RESEARCH POLICY AND PROGRAM OF THE PAN AMERICAN HEALTH ORGANIZATION

1. The Annual Report of the Director reviews progress and accomplishments of the PAHO research program in 1966, and reports on special studies and scientific meetings sponsored by the Organization on (i) migration of scientific personnel, (ii) multinational centers for advanced training and research in the health sciences, (iii) life at high altitudes, (iv) vaccines against viral and rickettsial diseases of man, (v) population dynamics and (vi) the Second PAHO/WHO Lecture in Biomedical Sciences*. Since the publication of the Report and with funds made available by the Commonwealth Fund of New York, by the National Library of Medicine of the USPHS/HEW, and by the Ministries of Health and of Education of the Government of Brazil, the PAHO Regional Library of Medicine for South America was formally established in the Faculty of Medicine of the Federal University of São Paulo. By providing increased access for specialists in the health sciences to a comprehensive collection of scientific and professional literature through modern communications technology, the new Regional Library will contribute to the acceleration and improvement of medical education, research and practice in South America.

2. The Sixth Meeting of the PAHO Advisory Committee on Medical Research was held on 12-16 June 1967 under the Chairmanship of Prof. René Dubos, and with Drs. Philip P. Cohen, of the University of Wisconsin, Herman Hilleboe of the School of Public Health and Administrative Medicine of Columbia University and Salvador Zubirán of the Instituto Nacional de la Nutrición of Mexico as new members. In its Report to the Director (See RES 6/21 attached) the Committee dealt mainly with two areas, research problems in the control of infectious diseases that are of special importance to the Western Hemisphere (See Paragraphs 2.1-2.3 below), and the multinational centers for advanced training and research in the health sciences in Latin America (See paragraph 2.4).

*Abel Wolman "The Unreasonable Man", PAHO Scientific Publication No. 152.
2.1 The immunological aspects of parasitic infections was the subject of the Committee's Special Session this year. With Prof. Otto Bier as moderator and with the participation of 15 distinguished immunologists and parasitologists from several countries, the Session directed the attention of the Committee to the outstanding problems in the host-parasite relationships of these infections and to the complexity of the antigenic structure of the parasite and of the response of the host. In its report of this Session the Committee indicated the need for intensive and multidisciplinary efforts in basic research in this field before practical steps can be sought for controlling these infections by immunological methods.

2.2 The First PAHO/WHO International Conference on Vaccines Against Viral and Rickettsial Diseases of Man highlighted the following among the many research accomplishments to date: (i) the existence of a highly effective live virus vaccine against measles, (ii) the development in the near future of equally effective vaccines against mumps and rubella, (iii) the availability of a vaccine against Mycoplasma pneumoniae, and (iv) the preparation of a rabies vaccine using virus grown in cell culture. The Committee remarked that the comprehensiveness of coverage and the promptness with which the conference report appeared made it a valuable reference text for research workers and students in this field throughout the world.

2.3 The symposium on Drug Resistance in Human Malaria organized at the request of the PAHO/ACMR made apparent the following observations: (i) certain strains of falciparum malaria isolated in South America and in Asia (but not thus far elsewhere) are resistant to 4-aminoquinolines, (ii) such isolations have been relatively rare and do not permit the drawing of major inferences, (iii) epidemiological studies are urgently needed to provide a basis for subsequent comparison, (iv) efforts should be made to develop models for detecting changes in drug resistant strains in epidemiological studies based upon present laboratory models, (v) meanwhile, solutions to logistical problems, such as the preservation and transportation of blood samples from isolated communities, should be sought.

2.4 Realizing the need for moderating the migration of trained scientific personnel from Latin America made evident by the Organization's "Study of Migration of Health Personnel, Scientists and Engineers from Latin America" the XVII Pan American Sanitary Conference, through Resolution XVI, requested the Director of PAHO to study means of expanding and augmenting the number of multinational centers for training and research in the life sciences and medicine in the Americas, and to present appropriate proposals to this meeting of the Directing Council.

The PAHO/ACMR, after reviewing the Organization's studies and proposals called for by this Resolution recommended that, in the implementation by PAHO of this program, emphasis should be given to the strengthening of existing biomedical centers for advanced training and research rather than the establishment of new multinational ones. It agreed that centers should not be strengthened in isolation but as integral parts of a network of institutes linked by discipline or by problem. It held valid the concept that the exchange of both students and teaching staff among
the centers should be multinational. The Committee also reviewed four studies in the fields of basic science, applied science, clinical science and scientific communications representing initial steps being taken by PAHO in planning a well-balanced program.

3. In compliance with the directive of the XVII Pan American Sanitary Conference, the attached document (RES 6/1, Rev. 2), summarizing the general principles and a program proposal for cooperative efforts to strengthen multinational activities in the biomedical sciences in Latin America, is submitted for the consideration of the Directing Council.

Annexes
PAN AMERICAN HEALTH ORGANIZATION

SIXTH MEETING
12-16 JUNE 1967
WASHINGTON, D.C.

ADVISORY COMMITTEE ON MEDICAL RESEARCH

REPORT TO THE DIRECTOR

Ref: RES 6/21
30 June 1967

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION
WASHINGTON, D.C.
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The Director opened the Sixth Meeting of the Pan American Health Organization Advisory Committee on Medical Research and welcomed three new Committee members, Drs. Philip Cohen, Herman Hilleboe, and Salvador Zubirán, and regretted the absence of Drs. Chagas, Hurtado and Roche. He commented on two significant events bearing on PAHO's research program, namely, the Declaration of the Punta del Este Meeting of Heads of State of the Western Hemisphere and the Resolution of the XVII Pan American Sanitary Conference authorizing the establishment in PAHO of a special fund for research.

