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THE ROLE OF IAEA IN PROMOTING HEALTH CARE SERVICES IN DEVELOPING COUNTRIES

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Introduction

When the International Atomic Energy Agency (IAEA) was established as an autonomous member of the United Nations family in 1957, a prominent assignment was to "seek to accelerate and enlarge the contributions of atomic energy to peace, health and prosperity throughout the world". The inclusion of "health" reflected the fact that medical uses of radiation and radionuclides were among the first and most widespread applications of "atomic energy". Although the World Health Organization has been given responsibility for the United Nations' main efforts in health, the close association of radionuclides with atomic energy was believed to justify a continuing role for the new Agency in their use in medicine and biology.

The scientific activities of the ongoing programme in these two areas are particularly guided to the problems closely associated with human welfare and alleviation of man's suffering. In general, the objective is to cooperate with Member States — especially in the third world — in the development and promotion of techniques for application of radiation and radionuclides in medicine and biology, in improving the accuracy and reliability of radiation dosimetric measurements, in having better understanding of the potential harmful effects of radiation and in the training of personnel, as well as dissemination of knowledge. Many of these activities are carried out in close collaboration with WHO.

The first use of radionuclide and radiation techniques in developing countries has often been in medicine. Medical specialists took part in the early missions to these countries to assist them in areas of nuclear medicine, radiotherapy, and medical dosimetry. Almost from the outset, the Agency also supported fundamental research in radiation biology, which was recognized as being necessary for a more complete understanding of radiation effects on living matter. Of course, it was also assumed that the other applications of atomic energy should themselves be conducted in a manner that did not compromise health.

Because of their diversities, medical and biological uses of radiation and radionuclides are performed in more countries and in more laboratories than any other application of atomic energy. This diversity establishes the character of the Agency's programme; instead of a few large projects, many small activities are supported, tailored to the needs and wishes of individual countries. Furthermore, the Agency's efforts are directed particularly to developing countries.

Mechanisms

Research programmes

It provides sponsorship of integrated research at a substantial number of institutions and in a considerable range of activities. The programme thus came to be heavily oriented, at an early stage, towards areas of relevance to developing countries; either by developing a new application or, more commonly, by adapting available techniques to local problems.

Initially, the programme generally made provision for the support of projects for a period of some 3 years, beyond which it was considered that the institutes themselves would be able to ensure further funding. The important factor from the outset was the willingness of the Agency to provide smaller items of equipment and supplies, if requested to do so by the contractor, for a portion of the funds made available. Another important factor was the requirement that scientific reports be submitted at appropriate intervals so that research progress could be judged accurately. Later, use began to be made of the chief scientific investigators involved in the research contract programmes as a pool of specialists, and arrangements for occasional meetings are made.

The limited funds available for support of research, combined with the international character of the Agency, provide strong impetus for the development of research programmes in which groups of institutes work on well-defined themes usually chosen for their relevance to the needs of developing countries. In order to ensure proper coordination, meetings of chief scientific investigators of the institutes are arranged at appropriate intervals. The role of the Agency in supporting research thus became not just a catalytic one, but also a coordinating one.

The use of research agreements was introduced, designed to provide for the participation of selected institutes in coordinated research programmes without reimbursement. However, provision is made in each case for inviting the chief scientific investigator to any coordination meeting held. At the outset, the institutes participating in coordinated research programmes through research agreements were all located in industrialized countries. Presently, however, some institutes from a number of developing countries also are participating in such programmes through research agreements.

Over $700,000 per year are distributed in this programme, and over 100 laboratories are receiving support at any one time.

Technical cooperation

Various mechanisms have been involved at different times for assisting Member States in the Agency's fields of activity. Most of the proposed activities are intended to benefit developing countries in particular, and it was expected that many divisions of the Agency would be heavily involved in these activities which, in the biomedical field, currently account for about 8% of the Agency's regular programme for technical co-operation (Fig. 1). During the last 10 years, funds for the Agency's programme on technical assistance have been more than tripled, as shown in Figure 2.

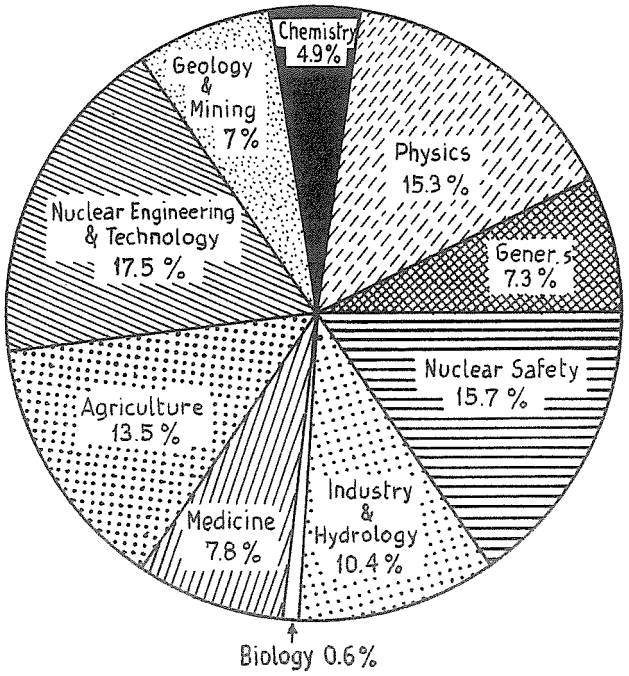

Fig. 1. – Distribution by field of activity of the 1983 IAEA regular programme for technical co-operation

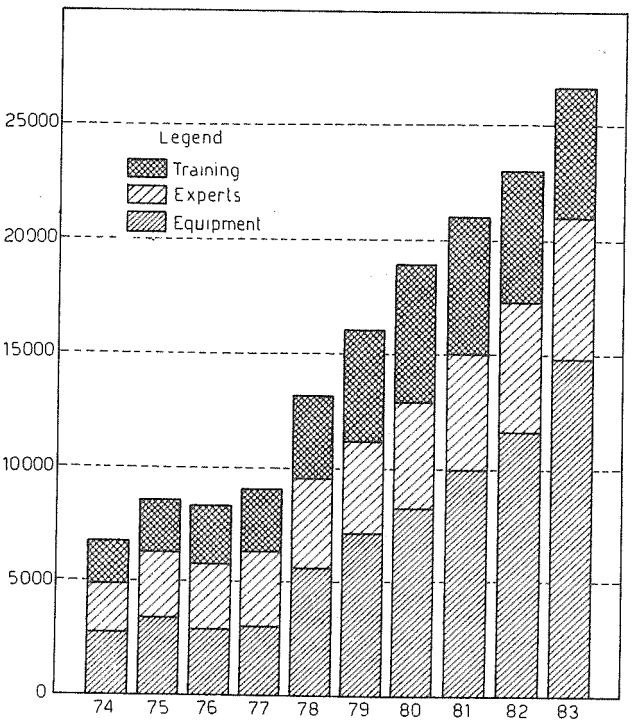

Fig. 2. – Assistance delivered by type of input, 1974-1983 (in thousands of dollars)

Training was given high priority in early years, later, the programme was expanded to include the provision of experts and equipment. The available resources include voluntary contributions and gifts in kind from Member States.

