunological and non-immunological methods.

Strategies and achievements - 1973-83. Studies at ILRAD focus on the complex interactions between trypanosomes and their hosts, especially on factors which influence host protective antibody responses and non-immunological host responses which play a role in resistance to trypanosomiasis. The analysis of protective host antibody responses has required the production of specific reagents which recognize the immunoglobulin classes and sub-classes of domestic ruminants and some species of wildlife.

Animals infected with trypanosomes characteristically produce antibodies against the variable surface antigens presented in successive parasitaemic waves. These antibodies are only able to kill parasites carrying the appropriate variable surface antigen type. The host/parasite interactions which are responsible for the induction of effective antibody responses have been analysed in laboratory animals of defined genetic structure infected with T.b.

brucei. The key factor appears to be the parasite growth rate. This is influenced by non-immunological host factors that determine the rate at which the parasites differentiate in the bloodstream from rapidly dividing to non-dividing forms. The non-dividing parasites stimulate protective antibody formation. The magnitude and specificity of the immune response and the factors which induce trypanosome differentiation are genetically determined in the host. However, different sets of genes control these two factors. Research will continue in order to identify the host factors responsible for controlling parasite differentiation, including factors derived from host-cell division. Similar studies are also being carried out on T. congolense and T. vivax infections in laboratory animals and domestic ruminants. This work uses in vitro cultivation systems which do not require the presence of feeder layer cells.

Other cells of the immune system are being studied, particularly macrophages which are capable of ingesting antibody-coated trypanosomes. The role of macrophage-secreted factors in maintaining trypanosome growth and inducing differentiation is also being investigated.

A hard swelling, called a chancre, usually appears in the skin 7 to 10 days after the bite of a tsetse fly infected with T. congolense or T. brucei. When trypanosome-resistant wild animals, such as buffalo, eland, oryx and waterbuck, are bitten by infected tsetse flies, they develop smaller skin reactions than susceptible domestic livestock. Parasites also appear much later in the bloodstream and the subsequent disease is less severe. This suggests that the resistance to trypanosomiasis exhibited by these wildlife species may be related to a capacity to control parasites in the skin. The events occurring after an animal is bitten by an infected tsetse fly are being investigated in domestic ruminants and certain wildlife species, with emphasis on the role of the immune response and the identification of biologically active molecules in the chancre which aid or impede parasite proliferation.

East African breeds of cattle, sheep and goats have been screened for evidence of resistance to trypanosomiasis, and preliminary findings suggest that Zebu cattle from trypanosomiasis endemic regions of western Kenya are more resistant to trypanosome infections than comparable Zebu cattle from non-endemic areas. This resistance appears to be genetic and not due to acquired immunity. One local breed of sheep also appears to be less susceptible to the anaemia induced by trypanosome infections than imported breeds. The factors involved in the resistance to trypanosomiasis shown by trypanotolerant N'Dama cattle have been studied in the Gambia. One objective of the study of comparative genetic resistance is to identify a marker system which correlates with degree of resistance as a basis for livestock improvement programs. Several promising research findings are being pursued in this respect.

Future strategies - 1984-93. Increased efforts will be made to elucidate the immunological and non-immunological mechanisms which confer increased resistance to trypanosomiasis. Emphasis will be given to T. congolense and T. vivax infections in susceptible and resistant domestic livestock, wildlife and laboratory animals. One

aspect which will receive attention is the interference observed when an animal is infected with trypanosomes and subsequently challenged with antigenically unrelated trypanosomes. In such situations, the established infection has a suppressive effect on the development of local skin reactions, parasitaemia and antibody production.

Previous studies on the mechanisms underlying the resistance of N'dama cattle will be continued at ILRAD, using animals transferred from West Africa by embryo transfer. A collaborative study will also be undertaken with a French and German project at the Centre de Recherches sur les Trypanosomiases Animales (CRTA) in Bobo Dioulasso, Upper Volta, to examine all aspects of trypanotolerance. Individual animals of trypanotolerant breeds which exhibit marked resistance to natural tsetse challenge have already been selected for this work. In vitro assays will be developed which indicate the degree of resistance to trypanosomiasis displayed by various species and breeds of domestic livestock and wildlife. These assays will be tested for correlation with levels of resistance exhibited by livestock covered in the ILCA/ILRAD trypanotolerance research network.

It is difficult to give more than approximate time scales for this research. It should be possible in the next 5 to 7 years to achieve a much better understanding of the mechanisms involved in acquisition of resistance to trypanosomiasis and perhaps to develop in vitro assay systems which correlate with resistance. Any consequent improvement in genetic potential for resistance, either by selective breeding or by gene transfer, will require considerable time. It is anticipated that the senior manyears allocated to this project area will increase from 6 in 1984 to 8 in 1985 and remain at that level at least until 1988 (see Table 3).