The Declaration specifically mentioned health and called for a regional scientific and technological development program by strengthening or establishing multinational institutions for research and training in science and technology at the graduate level, a step which is coincidental with the approach that the Organization has been developing over the past few years and which appears in the documentation presented to the Committee during this current meeting.

The Director commented on the items of this year's agenda and noted that they are illustrative of the thinking expressed by the Committee when it stated in 1962 that "fundamental science is not distinguished by the use of mathematical, physical or chemical methods per se, but rather by the relevance of the research to an intellectually and practically satisfactory solution of the problem at hand. The immediate purpose of supporting research in Latin America is to solve problems related to health in a manner which will promote human welfare."

Dr. René Dubos was appointed chairman of the Meeting, Dr. Abel Wolman vice-chairman, and Drs. Hilleboe and Zubirán rapporteurs.
1. **Multinational Centers for Advanced Training and Research in the Health Sciences**

1.1 The Committee noted the highly significant fact that the Presidents of the American States during their meeting at Punta del Este in April, 1967, recognized the importance of science and technology in the social and economic development of the hemisphere and in the future well-being of its people. The content and tone of the Declaration of Presidents at that meeting influenced the thinking of this Committee. The evolution, status and outlook for the program in science and technology adopted by the Heads of American States at Punta del Este was then reviewed for the Committee. The role that PAHO may play and its scientific and technical contribution to the total OAS program was also discussed.

1.2 The Committee reviewed the reports summarizing studies conducted by PAHO on strengthening existing centers of research and advanced training in Latin America and outlining the general principles governing such efforts. It was the consensus of the Committee that PAHO should emphasize the strengthening of existing centers for advanced training and research rather than the establishment of new multinational ones.

Centers should be strengthened, not in isolation, but as part of a network of laboratories linked by discipline or by problem for the benefit of all Latin American countries. The functions of this group should be to elevate standards of advanced teaching and research.

The Committee agreed that the PAHO program should not be called "multinational centers," but something like "cooperative programs to strengthen multinational activities in the health sciences." Collaborative arrangements should take into account the vast distances and high costs of transportation involved in cooperative arrangements among countries from the far north to the far south of Latin America. Regional groupings should be considered. The concept of having both teaching staff and students come from different countries is implicit in the composition of these centers.

The following four subjects - representative of basic science, applied science, clinical science and scientific communications - were chosen because
they had been studied by PAHO and other expert groups by the time of the meet-
ing at Punta del Este. They represent only first steps toward a well-rounded plan and the laboratories mentioned do not in all cases include all outstanding institutions.

1.3 Multinational Program for the Biochemical Sciences

The Ad Hoc Committee of Latin American Scientists for the Biochemical Sciences, an independently elected Committee more or less regionally representa-tive of biochemical and related sciences in Latin America, had been asked by PAHO to accept the responsibility for making a study and recommendations for the development of multinational institutes in the biochemical sciences in Latin America. The revised proposal presented to the Committee for a multinational institute to be developed in Mexico is an example of what might be developed.

With the information on the present status of biochemical research and training obtained from the members of the Ad Hoc Committee and from a few other biochemists, an effort has been made to identify, among the scientists engaged in biochemical work, those who might be considered productive and well established and those who are promising. It was readily apparent that high quality research nuclei have developed in Argentina, Brazil, Chile and Mexico. The reasons for the limitations in development and the unmet needs to achieve such developments were discussed.

The establishment of multinational centers - as defined by PAHO - for the biochemical sciences at least one in the north and at least one in the southern part of the Hemisphere was proposed.

1.4 Multinational Program for Research and Training in Arbovirology

Arbovirology was selected by PAHO as one field of biomedical science and microbiology that deserved early consideration because of the importance of arboviral diseases, e.g., Venezuelan encephalitis and dengue, in many parts of Latin America. There is a current potential for rapid advancement of knowledge in this field.

The Ad Hoc PAHO Advisory Group on Multinational Collaboration for Research and Training in Arbovirology, convened at the Universidad del
Valle in Cali, Colombia, 16-18 April 1967, recommended as first steps in a multinational program in arbovirology i) the formation of a Latin American Committee on Arboviruses (LACAV) and ii) multinational Latin American centers for training in three scientific fields basic to investigations of arboviruses and other viral zoonoses, namely, medical virology, medical entomology, and vertebrate ecology.

Possible functions of the LACAV would include training, research collaboration, enhancement of communication, a survey of arbovirologists and their facilities in Latin America, advice and assistance to governmental and other organizations, close affiliation with the PAHO/WHO Collaborating Center in Arboviruses in São Paulo, and coordination with the American Committee on Arboviruses in the USA.

1.5 Multinational Program for Research and Training in Pathology

Research has priority in the development of pathology as a specialty in Latin America. A proposal was presented to the Committee as the collaborative effort of four departments of pathology in Colombia, Mexico, Peru and Venezuela.

The Committee considers that in the study of pathology, disturbances in function should be viewed together with alterations in structure. Consequently, pathological physiology and pathological biochemistry should be represented with pathological anatomy in the research and training activities of the multinational centers in pathology.

Multinational centers should be an effort in the right direction in correcting the failure of many Latin American universities to develop research attitudes in staff and students. Pathology departments in Latin America frequently place emphasis on patient care rather than on disease processes. Such centers could favorably effect attitude changes towards medicine and science and assist in bringing about much needed reforms in pathology teaching and research in Latin America.