The Agency's fellowship programme provides opportunities for young scientists mostly from developing countries to undergo specialized training or do research in more advanced institutes, after nomination by their governments. The Agency's records show that many of the early fellows have been serving in leading positions in their countries for some time.

In addition, the Agency sponsors training courses and study tours (for 1984 see Table 1); 7 this year in the area of medicine and biology, for groups of about 30 candidates.

The Agency also sends experts in particular fields to institutions and laboratories in developing countries for periods of a week to a year or more. They install or introduce equipment and train local staff so that the activities continue after they depart.

Table 1. – *Human health programme. Training courses 1984*

1. Interregional course and study tour on nuclear medicine
2. Quality control of scintillation cameras
3. Workshop on maintenance of nuclear instruments
4. Train-the-trainers course on radioimmunoassay
5. Nuclear techniques for radiation therapy technologists
6. Workshop on brachytherapy for cancer of the cervix
7. Interregional course on radiation dosimetry

Moreover, the Agency provides specialized radiation measurement equipment or related apparatus to particular laboratories, often in conjunction with the work of the experts. Table 2 shows the distribution of funds among the 3 areas in 1983.

Table 2. – *Technical cooperation programme in medicine and biology (in 1983) (in thousands of dollars)*

Fellowships	Experts	Equipment	Share of total programme
993.0	432.6	1,127.7	2,553.3

It is important to note that all technical cooperation projects are channelled through governments; governments submit requests and are responsible for the effective use of resources provided. Figure 3 shows the geographical distribution of the programme in 1983.

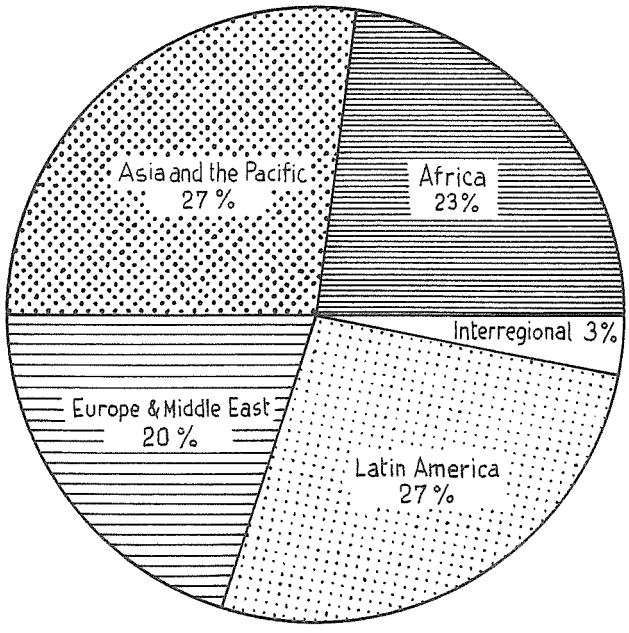

Fig. 3. – Distribution by region of the 1983 IAEA regular programme for technical co-operation

Information exchange

One prominent mechanism of information exchange is through meetings of various formats and publications of various types. Every year, the Agency organizes one or two symposia at which specialists from developed and developing countries review progress and present their latest findings on a specific subject. In addition, it convenes several smaller meetings of experts (advisory groups and consultants) to examine particular topics in depth, to plan future programmes or to review results achieved in research activities. An important component of the Agency's work is the provision of information via technical reports of various kinds, the proceedings or results from these meetings also being published by the Agency. All publications are publicly available, some free, some at cost.

Activities at the Agency's laboratory

The Agency operates a laboratory near its headquarters in Vienna to support some of its activities and to meet particular needs arising from the rest of the programme. The Agency staff members themselves engage in some creative activities there. The Dosimetry Laboratory assists particularly in the calibration of radiation doses, facilities are also available for neutron activities analysis, especially of biological samples, with provisions of reference material and reference measurements to upgrade the performance of laboratories in Member States. Moreover, on-site training for young scientists — mostly from the third world — is being offered in the laboratory.

Research programme of human health

The scientific programme of the Agency here includes 4 main areas:

1) nuclear medicine;
2) radiation therapy and dosimetry;
3) environment and nutrition;
4) applied radiation biology.

The programme in general is dynamic, changing according to the results obtained, the needs of Member States and the available budget. Completed components are phased out and new ones are implemented.

Nuclear medicine

The objectives of the programme are generally to apply nuclear medicine techniques effectively in developing countries to the diagnosis and management of patients in nuclear medicine units in about 60 countries as well as to investigations related to con-

trol of diseases distinctive to these countries, i.e. parasitic diseases.

This is accomplished by technical management of research projects including those in coordinated research on the diagnostic strategy for thyroid disorders in two major areas. The first is quality control of radioimmunoassay procedures of thyroid related hormones while the second is optimization of the various nuclear medicine techniques applied for the most cost–efficient diagnosis of these disorders. The programme also includes evalutation and support of technical cooperation field projects, technical organization of training courses in nuclear medicine in general, quality control of radioimmunoassay and on data processing as related to its procedures. Many of these activities are performed in collaboration with WHO, professional societies and outside experts. Information exchange is accomplished through seminars and symposia; an international symposium is scheduled next year on "Nuclear medicine techniques in developing countries".

An aspect which is closely tied in with the development of nuclear medicine but often neglected is the question of instrumentation. These types of instruments suitable for nuclear medicine application in developing countries may be rather different from those that have evolved in developed countries. Seven national workshops have been held on this subject in Latin America since 1980. A corresponding technical cooperation project for Asia and the Pacific was established in 1982 which included national workshops in 4 countries of the region.

A technical document on quality control of nuclear medicine instrumentation including detailed protocols for 5 different types of instruments will soon be published by the Agency. Two coordinated research programmes have also been set up for Latin America and the Far East in which each participating country would designate a local counterpart to visit each nuclear medicine laboratory and set up correct quality control procedures with annual follow–ups. As a joint effort with WHO, an imaging survey will be conducted using a liver phantom to determine specifically the quality of the imaging procedures. Results of a recent survey suggested that 10–20% of instruments are inoperable at one time. Subsequently, about 3 pilot laboratories in each of over 20 countries have given special support to study and solve the problems of maintenance. Annual workshops on maintenance of nuclear instruments are supported by the Agency's technical cooperation programme.

Nuclear techniques in parasitic diseases. – The Agency's component on the control of parasitic infections of man and of disease vectors by means of nuclear techniques is designed to encourage research into the development of new techniques, the evaluation of existing techniques and the development of expertise in such techniques in institutes in the developing Member States. The component is developed in consultation with WHO, and basically consists of a number of co–ordinated research programmes; associated with these are other activities such as training courses, advisory group meetings, research co–ordination meetings, etc. Every few years, there may be a symposium which provides a forum for review of the advances made in the development of techniques.