TRAINING AND OUTREACH

The successful implementation of any livestock disease control program requires an effective administrative infrastructure and adequate numbers of trained personnel. ILRAD's training program is designed to support the development of scientific and field personnel in Africa and other developing regions who can extend research on ECF, trypanosomiasis and other important animal disease problems and carry out the most effective control programs possible with the means now available. Participants in ILRAD's training program are also prepared to conduct pilot projects and field trials and to implement new disease control programs when improved methods are ready for introduction.

Opportunities for training on an individual basis are offered within the scope of ILRAD's research activities, and seminars, courses and conferences are held on topics related to improved ECF and trypanosomiasis control. All training activities are designed to complement ILRAD's research programs.

TRAINING PROGRAMS FOR INDIVIDUALS

As ILRAD's scientific staff has expanded, opportunities for specialized training have steadily increased. Since 1975, over 160 people have received training on an individual basis. Three levels of training are offered - for scientists and senior technicians, for post-graduate students and for post-doctoral fellows. The number of positions offered depends on the availability of supervisory staff, laboratory space, equipment and accommodation. Within budgetary limitations, a few individuals are also sponsored for training at other institutions.

Specialized technical training

Scientists and senior technicians come to ILRAD to learn the specialized laboratory and field techniques used in the research programs. Most of these individuals are staff members of government livestock ministries, university departments or national research centres. They come from developing countries, most often from Africa, and stay for periods ranging from a few weeks up to a year.

Each trainee is assigned to a member of ILRAD's scientific staff who has the primary responsibility for providing an appropriate training program. Training is offered on many different aspects of ECF and trypanosomiasis research and control, depending on the needs of the participant's home institution. Trainees might learn parasite recognition and characterization, basic serological, immunological and diagnostic techniques, methods for cultivating parasites and host cells in vitro, experimental pathology procedures, assessment of vector infection rates or parasite and vector control methods.

Technicians who receive training return to research and diagnostic laboratories in their home countries. They are generally responsible for routine procedures connected with ECF and

trypanosomiasis control programs, and they are expected to teach their junior staff the techniques they learned at ILRAD.

As ILRAD's research programs extend to pilot projects and trials in the field, more training opportunities will be offered to veterinary officers, animal scientists and biologists who supervise field projects. Training for field officers will involve a minimum of 6 to 12 months' practical experience in the management of experimental livestock, assessment of vector density and challenge levels, isolation of parasites, collection of samples and recognition of different diseases. This type of training will be offered at ILRAD and in the countries where field projects are conducted.

Post-graduate and post-doctoral training

Graduate students with good honours B.Sc. or M.Sc. degrees work at ILRAD for periods of 1 to 3 years to fulfil requirements for higher degrees. Most of these students are from Africa. They are recommended by deans of veterinary, medical or science faculties or directors of national veterinary services or other appropriate disease control agencies. Since 1975, five ILRAD research fellows have completed their doctorates and another five have been awarded M.Sc degrees. At present, 15 graduate students are working as research fellows at ILRAD and 2 are completing their studies at overseas universities with ILRAD support.

Candidates for post-doctoral positions are selected on an international basis, but preference is given to well-qualified scientists from African countries. They normally work at ILRAD for 2 years, contributing directly to the research program. Post-doctoral fellows who come from advanced laboratories frequently introduce new research techniques to ILRAD staff. A total of 14 post-doctoral fellows have completed their work at ILRAD, and 10 are now participating in this program. It is anticipated that a further four post-doctoral positions will become available in 1984-85.

For both the graduate and post-doctoral programs, a special effort is made to recruit students from francophone African countries where trypanosomiasis is a serious problem. When they finish their work at ILRAD, all participants in the training program are expected to return to their home countries and continue research on ECF or trypanosomiasis. Their experience at ILRAD should enable them to make a substantial contribution to national and regional programs to improve control of these two diseases.

TRAINING COURSES, CONFERENCES AND WORKSHOPS

In addition to training offered on an individual basis, ILRAD organizes regular courses, conferences and workshops on topics directly related to the research mandate. From 1977 to the end of 1983, 14 courses or conferences were held. Over 700 participants attended these sessions, about half representing 30 different countries in Africa.

Most of these activities are cosponsored by other organizations, including the OAU, FAO, WHO, IAEA, ILCA and the Rockefeller Foundation, among others. ILRAD cooperates closely with these agencies in the organization of the sessions, the choice of topics and the selection of participants.