1.6 Regional Library of Medicine

In view of the serious deficiencies in biomedical communications in Latin America and of the interest of Latin American physicians and scientists in acquiring the literature of the biomedical sciences, recommendations were made during previous meetings of this Committee to develop a regional library of medicine strategically located in South America to improve documentation and library services throughout this area of the world.
With commitments from the National Library of Medicine to provide technical support as well as access to its book credits in the U.S. Book Exchange, the Pan American Health Organization agreed to serve as the agency to administer the Regional Library of Medicine.

A search for funds to implement the program has resulted in a series of agreements between the Government of Brazil, the Pan American Health Organization, and the National Library of Medicine which would permit the establishment of the Center to take place during the current calendar year.

It is believed that the Regional Library of Medicine should be considered an essential communications element for the multinational centers for advanced training and research in the health sciences currently being developed by PAHO and OAS. It is reasonable to expect that upon successful demonstration of the capabilities of the Regional Library of Medicine that long-range sustained funding should come either from the Pan American Health Organization itself or from some other stable funding source.

It was suggested that, in every Latin American country, local offices be established with professional personnel available to offer consultation to facilitate transmittal of library materials in both directions.

The method whereby experts visit all countries in Latin America and report back to PAHO, as has been done in developing this proposal, is commended by the Committee and is suggested as a guide for similar projects.

1.7 The principles of the four proposals for multinational centers presented to the Committee were endorsed. However, the Committee recognized that many problems remained to be solved. Among these are:

- Appropriate means for ensuring that the larger participating laboratories will actually receive students and scientists from other countries;

- Practical problems, such as the kinds of expenses which may be put in budgets; and

- Care must be exercised to ensure that the total program is not simply one to make strong centers still stronger at the expense of the development of other centers.
The Director pointed out that the eventual aim of the multinational program was to create a network of existing institutions covering all fields of biology and medicine. Committee members suggested additional disciplines which might be considered for cooperative programs. Among them were population dynamics, health administration, social pediatrics, biophysics, nutrition and the biology of reproduction. It is recognized that a high priority must be given to certain problems in the application of research in biology and medicine to the improvement of health and social well-being. The Committee, however, emphasized that in order to insure an effective program of applied research an equally vigorous program of basic research must be carried on simultaneously.

The Committee noted that, after the initial phase of planning, criteria for adding new programs and extensions should be worked out. These criteria were suggested as a start:

- Priority should be given to areas of research which promise significant and rapid advances in levels of health;

- Support should be selective, and high priority should be given to centers capable of advanced training and high quality research; and

- Priority should be given to proposals which have the prospect of strengthening regional collaboration within Latin America.

The Committee felt a responsibility for building a strategy for the use of science and technology in social and economic development, and for evolving the general guides for a plan which would meet the challenge set forth by the Presidents at Punta del Este. The Committee was strongly of the opinion that the four proposals thus far developed were of the type to be undertaken - although requiring modification - but that they left a large and important strategic gap. This deficiency was defined as being a relatively ineffective link between research on the one hand and economic and social development on the other. Various means of attainment were proposed:

- More attention to research on the effective administration (organization and management) of health programs;

- Investigations of the process of planning, organizing and managing research itself; and
- A broad attack on the means by which all available knowledge - from the social and physical sciences and engineering as well as from biology and medicine - can be brought to bear most effectively on new means of solving both personal and environmental health problems (taking into account social, cultural, political and economic constraints) through changes in institutional forms as well as through applying specific technologies.

In connection with these concepts, the Committee thought that the creation of a new institutional form - possibly a new and extensive multinational center - should be thoroughly studied and suggested that a subcommittee be appointed by the Director to elaborate the general idea into specific terms.

2. PAHO/WHO Immunology Research and Training Center in Brazil

A brief presentation was given of the activities of PAHO/WHO Immunology Research and training Center established in the Department of Microbiology and Parasitology, Escola Paulista de Medicina, São Paulo. The Center is now in its second year of operation. Besides providing teaching at a post-graduate level, immunological research related to public health problems of local importance is pursued. It is believed that through the cooperation of visiting professors it will be possible to involve highly qualified immunologists in the study of the above problems. On the other hand, students participating in the Center's research under the guidance of visiting professors can be adequately motivated. It is hoped that this will help to mitigate the migration so frequently observed in scientists trained abroad.

The Center is financed by (i) PAHO/WHO contributing to the expenses involved with visiting professors and with the provision of equipment and drugs, (ii) the Escola Paulista de Medicina providing the laboratories and the services of the permanent staff and (iii) the Ministry of Education of Brazil, through the CAPES-FORD program, providing fellowships for the post-graduate students participating in the yearly course given by the Center.

As an example of the research activity developed in the Center, a detailed report was presented to the Committee of studies on "fogo selvagem", an endemic form of pemphigus foliaceus which is estimated to afflict about 1,000 persons per year in the central areas of South America. Five
hospitals in Brazil are devoted exclusively to the care of these patients. The disease is clinically and histologically indistinguishable from the non-endemic form of pemphigus foliaceus as it occurs elsewhere in the world. The epidemiology of the disease in Brazil is, however, quite different. It behaves like an arthropod-borne infectious disease. The non-endemic form of the disease is associated with autoantibodies against an intracellular component of stratified epithelium which were demonstrated in all active cases of "fogo selvagem" studied in São Paulo and at titers higher than those in the non-endemic form of the disease. Interestingly, the titers of autoantibody were correlated to the severity of the disease.