The programme on nuclear techniques for the detection of parasite antigens is designed to evaluate the use of immunoradiometric assays using monoclonal antibodies for the detection of circulating parasite antigens in patients with filariasis and schistosomiasis or malaria. The monoclonal antibodies for filariasis and schistosomiasis are supplied by the Pasteur Institute at Lille, France and the malaria antibodies by the WHO Institute for Research and Training in Immunology, Geneva. Six laboratories in Africa participate in the programme. These laboratories collect blood samples from patients before drug treatment, and again after treatment has been completed. One aliquot of the serum is assayed at the laboratories whilst the second aliquot is sent to Lille or Geneva for assay. Common protocols are used and the results compared.

The programme has run since late 1982 and in 1983 results obtained in the first year were reviewed at a co–ordination meeting. A laboratory workshop was also held during this meeting so that any discrepancies in the protocol could be eliminated. The results obtained in the first year showed that antigens can be detected in the circulation of filariasis and schistosomiasis patients. These antigens, however, continued to be in circulation for several weeks after therapy and this year the collection of sera will be continued for a longer period after therapy in an attempt to get to the point where the antigen disappears from the circulation.

The research programme on nuclear techniques for tropical parasitic diseases in Asian countries is a programme limited to the South–East Asia–Pacific Region. In this programme, the Bhabha Atomic Research Institute at Bombay acts as a central laboratory for assaying aliquots of sera collected by other participants in the region.

The research programme on development of nuclear techniques for monitoring malaria vectors basically concerns the evalution of an immunoradiometric assay for detecting malaria sporozoites in mosquitoes. This assay which uses a monoclonal antibody to a sporozoite surface antigen, was developed at the New York University Medical Centre. The technique provides a more rapid alternative to the conventional dissection of freshly killed mosquitoes for ascertaining sporozoite load. The assay can be carried out on dead mosquitoes which have been dried and stored for several weeks and the mosquitoes can be processed singly or in batches, making the technique potentially very useful for

epidemiological studies designed to determine vectorial capacity and transmission rate and for vector incrimination. The technique is particularly useful in areas where transmission is low so that dissection of individual mosquitoes would be laborious and frustrating.

The research project on use of radiation and radioisotopic techniques for the development of a defined antigen vaccine against schistosomiasis has developed from an earlier programme on preparation of radiation-attenuated vaccines for some human diseases. The earlier programme showed that irradiation augmented the protective properties of host migrating larval schistosomes with an optimum for γ irradiation of between 20-50 K rads. This also accelerated the development of the host's protected state, compared with natural infection. Despite this, pratical problems of technical feasibility, safety and logistics of this type of vaccine ramained serious obstacles to field application, and the new programme uses experiences gained from the use of irradiated larval schistosomes to attempt to develop a vaccine which is based on antigens present in irradiated larvae.

Since the programme is basically a developmental one involving sophisticated techniques, only 3 of the 10 participants are institutes from developing Member States. However, this proportion will change as more research workers from endemic regions get trained in such techniques through the Agency's training course and fellowship schemes.

Associated with the above programmes are training courses and fellowships under which scientists from developing Member States can be trained in the use of relevant nuclear techniques. Two training courses were held in the USA in 1980 and 1983 at which a total of 53 junior scientists were trained. A further training course is planned in 1985. In addition, each year about 5 scientists from developing Member States are awarded training fellowships to enable them to spend periods of six to twelve months at institutes in developed countries where they can learn new techniques.

Some of the persons trained then participate in the co-ordinated research programmes, under research contracts which provide funds for doing research in a relevant field.

Radiation therapy and dosimetry

Radiation therapy. – Of the several applications of radiation in the medical field, radiation therapy of cancer is by far the most frequent. In 1976 the Agency published a survey of the radiotherapy institutions throughout the world that use beams from radionuclide sources (Cobalt-60, Caesium-137) or high-energy X-ray machines. It showed over 2,000 institutions operating over 3,000 machines providing several tens of millions of individual treatments per year to cancer victims. The problem of providing proper treatment for these patients in the developing world is especially serious where equipment and trained staff are often inadequate.

The Agency has been recently concerned with the problem of setting up and promoting wider use of radiotherapy services and improving radiotherapeutic techniques in developing countries. This is mostly being carried out through the programme of technical cooperation. As an example of such kind of activity, the Agency — in cooperation with WHO — has launched a project in Egypt for promotion of wider use of intracavitary radiation therapy for cancer of the cervix. It mainly comprises training of young physicians and physicists on the proper use of this kind of radiation treatment and subsequently supplying them with required radiation sources and applicators to carry on the procedure in their hospitals. This project has started in 1983 through a generous financial contribution from the Italian Government and is expected to continue until 1986. The experience to be gained from this project will be used in the future for implementation of similar cooperative programmes in other developing countries.

Other activities related to radiation therapy are a research programme on improvement of cancer treatment by combined radiation and chemical and physical means, and the assessment of the effectiveness of high LET radiation for treatment of cancer. The Agency is planning to hold an international symposium on radiation therapy in developing countries in 1986.

Radiation dosimetry. – Public concern about all aspects of radiation safety has generated a strong demand for accurate and reliable measurement of ionizing radiation, a demand that applies not only to the protection of man and his environment but also to those activities in which radiation plays an essential role, *i.e.* radiotherapy and industrial radiation processing of foodstuffs.

The Agency's dosimetry programme consists of 3 main components:

1) An international network of secondary standard dosimetry laboratories that are authorized to perform calibration and verification of instruments used for measurement of radiation exposure and radioactivity. This network has started in 1976 by a joint effort of WHO and IAEA, the latter's dosimetry laboratory near Vienna acting as central laboratory. At present, 46 member laboratories, mainly located in developing countries, are actively supported by 5 collaborating international bodies. The staff of the IAEA Laboratory and other experts visit the SSDLs to render advice in the setting up and proper operation of the laboratories. Technical cooperation in the form of equipment is also provided to them. During the last few years, about $ 2 million in direct support has been invested by the Agency for the SSDL network.

2) Postal dose calibration intercomparisons for Cobalt–60 machines in radiotherapy institutes are being routinely performed by the Agency's Laboratory using thermoluminescent dosimeters. The results of such intercomparisons are sent to those laboratories with advice for more accurate measurements, if required.

3) A programme for implementation of high dose standardization and intercomparison for industrial radiation processing facilities was developed since this application for accurate dosimetry were recommended for preservation of food by radiation for reasons of wholesomeness and public acceptance. An international symposium on high dose dosimetry is planned by the Agency this year.

Environment and nutrition

Nuclear analytical techniques have many applications in studies of stable trace elements and isotopic tracers. In this connection the Agency's Human Health programme is currently supporting a number of projects dealing with health–related environmental research and with nutritional studies of trace elements.

From the analytical point of view, nuclear techniques have been shown to be competitive with other methods of analysis for at least 16 of the minor and trace elements currently considered to be of nutritional or bioenvironmental interest; for several of these elements they are the only applicable methods. The most important technique is neutron activation analysis, which is usually applied with the aid of a research nuclear reactor. At present, there are approximately 160 such reactors in operation in more than 40 of the Agency's Member States, many of them developing countries. Neutron activation analysis is one of the most important practical applications of the facilities to be found at such research centres.