Future plans include one 6-week training course and at least one workshop or conference every year. To give an indication of the type of courses and conferences that are planned, a tentative schedule of topics for 1984 to 1987 is given in Table 2.

The training courses will cover laboratory techniques required for research and control programs, focusing on ECF and trypanosomiasis in alternate years. Twelve to 16 senior technicians will attend each course, and some will remain at ILRAD for further individual training in the specific techniques required by their home institutions. Similar courses may be conducted in francophone countries of Central and West Africa, with contributions by ILRAD staff.

Table 2. Proposed ILRAD courses and conferences, 1984-87.

1984	
May	Basic course on the diagnosis of haemoprotozoan diseases - with emphasis on trypanosomiasis
	Workshop on the use of nucleic acid characterization methods in the study of parasitic disease
	Seminar/course in francophone West Africa on the basic diagnosis, treatment and control of trypanosomiasis
September/ October	Workshop on parasite antigens and pathogenesis
1985	
May	Conference on biological and economic aspects of livestock production under trypanosomiasis risk
September/ October	Course on the development and application of improved diagnostic techniques to parasite disease
1986	
May	Basic course on the diagnosis of haemoprotozoan diseases - with emphasis on East Coast fever
September/ October	Workshop on integrated approaches to the control of protozoan diseases
1987	
May	Basic course on the diagnosis of haemoprotozoan diseases - with emphasis on trypanosomiasis
September/ October	Conference on immunization against vector-borne diseases

PUBLICATIONS

The search for immunological measures to control ECF and trypanosomiasis involves scientific research of a very high standard. The results of research carried out at ILRAD are made available to the general scientific community through the regular publication of articles in scientific journals and books and through papers presented at conferences and meetings of international agencies. ILRAD staff members have published over 250 articles in scientific journals since 1975.

Information published through these channels may not always reach scientists and laboratory and field staff working on the practical aspects of ECF and trypanosomiasis control. For this reason, ILRAD publishes a general account of recent research findings in an annual report which is distributed widely. In 1982, a series of brochures was produced describing the research and training programs and listing publications by ILRAD scientists. These brochures will be brought up to date and reissued periodically. In 1983, ILRAD began publishing a quarterly newsletter, ILRAD Reports, which summarizes research and training activites for a broad audience.

In view of the importance of trypanosomiasis in francophone Africa, ILRAD's annual report, brochures and newsletter are all published in French as well as English. These publications are distributed around the world to individuals and organizations concerned with theileriosis and trypanosomiasis control. Distribution is increasing steadily as researchers and field workers write in for more information about ILRAD and for reprints of articles by ILRAD scientists. Single copies of all publications are issued free of charge.

In addition to ILRAD's regular publications, comprehensive training manuals are needed on the diagnosis of ECF and trypanosomiasis. At present, relevant material is scattered over a number of sources which are seldom available to scientists in developing countries. Training manuals are needed to serve as a basis for courses conducted at ILRAD and for participants to take back to their home institutions to review what they have learned and instruct their colleagues. One manual has already been prepared in English and French for field staff working in the ILCA/ILRAD trypanotolerance research network. Additional manuals are planned to support ILRAD's training activities, and audio-visual materials will also be produced.

REQUIREMENTS FOR STAFF AND RESOURCES, 1984-93

STAFF

As ILRAD's building program reached completion and the laboratories became operational, the staff increased from 1 manyear in 1974 to 209 by 1978. From 1979 to 1983, senior scientist manyears increased from 33 to 47 and support staff increased from 314 to 338.

Almost all the established 51 senior scientific and administrative positions are expected to be filled by the beginning of 1984. The proposed distribution of staff among research project areas and administrative units is shown in Table 3.

Table 3. Senior scientific and administrative positions proposed for 1984-88, and possible additions in 1989-93.

	1984	1985	1986	1987	1988	1989-1993
Research						
Theileriosis						
1. Epidemiology and control	3	4	4	5	5	1
2. Sporozoite immunization	8	8	8	7	7	
3. Schizont immunization	8	8	8	8	8	
	19	20	20	20	20	
Trypanosomiasis						
1. Epidemiology and control	3	4	5	5	5	1-2
2. Trypanosome antigenicity	11	9	8	8	7	
3. Comparative immunology	6	8	8	8	8	1
	20	21	21	21	20	
Research support	3	3	3	3	3	
Training and conferences	1	1	1	1	2	1-2
Information services	1	1	1	1	1	1-2
General administration	3	3	3	3	3	1
General operations	2	2	2	2	2	
Total	49	51	51	51	51	57-60

The current plan is to have a full complement of 51 senior staff members from 1985 to 1988. Some positions will be shifted as certain research areas receive greater attention, but no increase in total number is planned for this period. There will be approximately 360 support positions during this time.