The above observations now afford an opportunity for investigating the pathogenesis of the disease, better methods of treatment, and its epidemiology. The need for virologic research was particularly emphasized. The cooperation of a qualified virologist in the project on pemphigus foliaceus was specifically stressed by the Committee.

In relation to the operation of the Center, it was pointed out that the low salaries paid to the local staff of immunologists should be supplemented in order to assure continuity in the functions of the Center. The Committee recognized this need and gave its support to the request of a more substantial contribution from PAHO for the further development of the Center.

3. Survey of Research Facilities in Parasitology

The Committee heard the report of a visit to Belo Horizonte and Mexico City in which research potentials in parasitology were briefly surveyed.

In Belo Horizonte, the caliber of the scientists and their programs is high and it would be an excellent choice for training in parasitology. There is a real and immediate need for greater support of the scientific community's salaries. In addition, the costs of supplies and equipment are often so great as to be inhibitory to research.
In Mexico City, the clinical center at the Instituto de Enfermedades Tropicales is outstanding and would be excellent for international collaboration in clinical and basic training in parasitology. A well prepared immunologist is willing to train parasitologists in his field in the projected PAHO/WHO Immunology Center in Mexico City.

The Committee considered the survey to be very useful as a start and should be extended to include other sites in the development of a multinational program in this field.

4. Population Dynamics

A report on the background to the three annual PASB conferences on population dynamics was presented and a review given of the highlights of the last one emphasizing training programs in Latin America. Those in attendance left the conference with a sense that achievements had been made in this field and that a most useful exchange of information had taken place. One could not fail but feel heartened at the substantial evidence emerging from the many and diverse areas that political and theological considerations are being brought into harmony with scientific solutions to the problems of population.

The Committee was informed that the Organization continues with its program of collecting, organizing and publishing data through its Population Information Center, promoting research and training, and rendering advice to governments upon request in family planning as part of maternal and child health programs. Discussion by the Committee centered on the importance of introducing the subject into the curricula of schools of medicine and of public health, and on the desirability of supporting and coordinating on-going research both in the biology of reproduction, at animal and human levels, and in demography.

The Committee also heard a report on a Latin American teaching program started in May of 1967 to train physicians in reproductive biology. The subject is being approached comprehensively to include the structural, biochemical and physiological bases as well as the clinical applications and the demographic aspects. The course, consisting of two parts of six and 18 months
each, has been organized by the cooperative efforts of several research and training centers located in Buenos Aires, Montevideo and Santiago. These centers complement each other since they specialize in different aspects of reproductive biology. The coordination between the cooperating units is obtained by the action of a central committee in which all units are represented. The trainees are selected from all Latin American countries. For the first year more than 60 application from 16 countries were received.

The Committee considered the reproductive biology training program as presented to be an excellent example of a multinational research training subject for inclusion among those being developed by PAHO with the funds that might be obtained from the Program on Science and Technology adopted by the Heads of American States at Punta del Este. Research centers for reproductive biology should be supported and extended because of the great relevance studies coming out of these centers would have to family planning and population dynamics.

5. Migration of Health Personnel, Scientists and Engineers from Latin America

The PAHO report* has been well received and has stimulated further investigations of migration. The number of studies in this field from Latin America has increased over the past year and includes studies by established investigators, younger students preparing dissertation, studies financed by private foundations in Argentina and the United States, and expanded studies by governments particularly the United States. The most extensive investigation is a worldwide review of the movement of university-trained people from poorer to richer countries to be undertaken with the assistance of a grant from the Rockefeller Foundation.

General discussion by the Committee developed the following points:

- Migration is harmful to many Latin American countries but most of the steps required to moderate migration from those countries must be taken by the countries themselves.

*Migration of Scientists, Engineers and Health Personnel from Latin America, PAHO Scientific Publication No. 142.
- The problem should not be dealt with by restricting entrance into the United States.

- Migration does not result from economic differentials alone. Such factors as prestige, opportunities for research, and political stability are very important.

- It is easier to take measures that will reduce the migration of scientists than it is to take measures that will reduce the migration of physicians. There are fewer scientists and the expense of giving them adequate facilities is not high. Very extensive and costly changes in the entire systems for providing medical care are necessary to deal with the migration of physicians.

- Migration is a symptom of more basic phenomena, namely, the economic, educational, political and social dislocation that appear to be an inevitable consequence of the process of development itself. Attention to migration leads quickly to consideration of more basic issues.

- While further studies are needed, enough is now known to point the way to the kinds of actions required by governments. The most significant action over the past year relating to migration of scientists, engineers and physicians is probably the Declaration of the Heads of American States at Punta del Este. It is widely recognized that a major cause of migration of scientists engineers and physicians is the absence of satisfactory career opportunities. With respect to those working in scientific and technical fields, the Declaration stated that "the establishment of conditions favoring scientific and technological potential for solving the economic and social problems of Latin America, and to prevent the exodus of personnel qualified in these fields" is a major element of national policy. With respect to physicians, the Presidents decided "to expand national plans that will strengthen infrastructure in the field of health ... and to mobilize the internal and external resources ... for financing these plans." Effective implementation of these measures will deal with the basic causes of migration.

6. Standing Advisory Committee for Medical Research in the British Caribbean

The Standing Advisory Committee is concerned with only a small area of about 4 million inhabitants in all. Nevertheless, its experience during the 12 years of its existence might provide some useful guidelines for future development elsewhere.