Some of the trace elements that can be studied by these means play an important role in human health and disease. Fifteen trace elements are now considered to be essential for health, of which 8 were discovered only during the last 25 years. Many naturally–occurring diseases in man and animals are associated with nutritional deficiencies of trace elements (particularly of iron, iodine, fluorine, selenium and zinc) or with genetic predisposition (copper and zinc). Worldwide, hundreds of millions of people, most of them in developing countries, are known to be affected by trace element deficiencies. Some of the toxic trace elements (particularly lead, cadmium and arsenic) also have important health effects, having led to hundreds of deaths and thousands of persons affected during the last 30 years.

Current coordinated research programmes (CRPs) are concerned with the use of hair as a means for monitoring internal body burdens of environmental mineral pollutants; with occupational health studies; and with dietary intakes of nutritionally important minor and trace elements. At one time, approximately 30 research contracts or research agreements are active. The total financial support provided by the Agency for this work presently runs at the level of approximately $100,000 *per annum*. A recently completed CRP, concerned with the elemental composition of human milk, provided data on 24 elements in human milk specimens collected from 6 different Member States. The results are leading to a re–assessment of the nutritional requirements of young babies. Another CRP has shown that hair can be used as a valuable first level monitor of environmental contamination.

Many of these programmes are also supported by work in the Agency's laboratory, in which a number of new analytical reference materials have been developed, and where analyses are carried out by neutron activation analysis using the Austrian Astra research reactor. Typically, the laboratory each year provides analytical quality control services of various kinds (for environmental and nutritional studies) to around 200 institutes in more than 40 Member States.

Recent technical reports include: 1) the comparison of nuclear and non–nuclear techniques for the determination of trace elements in biological materials (1980), 2) the elemental composition of human and animal milk as determined by activation analysis and other trace analysis techniques (1982), 3) a survey of currently available reference materials for use in connection with the determination of trace elements in biological materials (1983), 4) nuclear–based techniques for the *in–vivo* study of human body composition (in press), and 5) quality assurance of biomedical neutron activation analysis (in press).

Applied radiation biology

The quality and standard of public health in general rely upon national health care services including control of cross infection and diseases.

Radiation sterilization. – The microbicidal effects of penetrating ionizing radiation have proved to be an effective means for sterilization of medical supplies even in a pre–packed hermetically sealed condition. This technique was found to be far more advantageous over other conventional methods such as heat and ethylene oxide gas. Being a "cold" sterilization process, ionizing radiation is applicable for a vast range of heat sensitive medical supply components as well as their packaging materials. Moreover, autoclaving is inapplicable to the heat sensitive items while ethylene oxide leaves toxic residues in the medical supplies, apt to cause health hazards. The pre–packed sterile ready–to–use medical supplies have successfully sustained a quality health–care service even under exceptionally adverse circumstances of rural remote settings. They are

particularly suited to services by mobile dispensaries, camp hospitals and similar facilities.

The Agency's programme in this area has promoted research, technical information generation and dissemination, and is helping to introduce and commission large production–scale irradiator facilities in Member States. The Agency also assisted to formulate expert recommendations on the Code of Practice for Radiation Sterilization of Medical Supplies and published a manual on the topic to serve as a valuable guidebook. This document receives periodic updating revisions in the light of growing experience. The Agency has also helped to build up trained technical manpower in developing Member States.

Another related area on which the Agency has embarked, is establishing feasible technical processes and criteria for radiation sterilization of non–viable tissue grafts (bone, cartilage, tendon, nerve, skin dressing, etc.) as implants in reconstructive surgery of disabled patients. Tissue banking of radiation sterilized grafts has been supported in the developing regions of Asia and the Pacific.

A seminar on tissue banking of radiation sterilized grafts was held this month in Manila and another one on radiation sterilization of medical supplies is scheduled for next year for the region of Africa and the Middle East.

Radiation treatment of sewage. – Population habitats generate increasing bulks of sewage sludge and waste water. Appropriate treatment and disposal of sewage is essential to protect infectious contamination of surface and ground water resources, agricultural fields, biological and food chains.

Certain categories of sewage sludge include constituents reusable as fertilizers or soil conditioners. This sewage may be viewed as a reusable resource provided the pathogenic and parasitic infective germs (bacteria, viruses, insect eggs/larvae, etc.) are destroyed. Many conventional sewage treatment processes are not totally effective to eliminate all bioburden in it and supplementary treatment with ionizing radiation has proved effective. Technologies and protocols have been formulated in a number of advanced Member States (USA, USSR, FRG, France, etc.) and radiation practices have been implemented to handle municipal sewage. Nuclear techniques further bear sigificance for disinfecting highly contaminated wastes from hospital wards, as well as establishments like slaughter houses, prior to their regular disposal.

IAEA co–ordinates current information on the radiation treatment of sewage sludge for disinfection and improvement of sludge management parameters (*e.g.* physico–chemical effects of radiation on sludge settling properties; disintegration of noxious components, etc.) and their possible reutilization as a resource.

Development of biological dosimeter for radiation protection. – Concomitant to the promotion of beneficial applications of nuclear techniques and technology, the Agency programme is also active towards the protection of human health against potential hazards of accidental exposures to radiation doses.

The discipline of radiation biology has early elucidated the quantitative relationships of absorbed radiation energy and the resultant biological damage as may be measured in the form of induced chromosomal aberrations, carcinogenic transformation, gene mutation and cellular inactivation and cell killing.

Sample of lymphocytes from the peripheral blood of an accidentally exposed worker can be analyzed for radiation dose–induced chromosomal aberrations. Those yields of aberrations could then be computed from the dose–response standard curve for radiation cytogenetics to evaluate the amount of radiation dose absorbed by the body. This is the basic principle of "biological dosimetry".

Under the Agency's programme the radiation cytogenetic parameters were investigated to formulate a reliable protocol for use in occupational personnel accident dosimetry. Studies are still continuing to assess the performance and technical feasibility and limitations of the chromosome–based biological dosimetry for nuclear accident monitoring of occupational health.

Epidemiological studies on nuclear impacts from low level radiation. – Modern technology in industrial, medical and scientific applications has exploited ionizing radiations to such an extent that hundreds of thousands of workers are involved and millions of people may become exposed by environmental release of radioactivity. Industrial and agricultural development, including especially nuclear energies, produce a vast amount of potentially harmful factors. The only way to obtain direct information on the harmful action in man of these factors, the first and foremost of which is low level radiation, is to conduct epidemiological studies.

The programme implemented by the Agency in this area aims at collecting and analyzing the existing methods of epidemiological studies of the harmful effects of low level radiation to man. In addition, the project is concerned with methodological approaches for comparing impacts on man's health of ionizing radiations and other harmful environmental factors for both radiation workers and the general population. Analytical quality control of methods of multivariant regression analysis is expected to provide best evaluation of the results obtained.