Any increase in staff after 1988 will depend on research results and financial resources. Table 3 indicates the areas where increases in scientific staff might occur. The number of support positions would rise in relation to increases in senior scientists, but

probably would not exceed 400. If the research programs are successful, there will be a need to increase activities in epidemiology and control. This would also be supported by an increased effort in training.

As results become available from research conducted in the laboratory, it will be appropriate to initiate field programs in other countries. These activities will be funded by bilateral projects formulated by the countries involved - core research positions will not be used for field investigations outside of Kenya.

CAPITAL REQUIREMENTS

Construction of the laboratories was completed in 1978 and staff housing in 1983. No major construction projects are forseen at this time, though some additions or modifications to existing buildings may be anticipated.

Even though all laboratories are well equipped, there will be a continuing need to purchase new equipment as technological advances are made. For this reason, an annual capital expenditure of US$ 500,000 is anticipated over the next 5 years. This may vary somewhat from year to year depending on specific needs.

Almost an equal amount will be required each year for equipment replacement and for maintenance of existing buildings and equipment. These costs will increase as ILRAD's initial equipment reaches the end of its useful period of service.

OPERATING COSTS

Core operating costs have increased in an irregular pattern since ILRAD was established. This has been due in part to construction needs and program development and to changes in management.

Costs increased significantly from 1979 to 1980, but expenditures remained at the same level through 1982. As a result, real costs decreased over the period (see Table 4). Operating costs increased again in 1983 because of a significant increase in the number of senior staff.

There will be an increase in operating costs in 1984 as support costs grow to meet the needs of the added senior staff. Estimates of operating costs for 1985 to 1988 are based on about 2% real growth per year.

Costs for 1989 and beyond can only be anticipated in general terms. If senior staff numbers were to increase to 60 by 1993, the operating budget in terms of 1984 dollars would approach US$ 13 million.

Table 4. Expenditures for core operations and total budgets (US$'000) and senior positions (manyears).

	Core Operations	Total	Manyears
Actual			
1979	5,611	7,383	33
1980	7,226	9,396	34
1981	7,445	9,745	36
1982	7,452	8,818	38
1983	8,500	9,300	47
Anticipated*			
1984	9,900	10,700	50
1985	10,000	10,500	51
1986	10,200	10,700	51
1987	10,300	10,800	51
1988	10,600	11,100	51
1993	13,000	14,000	up to 60

*Expenditures based on 1984 dollars.

FUTURE PROGRAM CONSIDERATIONS

ECF AND TRYPANOSOMIASIS VACCINE PRODUCTION AND DISTRIBUTION

The identification of effective immunogens for the prevention of ECF and trypanosomiasis would bring into prominence questions of how to produce and distribute suitable vaccines.

It is difficult to predict the form vaccines against ECF and trypanosomiasis are likely to take. However, they will probably not consist of complete parasites or parasitized cells, but rather they are likely to consist of isolated parasite or, possibly, host molecular components. An ideal vaccine would be easy to produce, and safe to use. The production technology would be straightforward and production capacity would be easily established in each affected country. Manufacture could be based in government laboratories. The development of such a vaccine would involve local, national and regional trials, training in its use, the provision of production facilities and transfer of appropriate production technology.

A more complex vaccine, synthesized chemically or produced by DNA technology, would require advanced techniques for manufacture. A vaccine of this nature could not be placed lightly into diverse manufacturing environments - it might have to be produced by one central establishment.

The transfer of production technology to national programs will require adequate infrastructure and trained personnel. The importance of establishing cadres of scientists, technicians and field officers with experience of all aspects of ECF and trypanosomiasis research and control cannot be overemphasized. Contacts with potential vaccine recipients and experience in various countries are being developed in the course of current activities.

The donor agencies which support ILRAD's research programs generally provide funds without restriction. ILRAD's policy, in turn, is to make useful results available to developing countries similarly without restriction. The development of vaccines against ECF and trypanosomiasis would present an attractive commercial prospect to organizations dealing with animal health problems. All useful discoveries should therefore be protected by legal means to prevent inappropriate exploitation and ensure proper application.

ILRAD's policies with regard to the protection and dissemination of research results have recently been reviewed by the Board of Directors with the help of specialized consultants. Revised guidelines are being prepared to ensure the proper use of discoveries made by ILRAD scientists, visiting scientists or ILRAD staff working in collaboration with other organizations.