6.1 The Standing Advisory Committee has successfully maintained its existence as a multinational body in spite of drastic political changes. The question has been discussed whether it should be extended to cover not only the
ex-British and British territories but also the other countries of the Caribbean region. It is considered, however, that such an extension, if it is to occur, is more properly the responsibility of PAHO.

6.2 Because the Caribbean area is technically under-developed, most of the support for medical research in the region comes from outside, mainly from the United Kingdom. It is the policy of the United Kingdom to decentralize as far as possible decisions on allocations for overseas research. In principle, grants for medical research in the Caribbean are made only on the advice of the local Committee, which is in a better position to assess the value of a project and the competence of the people who propose it.

6.3 The Standing Advisory Committee has at its disposal funds from which small non-recurrent grants can be made to individual investigators in medical schools, government medical officers or private practitioners. Much importance is attached to this as a means of encouraging a research tradition, which will not be confined to laboratory workers and specialists. It is of great value that the grants can be made with the minimum of formality and delay.

6.4 The PAHO/ACMR, in accepting the above report, hoped that similar regional funds for making such grants might be set up in other parts of Latin America.

7. Textbooks for Medical Students

The proposed program aims to supply textbooks in the biomedical sciences having a new pedagogical approach and at a cost within the economic possibilities of students in the medical schools of Latin America. This is part of a broad program of the Pan American Health Organization for improving the professional training of physicians and of other health personnel in the Americas.

After consultation with faculty members, committees of experts on the most important subjects in the medical curriculum will be appointed to assist PAHO in selecting the best textbooks. The cost of books will be kept low by issuing large press runs of books of modest appearance. Books will be advanced by PAHO
to medical schools which in turn will sell or rent them to students. Funds will revert to PAHO for a new supply of books, thus establishing a revolving fund.

Several suggestions were made by the Committee to improve and maintain the quality and usefulness of the proposal:

- The textbook program should be complemented by others, such as assistance to medical libraries in order that the students and faculty have access to several books on the same subject. Nevertheless, the value of having at least one book available was emphasized because basic scientific principles do not change.

- The content should elicit a critical response to concepts.

- Experiments should be tried on sectionalizing parts of textbooks to keep material up-to-date without rewriting a whole book.

- Inexpensive textbooks should be complemented by new teaching methods, e.g., programmed instruction and audiovisual aids.

- A conceptual approach to health should be incorporated into the content of books to help students acquire lasting knowledge and skills.

The Committee approved of the program and recommended its continuation and expansion.

8. Study of Health Manpower and Medical Education

The Government of Colombia, through its Ministry of Health, and the Colombian Association of Medical Schools with the collaboration of the Pan American Health Organization and the Milbank Memorial Fund have developed a study on health manpower and medical education. In essence the study in Colombia attempts to examine the teaching programs and patterns for medical education.

The three-fold objectives of the study are:

- Development of a method that can be used in other Latin American countries to obtain data for more rational planning in the education and training of health personnel.

- An educational experience for faculty and students of the medical schools of Colombia that will give them a better knowledge of their country's health conditions and needs.
Development of a closer understanding - for a more effective joint action - between health authorities and those responsible for medical education for attaining a common goal of rising health standards in Colombia.

The Committee was of the opinion that medical manpower studies of this type should be extended as soon as possible to non-medical manpower needs, i.e., in the environmental health field and in health administration - problem areas equal in importance to those of personal health.

In order to translate mortality, morbidity and disability data from such studies into actual priority goals for a country other factors of administrative and political nature should be taken into consideration. For this administrative and biostatistical research is needed.

The manpower shortage may not be primarily the cause of difficulties in providing adequate health services. It may well be a symptom of a serious deficiency in the way health services are organized and delivered. Fundamental research is urgently needed to identify the basic defects of the system.

The Committee expressed the hope that, because of their great importance, PAHO will continue to encourage similar studies in other countries of the Hemisphere.

9. First PAHO/WHO International Conference on Vaccines Against Viral and Rickettsial Diseases of Man

The highlights of this successful Conference* were presented to the Committee.

Essentially, a highly effective live virus vaccine affording lasting protection against measles now exists. Vaccines of equal effectiveness against mumps and rubella are on the horizon. Effective control of certain respiratory viruses seems probable in the foreseeable future. Effective vaccine against Mycoplasma pneumoniae has been developed and great progress toward parainfluenza

* Proceedings of the First PAHO/WHO International Conference on Vaccines Against Viral and Rickettsial Diseases of Man, PAHO Scientific Publication No. 147.
and respiratory syncytial virus vaccines has been made.

Influenza vaccine, while effective, requires continued surveillance because of antigenic changes. The effective adenovirus vaccines are now in question because of carcinogenicity for animals of a large number of serotypes including 3 and 7; a new live oral fed type 4 vaccine has been found effective. The heterogeneity of common cold viruses precludes practicable immunological control. Live poliovaccine is very effective but interference by other enteric viruses may prevent a positive take. Arboviruses, aside from yellow fever, appear best attacked by vector and reservoir control.

Sequential administration of live viruses grown in cell culture holds promise in broadening the response to these heterogenous agents. Smallpox vaccine may be reduced in virulence by further attenuation. Rabies vaccine has been prepared using virus grown in cell culture. Vaccines developed against B virus and Herpes simplex require further evaluation. Apparent infection of marmosets to hepatitis holds promise of a major breakthrough. Control of trachoma by vaccines may be of some value.