In relation to prospective studies, the Agency's programme aims at trying to elaborate a generally–accepted methodology and structure of a typical follow–up system for radiation workers which can — if elaborated properly — be used in develop-

ing countries for the planning of their economic development and for their system of public health.

The product. – Table 3 illustrates the manpower of the programme of human health which includes 15 professionals taking care of 21 coordinated research programmes. The regular budget of the division is about $5.0 million equally divided among the division's own programme and technical cooperation activities: the latter includes 97 projects.

Finally, Table 4 shows the symposia and seminars organized by the Agency in the area of medicine and biology, for this year and those scheduled for the next 2 years. We try to cover — through this function — as many of the different activities related to the programme of human health as possible.

Table 3. – *Human health programme*

No. of Professionals	15
No. of Coordinated Research Programmes: (1985–1986)	21
Regular Budget (1985)	US $ 2,5 million
Technical Cooperation Programme 1983 Budget	US $ 2,5 million
No. of Projects	97
No. of Publications (1982–1983)	8

Table 4. – *Human health programme. Symposia and Seminars*

1984

International Symposium on High Dose Dosimetry

Seminar on Quality Control in Radioimmunoassay (Asia)

Seminar on Tissue Banking of Radiation Serilized Grafts for Clinical Use

1985

International Symposium on Medical Applications of Nuclear Techniques in Developing Countries

Seminar on Quality Control in Radioimmunoassay (Latin America)

Seminar on Practices of Radiation Sterilization of Medical Supplies (Africa and Middle East)

1986

International Symposium on Radiation Therapy in Developing Countries

Seminar on Quality Control of Nuclear Medicine Instruments (Africa and Middle East)

Seminar on Stable Isotopes in Medicine

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FAO CONTRIBUTION TO PUBLIC HEALTH THROUGH LIVESTOCK DISEASE CONTROL WITH EMPHASIS ON VIRAL DISEASE

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The Food and Agriculture Organization of the United Nations (FAO) is an autonomous agency grouping over 150 nations. The main economic and technical programmes of the FAO deal with agriculture, fisheries and forestry. Among many other activities, FAO spreads advance techniques across the world, combats epidemics of animal diseases, and provides technical assistance in such fields as nutrition and food management.

Let me focus my attention on activities of the Animal Production and Health Division of FAO (Fig. 1 and Table 1), particularly its Animal Health Service on the control of the viral diseases of livestock.

Table 1. – *FAO activities on animal health*

REGULAR PROGRAMME:	
Organization of expert consultations, seminars, workshops, training courses, publications including *World animal review* and FAO/WHO/OIE *Animal health yearbook*, research contracts	
FIELD PROGRAMME:	
Field projects: National	Financed by international agencies and trust funds
Regional	
Sub-Regional	
In 1983: Total of 87 projects, with 92 experts and 26 consultants	

Selection of animal viral disease for illustrating FAO activities on public health originates from their importance for livestock and poultry production and in international trade. Their products are the main source of animal proteins and other components necessary in normal human nutrition. The seriousness of virus diseases is not solely that of the effect of the disease in the infected flock or herds; it is also because of interruptions in international trade resulting from disease-free countries placing embargoes on the importation of animals and animal products from affected countries. The presence of a potentially disastrous animal disease in a country or region, or even suspicion of the existence of such a disease, constitutes a disease emergency (Table 2).

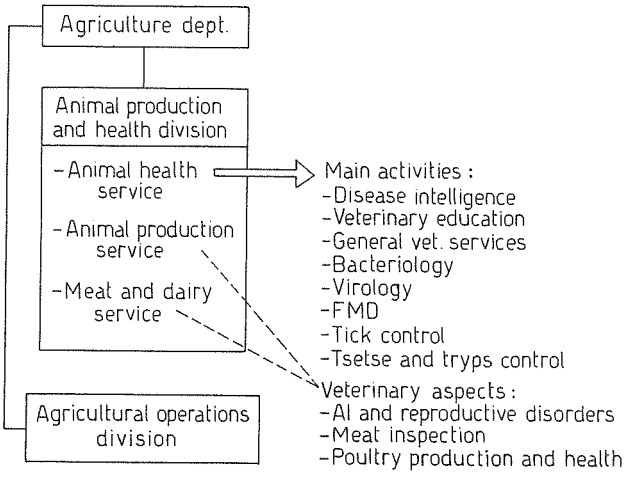

Fig. 1. – The Animal Production and Health Division at FAO Headquarter, Rome

Table 2. – *Viral emergency diseases*

Vesicular diseases:	
Foot-and-mouth disease	A
Swine vesicular disease	A
Vesicular stomatitis	A
Vesicular exanthema	
Rinderpest	A
Peste des petits ruminants	A
Pox (sheep, goat and lumpy skin disease)	A
Bluetongue	A
African horse sickness	A
Classical swine fever (hog cholera)	A
African swine fever	A
Teschen disease	A
Rift Valley fever	A
Newcastle disease (viscerotropic/velogenic)	A
Fowl plague	A
Rabies	
Equine encephalitis	
Japanese encephalitis	