RESEARCH ON OTHER MAJOR LIVESTOCK DISEASES

Other forms of theileriosis, caused primarily by T. annulata and also by T. hirci and T. sergenti, affect livestock production in

extensive areas of North Africa, the Middle East and Asia. Research on the control of these parasitic infections is being undertaken by other organizations, but many of ILRAD's findings could be applied through collaborative projects. Techniques for the cultivation of Theileria parasites, identification of parasite strains (especially related to immunization by infection and treatment) and identification and isolation of parasite antigens would be particularly useful.

Another tick-transmitted protozoal disease, babesiosis, and two tick-transmitted rickettsial diseases, anaplasmosis and heartwater, are also significant problems. Babesiosis and anaplasmosis occur in cattle in Africa and elsewhere. Immunization methods have been developed using attenuated parasite strains, but the available vaccines can induce anaemia in a proportion of the animals treated. Research is in progress in several laboratories to improve these procedures by identifying and using isolated parasite antigens.

Cowdriosis, or heartwater, caused by Cowdria ruminantium, is also a significant livestock disease in Africa. Cattle can be immunized by inoculation with material from an infected animal and subsequent treatment with antibiotics, but efforts to develop a better vaccine have been constrained by the inability to cultivate the pathogenic organism in any quantity in the laboratory. Cultivation of this organism may require in vitro tissue culture systems, a field in which ILRAD has considerable expertise. If this can be achieved, it may be possible to produce an improved vaccine using techniques such as those being employed at ILRAD for T.p. parva.

If at some time it appears appropriate to initiate research aimed at developing improved vaccines against these other tick-transmitted diseases, ILRAD will seek advice from others working in the field and will consult with all interested parties before presenting a recommendation to TAC for review. The progress of research in other laboratories concerned with these diseases would be a significant factor in ILRAD's decision.

There is evidence that cattle can acquire immunity against ticks by repeated natural exposure. The immune response affects tick attachment, feeding and reproductive ability, and reduces their effectiveness in transmitting T.p. parva. A preliminary collaborative study has been carried out with ICIPE in this area, and further studies will continue over the next 3 to 5 years. Tick antigens which induce immunity will be identified, isolated and characterized and the possibility of using these antigens in a vaccine will be investigated. This work will be carried out initially with R. appendiculatus. A successful vaccine against ticks would be a useful adjunct to an ECF vaccine because resistance against ticks would reduce the transmission of other tick-borne pathogenic parasites.

In the case of trypanosomiasis, T. evansi infections cause extensive livestock losses in South and Central America, North Africa, the Middle East and Asia. The similarities between T. brucei and T. evansi indicate that a project to apply results of research from work on tsetse-transmitted trypanosomiasis to mechanically-

transmitted T. evansi would have substantial benefits. Mechanically transmitted T. vivax infections also occur in cattle in the northern countries of the South American continent, and a project to apply the results of research on tsetse-transmitted T. vivax would have substantial benefits. ILRAD's expertise in parasite cultivation, antigen identification and isolation, development of diagnostic assays and analysis of protective immune responses could be disseminated through collaborative projects.

CONCLUSION

Ten years after establishment and 5 years after completion of the facilities and initiation of fullscale research programs, ILRAD has made significant progress towards achieving the goals expressed in its mandate. Basic research programs are well established and applied research programs are being initiated in locations throughout Africa.

Research results indicate that effective immunization measures can be applied today to protect particularly valuable livestock, and that improved, more widely applicable, vaccines are likely to be available in the next few years. In the case of trypanosomiasis, control based on immunological means alone is not likely to be achieved within the next decade. However, livestock productivity should improve significantly in areas affected by trypanosomiasis. On the basis of current research findings, this would be achieved by the greater exploitation of trypanotolerant livestock, improved use of chemotherapeutic and chemoprophylactic agents and integrated vector control programs.

While ILRAD has an important role in the development of improved measures to control ECF and trypanosomiasis, effective implementation can only be achieved with sufficient resources and the support of national governments. To this end, ILRAD is making a considerable effort through collaborative research, training and outreach programs to ensure that research findings are made available to scientists in the countries affected by these two diseases.

The economic impact of theileriosis and trypanosomiasis throughout the world is enormous - incalculable when considered in relation to agricultural production as a whole and not simply in terms of livestock losses. The development of improved measures to control these two diseases will have an important effect on agricultural productivity in Africa, Latin America and Asia, considerably alleviating the chronic food shortages experienced in these regions. By sustained research in the next decade - and beyond - ILRAD hopes to achieve this task and perhaps to begin research on other important livestock diseases, thus fulfilling the expectations of ILRAD's founders and justifying the confidence of those who have given financial support.