Immunologic adjuvants are of prime importance for the future and a rapid metabolizable adjuvant now holds considerable promise. Limited effectiveness of drugs for prophylaxis or therapy of ocular Herpes simplex (Iododeoxyuridine, cytosine arabinoside, trifluorothymidine, methylamino deoxyuridine), smallpox (Isatin Beta-thiosemicarbazone) and influenza A2 (adamantanamine) were reported. Stimulation of host response utilizing the interferon mechanism holds great promise for future control of viral diseases.

The Committee was most impressed with the comprehensiveness of the conference report and especially with the promptness of its publication. This volume should serve as a valuable reference to groups and individuals throughout the world concerned with these viral and rickettsial diseases.

The Committee expressed an interest in the question of what would now constitute a total vaccination program and the practical problems associated with effecting it.
10. **Special Session on Immunological Aspects of Parasitic Infection* 

The antigenic mosaic of parasites presents a very complex picture. Specialization in the stages of the life-histology of the parasite is reflected in antigenic structure and each stage of the life cycle may develop certain unique antigenic characters. Further modification of parasite morphology, physiology and antigenicity may follow host immune reactions. In chronic infections with some protozoa, additional and repeated antigenic changes occur without obvious alterations in parasite morphology. In this way some protozoa avoid the full consequences of the host's immune reactions. 

Protective immunity may need to be directed specifically against each antigenic form as it appears, but a more generalized immunity often develops and may be limited to common antigens. Generalized immunity may depend on the use of a live rather than a dead vaccine. 

To immunologists and biochemists, the complexity of the antigens of parasites is very impressive, and it was suggested that attention should be concentrated on a small selected group of antigens for detailed studies at genetic and subcellular levels. 

The desirability of correlative studies with trypanosomes and *Paramecium* was stressed, especially in relation to "secreted" exoantigen and surface antigens. 

The chemical characterization of parasite antigens is being attempted in many laboratories. Because of their complexity very few antigens have been isolated in sufficiently pure form for exhaustive study, but some progress has been made in the preparation of antigens for use in the immunodiagnosis of parasitic infections. The development of purer and more specific antigens will increase the efficiency of diagnostic tests. 

A complex antibody response is induced by parasitic infections but relatively little is known about the characteristics of antibodies. Recent advances in knowledge of the immunochemical heterogeneity of immunoglobulins require a better understanding

*The full proceedings of this Session will appear as PAHO Scientific Publication No. 150.*
of the functional significance of the heterogenicity of immunoglobulins in terms of complement fixation, tissue sensitization and anaphylaxis, cytophilic and opsonic properties of immunoglobulins, how immunoglobulins appear in external secretions, etc. The characterization of these antibodies might also shed light on the mechanisms of parasitism and host response. At the moment the majority of demonstrable antibodies cannot be correlated with the protective state of the host, although in many infections passive protection with serum has demonstrated that humoral agents must have some role in immunity. It was suggested that parasitologists should seriously consider reinvestigating the anti-enzyme hypothesis of parasite destruction.

Reaginic antibodies are an important feature of the antibody response to helminth infections, but again their role in the host-parasite relationship is not clear. Helminth infections, however, will provide useful systems for the investigation of the function and properties of reagins including the possibility that they are important factors in immunity in certain parasitic infections.

Parasites usually induce a marked increase in serum immunoglobulins and the current evidence suggests that most of the increase is not due to antibody specifically directed against the parasite. The need to study the chronology of the different immunoglobulin responses during infection was stressed; the value of this was illustrated in toxoplasmosis, where, when infections occur in the fetus or the neonate, IgM antibodies are detected. Since maternal IgM antibodies do not cross the placenta, their detection in the newborn is diagnostic of congenital toxoplasmosis.

In view of the paucity of information on humoral antibodies involved in destroying parasites, it is essential that the cellular reaction to parasitic infections should be studied in detail. In some infections, especially some helminths and intracellular protozoa, certain analogies with homograft immunity can be drawn. **In vitro** cell systems, familiar to immunologists working on cellular immunity can and are being profitably applied to parasites. In one **in vitro** system, lymphocytes from immune hosts, after stimulation with specific antigen, will attach themselves to larval parasites. This reaction may be correlated with the protective state of the host.
It was pointed out that different immunological mechanisms may be involved in response to different types of parasites. For instance parasites with a very resistant surface, such as the nematodes, may only be affected by a cellular mechanism, whereas humoral antibodies would be able to deal more effectively with protozoa.

The importance of the reticulo-endothelial system in ncn-specific immunity was stressed especially in rodent malaria.

The effects of the immune response on parasites are manifested in a wide variety of ways. Most studies have addressed themselves to one particular facet only, e.g. structural damage, morphologic changes, physiologic and biochemical alterations, etc., reflecting the particular interests of the experimenter. In few instances has there been a systematic attempt to study and interrelate the variety of consequences to a parasite that may follow the occurrence of an immunological event.

Comparable studies of antibody effects on cells conducted in other fields of research and recent investigations by immunologists concerned with the action of complement should be reviewed carefully with regard to applicability to parasitic systems. Equally important, unicellular and multicellular parasites offer valuable tools with which to investigate antibody effects on cells, and it is apparent that their exploitation in a systematic manner has occurred in relatively few instances.

It was suggested that most of the mechanisms which lead to elimination of parasites or immunopathological lesions may be triggered by the action of antibody on the parasite but actually involve secondary processes which require further study. These include activation of various complement components and kinins, release of enzymes from lysosomes, changes in cell glycolysis and tissue pH, etc.