A – list of the International Zoosanitary Code

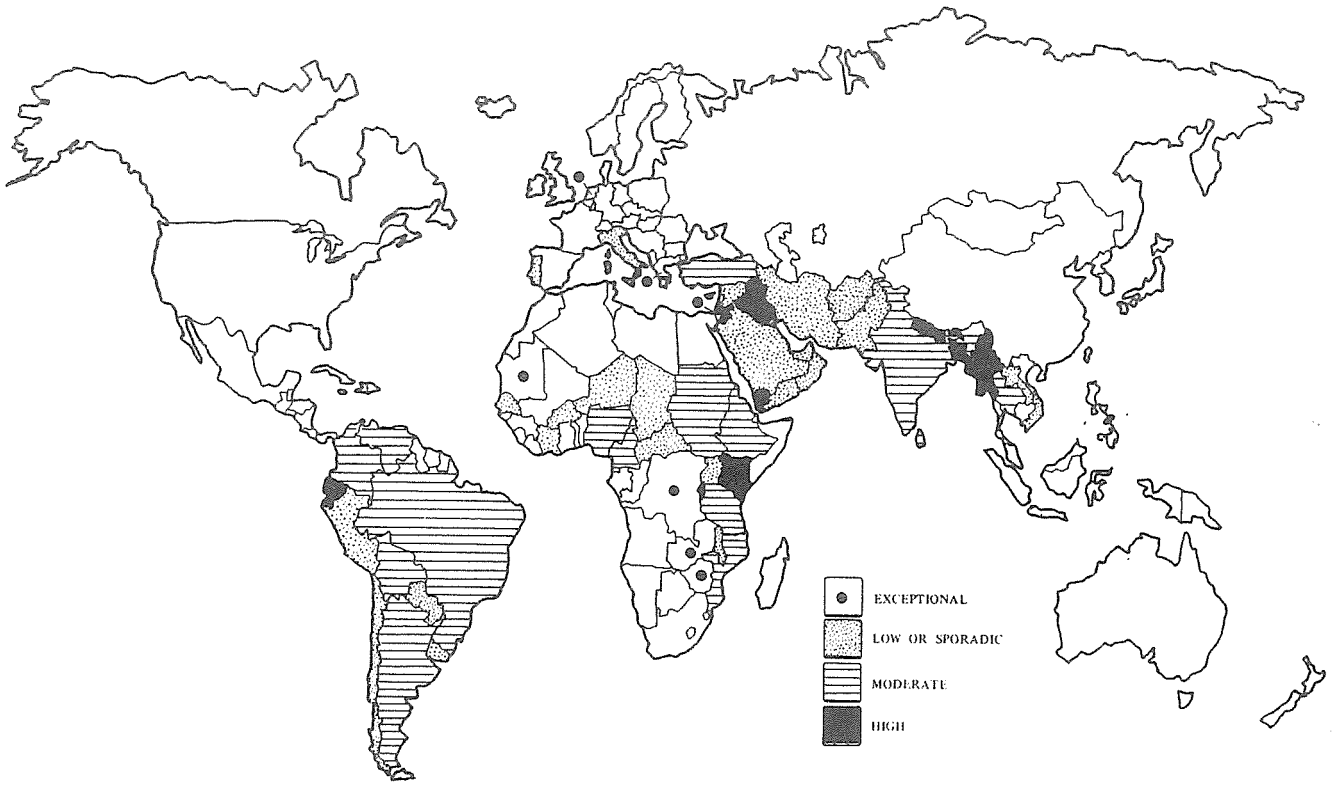

Fig. 2. – Countries reporting outbreaks of foot–and–mouth disease recently

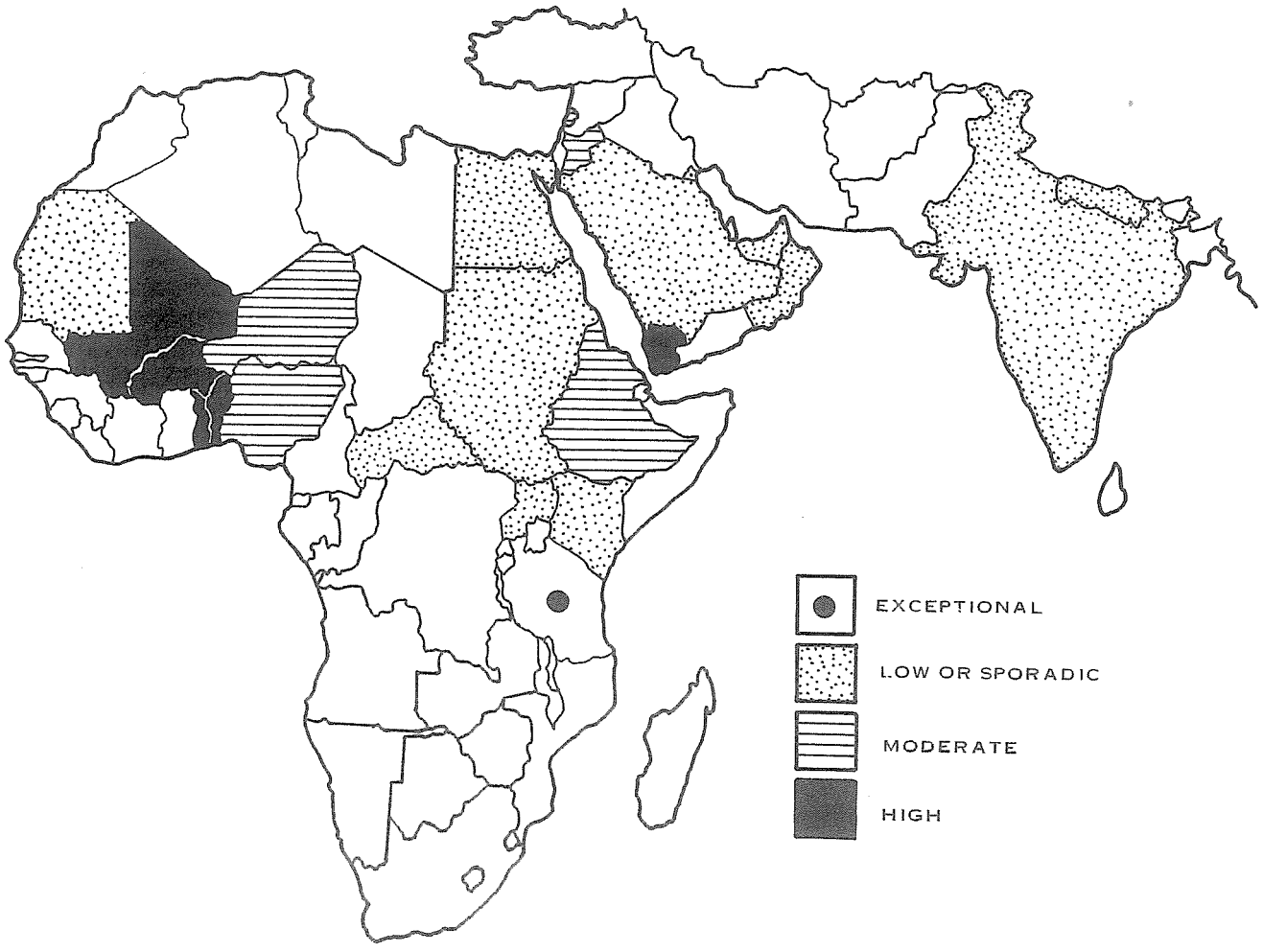

Fig. 3. – Countries reporting outbreaks of rinderpest recently

Foot–and–mouth disease is probably the most feared virus disease of the world livestock industries (Fig. 2). At present there are 7 serological types with 60 subtypes identified. After the foot–and–mouth disease (SAT 1) virus invasion of the Near East in 1962, another FMD virus, type A 22, spread from its original areas in Eastern Africa to the Near East and involved southeastern Europe, Near East, India and Nepal. Thus the potential threat of an invasion by an FMD virus crossing continents is real and continues.

Introduction of FMD to United Kingdom (1967/68) has led to slaughter of nearly half a million of livestock in efforts to contain and eradicate the disease. In many countries FMD is endemic and vaccination is widely applied.

An important factor contributing to the success of FMD control in Europe has been the initiative taken by FAO in protecting the European continent from invasion by exotic types through the establishment of buffer zones in southeastern Europe. It is necessary to plan and implement similar long–term programmes for FMD control in other regions such as the Near East, south and southeast Asia, Africa and South America.

Fig. 4. – Pan–African campaign against rinderpest and pleuropneumonia (CBPP) as planned in 1984. (The campaign will take place on a reduced scale, 1985)

Rinderpest first infected the African continent in 1889, killing in a devastating epizootic almost 90% of the African cattle. The methods available to control this disease have developed with the introduction of new vaccines, field equipment, laboratories and well-trained veterinary personnel. These, together with adequate funding and coordination of activities, made vaccination campaign possible during 1962/1976. The JP 15 Campaign involved 15 countries. Due to unforeseen circumstances vaccination coverage was inadequate and rinderpest remained enzootic in several areas of the continent (Fig. 3).

The emergency situation in regard to rinderpest in ten countries of West Africa resulted in an immediate international campaign (including FAO) in 1981, and further action taken by FAO since 1982.

The new vaccination campaign is now being prepared: 10 years Pan-African Rinderpest Campaign – whose aim is to eradicate the disease from the continent. Action is going to take place in 28 African countries to vaccinate about 120 million cattle. The role of FAO will be to advise on the organization, strengthen diagnosis, vaccine production and quality control, distribution of vaccines and provide the relevant training (Figs. 4 and 5) *.

In Asia rinderpest is endemically present in many areas especially the Indian sub-continent. FAO/APHCA "Expert Consultation on Requirement for Rinderpest Campaign in South Asia", held in 1983, recommended a five year campaign with application of TC vaccine. At present the disease is also reported in the Arab Peninsula and Middle East countries. FAO assists in strengthening diagnosis, vaccine production and field vaccinations.

The global threat of *African swine fever* became apparent outside Africa invading, after 1957, Portugal, Spain and France. In 1978 the disease appeared in Malta, Sardinia (Italy), Brazil and the Dominican Republic and in 1979 in Haiti, Cuba and Sao Tome. FAO provided immediate assistance to the majority of these countries and to 12 other countries at high risk. FAO assistance to Haiti, Brazil and five Andean Pact countries will continue.

In 1980 a "FAO Expert Consultation on Emergency Disease Control" called on governments to review existing regulations, to enable them to function effectively in an emergency to develop national Emergency Task Forces, to identify the sources of the assistance they may require and to organize a training programme. Training on exotic disease has been initiated by FAO for participants from many continents. FAO reference laboratories for rinderpest, African swine fever, foot-and-mouth disease and other emergency viral diseases have been designated (Fig. 6).

In 1976 the FAO Technical Cooperation Programme was introduced to provide immediate assistance to countries affected by, or exposed to, emergency situations affecting agricultural production.

Recent technical developments and research on viral laboratory diagnosis and vaccine production

For laboratory diagnosis see Table 3.

The *Enzyme Linked Immunosorbent Assay* (ELISA) differs from conventional seroassays by its indicator (marker) system and is based on enzymic conversion

Table 3. – *Laboratory diagnosis of some animal viral emergency diseases*

Disease	Tests applied	Methods being developed
Foot-and-mouth disease	Complement fixation, SN Isolation on tissue cultures ** ELISA, pH gradient electrophoresis, RNA fingerprinting and sequencing	Monoclonal antibodies (Mabs)
Rinderpest	– agar gel immunodiffusion (AGID) – counterimmunoelectrophoresis (CIEP) – cultivation on cell cultures, virus isolation – identification by the immunoperoxidase staining, indirect immunofluorescence (IIF) – microseroneutralization test	ELISA Mabs
Hog cholera (classical swine fever)	Direct immunofluorescence (DIF) of of lymphopoietic tissues Microseroneutralization test (detection of an antigen by IIF or use of a cytolitic strain of the virus) ELISA	Mabs
African swine fever (ASF)	– haemadsorbtion in leucocyte cultures (HAD) – immunoelectroosmophoresis (IEOP) – ELISA	– semi-automatic fluorometric assay (SAFA) for ASF -IgG detection and quantification – detection of ASF virus by DNA-DNA hybridization

* The campaign will take place on a reduced scale (1985).
** Methods applied only in specialized laboratories

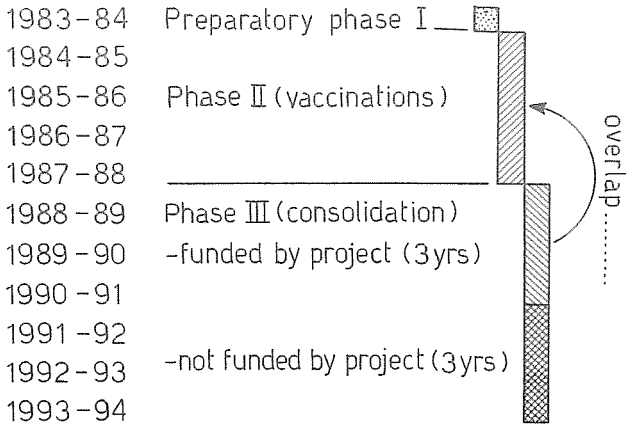

Fig. 5. – Pan-African rinderpest campaign (as planned in 1984)

of substrate to a coloured product. The test is faster, less expensive and less tedious than most of the other procedures commonly used.

The usefulness of the ELISA for field work has been proved for the majority of viral emergency diseases especially FMD, ASF and rinderpest. A modification of the ELISA with the *Staphylococcal Protein A — horseradish peroxidase* proved to be an excellent method for detecting viral antibodies correlating well with SN. This protein has also been used as a substitute for IgG sera in radioimmunoassay, immunoferritin technique and immunofluorescence. The protein A modification of ELISA, at present used by FAO reference laboratories, has potentials for wider field application.

A *Computer-assisted kinetic-based enzyme linked immunoassay* (KELA) has been developed, which allows for standardization based on totally objective criteria. The method is only applied in some larger reference laboratories. A Simplified Immunofluorescence Assays (Track System) based on the same reference sera concept as the KELA, but using fluorescence as the indicator has been developed. It may have substantial application for FAO activities in countries where laboratory services are inadequate.

The monoclonal antibodies (Mabs) based on fusion myeloma and spleen cells from immunized animals have been developed for many viruses such as FMD, rabies, vesicular stomatitis and bluetongue. Monoclonal antibodies are being used by FAO projects to identify different strains of *Theileria parva.*

Virus diseases are usually diagnosed by serological methods provided specific antisera are available. With a "new" virus, however, knowledge of its physical and chemical properties are necessary before it can be assigned to one of the existing families.

If a specimen contains sufficient virus, *electron microscopy* is the valuable first test often allowing the agent to be placed immediately into a virus family. It is applied in more sophisticated laboratories using negative staining or cryo- and/or immunoelectronmicroscopies.