The question of interferon was raised. It has recently been shown that interferon is produced in response to Toxoplasma infection, although it does not appear to effect the parasite. How important is interferon on other intracellular infections?
The effects of the immune response on the host were discussed with special reference to granuloma formation around parasite eggs in schistosomiasis. The host-parasite balance characteristic of chronic, natural infection is the result of vigorous counteravailing mechanisms of both host and parasite, rather than of unresponsiveness on either part. Illness in the host is usually the product of gradual and progressive accretion of granulomatous lesions leading to structural distortion and impairment of flow in sensitive vascular territories.

In the general approach to immuno-parasitology, the potential of the whole viable cell rather than isolated cell components should be recognized. Specific immunological or biochemical effects are induced by the complex interactions of the whole organism.

The hallmark of the Special Session has been "complexity": complexity in antigenic structure and complexity in the response of the host. The elucidation of the problems of this particular aspect of the host-parasite relationship presents a tremendous challenge. There is still a need to concentrate on basic research. Cooperation among experts in a variety of disciplines is necessary to generate substantial information before practical steps can be taken.

Although much still needs to be done, substantial progress during past years gives rise to optimism and there is every reason to believe that, with continual effort and drive, practical steps towards controlling parasitic diseases of man by immunological methods will be possible in the future.

The PAHO program for research and training centers could be an important factor in providing support and trained personnel which are essential if research in the parasitic diseases is to be carried on in the countries where the diseases exist.
11. Drug Resistance in Human Malaria

11.1 Resistance of Human Malaria Parasites to 4-Aminoquinolines

It has long been known that naturally occurring strains of the four species of malaria parasites vary in their response to antimalarial drugs. The generally accepted definition of relative drug resistance is as follows: Ability of a parasite strain to survive and/or to multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within the limits of tolerance of the subject.

Resistance and sensitivity to chloroquine in falciparum malaria are not absolute qualities. Between full sensitivity and complete resistance there is a wide spectrum of response. The recent (1967) WHO Scientific Group on Chemotherapy of Malaria recommended a 3-step grading ($R_1$, $R_2$, $R_3$) of tolerance or resistance of malaria parasites ($P. falciparum$) to 4-aminoquinolines. The standard of sensitivity which has been generally accepted for $P. falciparum$ malaria is permanent cure after rapid response to the treatment with 1500 mg chloroquine base (25 mg base/kg) given in three days. The existence of 4-aminoquinoline-resistant strains of $P. falciparum$ has been confirmed only in some areas of South America and Asia.

It is urgent that the response of malaria infections to chloroquine should now be widely investigated particularly in areas where falciparum malaria is endemic, to provide baselines for future consideration of resistance.

There is no single explanation of the conditions in which resistance to 4-aminoquinolines emerges and at the present time these drugs will continue to be used in malaria eradication programs, wherever appropriate, with the addition of sporontocidal and anti-relapse compounds (pyrimethamine, 8-aminoquinolines). However, there is great need for special measures in malaria eradication areas where resistance to antimalarial drugs has been confirmed. The main lines of action should be directed toward elimination of the focus of the resistant strain or prevention of its possible spread by an effective attack on the vector.
11.2 Studies on the Response to Drugs of Blood-Induced Falciparum Malaria: South American Parasite Strains

Highlights were presented in a formal report covering two years of work in a mental hospital in Brazil on 131 subjects testing 18 suspected resistant strains of malaria from Brazil, Venezuela, and Colombia. There were 128 treatments of first attacks and 103 treatments of recurrences.

11.2.1 Cases were treated with various dosages of chloroquine from 1500 mg to 5400 mg and some failures were noted with all doses. Responsiveness often varied with the same strain. The failures were mainly of the $R_1$ type (68% of all cases), showing a temporary relief of fever and clearance of parasites, followed by a recurrence of parasitemia with or without fever in from 2 to 40 days; 11% were $R_2$ and 5.6% $R_3$, showing so little response to even large doses of chloroquine that quinine was added for the protection of the patient.

11.2.2 Trials were also made with pyrimethamine, mepacrine, proguanil, sulfonamides, and quinine, seeking the most effective alternate methods of treatment. Resistance was seen to all of these drugs in one or more strains. One attack was not cured by 26.5 gm of quinine in 17 days, which suggests resistance, but 11 out of 13 cases receiving 14 or more grams in 7 or more days were cured.

11.2.3 Resistance to pyrimethamine was present in most strains, but the combination of pyrimethamine and sulfonamides was effective in curing all cases, even those with strains resistant to one or the other of these drugs, if adequate doses were given.

PAHO is interested in the immediate application of new knowledge to field problems and directed the study of the combination of pyrimethamine and sulfonamides in chloroquine-resistant cases. The results were so good that field trials were initiated in northeastern Brazil in 1965 using a two-day schedule with long-acting sulfonamines with excellent results. These field trials are being continued in other parts of Brazil.

11.3 Research in the U.S.A. on Drug Refractory Malaria

The current malaria research program sponsored by the United States Army was summarized and the background against which the program developed was noted.
The several components of the program (basic biology, screening, chemistry, pharmacology, and clinical testing) were indicated and examples of the interplay between these areas were presented. Particular emphasis was placed on the role of the four U.S. centers for testing in volunteers, both for delineation of the problem of drug-refractory \textit{Plasmodium falciparum} malaria and for approaches to solutions. It was concluded that drug-refractory malaria will constitute, for some time to come, a serious problem when non-immunes enter an area with high transmission rates, and that a research program, utilizing all approaches to the problems, must be maintained.