Fig. 6. – FAO Reference Laboratories for viral diseases of food animals

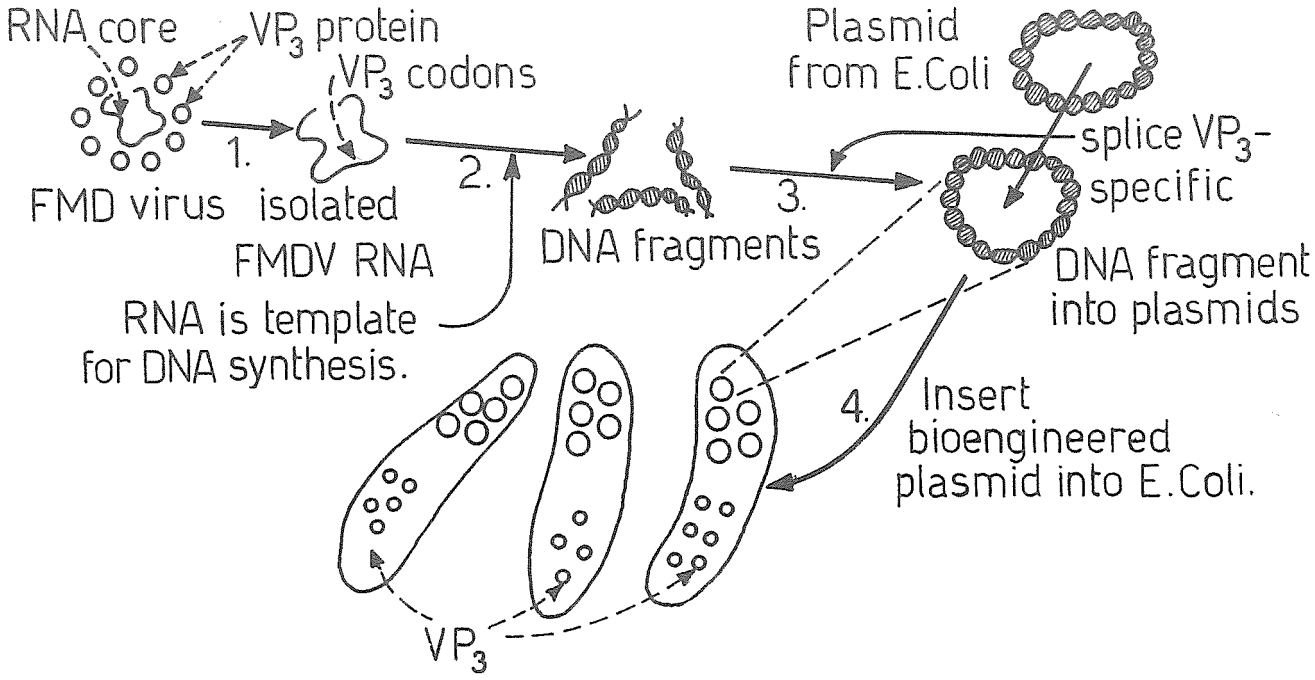

Fig. 7. – Recombinant DNA strategy for making FMD vaccine. Growing *E. Coli* bacteria may produce VP_3 for use as vaccine for FMD. No virus or infectious RNA is produced by the harmless bacteria strain

Table 4. – *Candidates for subunit veterinary vaccines**

Family	Virus	Immunogen		
		Isolated from virus	Cloned	Synthetic
Herpetoviridae	Marek's disease	Cell membrane proteins	ND	
	Infectious bovine rhinotracheitis	Glycoprotein	IP	
	Pseudorabies	Glycoproteins	IP	
Parvoviridae	Canine parvovirus	Capsid proteins	Yes	
Orbiviridae	Bluetongue	Protein p2	IP	
Picornaviridae	Foot-and-Mouth Disease	VP_1 (VP_3)	Yes	Yes
Togaviridae	Tick-borne encephalitis	Glycoprotein V3	ND	
	Hog cholera/bovine viral diarrhea	Split virus E_{1-2}	ND	
Coronaviridae	Transmissible gastroenteritis	Glycoprotein	ND	
Orthomyxoviridae	Fowl plague	Hemagglutinin	Yes	
Bunyaviridae	Rift Valley fever	Glycoproteins G_{1-2}	IP	
Paramyxoviridae	Newcastle Disease	Hemagglutinin, neuraminidaze	IP	
	Parainfluenza-3	Protein F	IP	
Rhabdoviridae	Vesicular stomatitis	Glycoprotein G	Yes	
	Rabies	Glycoprotein G	Yes	

ND: not done to our knowledge
IP: in progress
*Modified from: Bachrach H.L. *et al* 1983

The methods applied only in some FAO virus reference laboratories include: time–resolved fluoroimmunoassay in detection of viral antigens; high resolution protein separation and identification; electrofocusing of structural and induced proteins; detection of viral enzymes; RNA fingerprinting and sequencing to the characterization of exotic RNA viruses; hybridization methods to the demonstration of viral nuclei acids; and restriction endonuclease patterns.

Assays of cellular immunity are used for basic immunopathological studies of African swine fever in FAO reference laboratories. In case of FMD vaccines due to problems of both live attenuated and inactivated vaccines, and also because of the very large market for an effective safe vaccine, research in recombinant DNA technology has been undertaken for the preparation of subunit vaccines (Fig. 7). Surface proteins have also to be cloned for the viruses of fowl plague, influenza, vesicular stomatitis, and rabies.

Synthetic polypeptide vaccines are also in experimental stage. The use of chemically synthesized antigenic fragments of VP_1 has recently been reported and these synthetic fragments appear to be potentially better at producing immunity to FMDV than the whole genetically engineered VP_1 protein. We are still far from practical application of biologically engineered subunit and synthetic vaccines (Table 4).

New methods and technologies are being developed in different scientific institutions or FAO reference laboratories partly as a result of research contracts with FAO. Generally the purpose of such contracts is to work out methods applicable under field conditions for diagnosis or vaccine production. In this way FAO is supporting work on: simplification of rinderpest diagnostic tests, rinderpest in wildlife and identification of isolated strains and preparation of diagnostic reagents; an African swine fever simplified ELISA kit, prepared by FAO reference center after worldwide testing, will be distributed on request by laboratories; finally, research on immunology of ASF, hopefully leading towards the prototype of a vaccine, is being carried out.

The role of FAO field projects on Animal Health and Livestock Production is a very important element of the progress. Highly qualified experts on many aspects of the above–mentioned specializations and also on viral diseases are assigned in developing countries. They are involved in organization of laboratory infrastructures, and training of counterparts.

The common problems in *tissue culture work* in developing countries are: contamination, poor cell growth and loss of cell lines.

Application of sterile microflow cabinets, prepared media, antibiotics and fungicides or disposable plastic laboratory glassware, is very useful. Utilization of microsystems for serological tests or titration of the virus is becoming a common practice. Fluorescent microscopy is commonly used by field laboratories. In vaccine production, the roller bottle system is being introduced in many countries. In the case of FMD vaccine production method of BHK–21 cultivation in stainless steel fermentors is commonly used and vaccine is prepared in well designed high security laboratories. New generations of freeze–drying equipment are being introduced and the main problem is the maintainance of equipment and its full utilization. Distribution of vaccines, from manufacturers to the field, requires a well organized cold chain. In tropical countries solar photovolter refrigerator or freezer systems for vaccine storage are under testing. Deterioration of vaccines in the field can be detected by changing colour stickers/indicators sensitive to temperature changes.

FAO is also participating in the planning, the designing and implementation of research through cooperation with international organizations, institutions, committies, and UN agencies.

Concluding, the progress in livestock production and provison of more animal proteins to the world population should be continuous and uninterrupted. The prophylaxis, control and eradication of viral animal diseases is a part of these efforts.