1.4 The question of drug resistant malaria (specifically chloroquine-resistant falciparum) can only be characterized in the broadest of terms. There are several reasons for this situation: i) Resistance is not absolute but is a continuous spectrum of increasing tolerance; ii) there have been no field studies with an \textit{in vitro} or other laboratory models for identification of drug-resistant strains; iii) an end-point of no post treatment recrudescence has been taken as a criterion of drug-susceptibility in malaria in humans; iv) the incidence of post treatment recrudescence is related to the speed with which treatment is initiated after the start of infection and to this extent is independent of time-dose relationships of the drugs; v) parasitemia of asexual forms, as determined by microscopy, can be affected by changes in humoral immunity and hence can fluctuate widely within relatively short time periods.

The practice of regarding all therapeutic failure as "drug-resistance" has understandably led to a typology of resistance 1, 2, and 3. The \textit{R}_3 type is defined as instances in which administration of drug in presumed adequate time-dose relationships is followed by no discernible effects on asexual parasitemia. It is only this type that would be considered as drug-resistant in the drug treatment of microbial diseases.

Finally, it can be said that whereas the actual observations thus far may not be sufficient to create an alarming situation, the existence of various forms of resistance \textit{per se} is nevertheless a cause for disquiet. This is particularly the case because such large numbers of persons infected by the parasite are involved, and because the density of population malarious areas provides the opportunity for possible spread of resistant forms.

For these reasons about all that can be said at present is:
- Certain strains of falciparum isolated in South America and in Asia (but not thus far elsewhere) are resistant to 4-aminoquinolines.

- Thus far, such isolations have been relatively rare events, so that no inferences concerning the actual incidence of drug resistance are possible;

- Epidemiologic studies to provide a basis for subsequent comparison are an urgent need;

- Every effort should be made to adapt present laboratory models, e.g. the in vitro or mosquito models, to establish a model for detection of drug-resistant strains in epidemiologic studies so that changes in the situation can be detected;

- Pending the development of such an indicator for use in community-wide studies, "targets of opportunity" should be exploited such as the preservation and transport of blood specimens from isolated communities (such as aboriginal people) for testing by the more elaborate processes now available in the malaria research centers.

12. **A Further Look at Some Indian Populations of Brazil and Venezuela**

Results were presented of recent studies among the Yanomama Indians of Brazil and Venezuela, with particular reference to the prevalence of malaria.

All three species of malaria parasites were encountered in blood films obtained in villages of Venezuela and Brazil. Splenic indices varied from zero to 86% in different villages. In some villages no individual had parasitemia whereas in others 21% of the sample had *P. falciparum*. Thus on the basis of this limited information there is a very uneven distribution of malaria in this region. It will be recalled that this area had been identified in previous studies as one in which the malaria parasites often exhibit relative drug resistance. Because of the terrain and the habits of the Indian, malaria control in this region would be extremely difficult.
It is suggested that it would be important at this time to obtain base-line studies which would accurately characterize the status of malaria in this region, so that in the future firm bases may be obtained for conclusions concerning changes in the situation and the results of control programs.

13. **Study Group on Chagas' Disease**

When in the past the problem of Chagas' disease was reviewed by PAHO so as to develop a plan of action, it became obvious that serologic diagnostic techniques needed strengthening. The complement-fixation test is the serologic test of choice at this time and it is widely used. The method used for the test and the antigens employed, however, are not the same in the various laboratories making the results obtained of uncertain value and making it difficult to compare results of one laboratory with those of another.

It was decided, therefore, to sponsor a review of the complement-fixation test as used for diagnosis of Chagas' disease. A group of ten specialists from six countries were assembled and were asked to study the test and to recommend a course of action. The Group recommended that the test be a quantitative one and that the antigens now employed be evaluated for sensitivity and specificity. Moreover, it recommended a method for carrying out the above through participation of Group members. As a result, six laboratories in five countries are now making preparations to test at least ten antigens against a large series of sera in a blind study. It is hoped that the study will reveal an antigen that can be recommended as a standard.

A standard antigen and a standard test will permit the measurement of prevalence, the evaluation of progress of research and control programs, the diagnosis of infections with greater confidence, and will aid blood banks to detect blood that may contain *Trypanosoma cruzi*.
The Chagas' Disease Chemotherapy Research Group continues along lines set down when it was organized in 1963. Its second meeting last summer indicated that its objectives of exchanging information, encouraging research, and providing a means for the prompt movement of interesting compounds from the laboratory to the clinic are being pursued. The Committee recommends extension of these activities.

It should be pointed out as that addition to the tissue culture studies, new information along those lines is steadily accumulating from investigations both within and without the Group, relating to host cell toxicity and infectivity, as well as to intracellular and extracellular growth. Much exploratory work has been done leading to the establishment of methods useful in examining the action of drugs in a number of tissue culture systems.

It should be noted that extensive empirical examination of many diverse substances for activity against *T. cruzi* has brought to light a number of types of chemical compounds hitherto not known to be active in Chagas' disease. Even if they turn out to be only leads rather than products, they lend both support to the approach and encouragement to continued search.

The Committee heard a report of a Study Group on Toxoplasmosis and of some characteristics of the infection.

Toxoplasma, in the acute stage is capable of spreading throughout all viscera. After antibodies appear, the proliferation of the protozoa is restricted to the central nervous system to a great extent although cysts may persist in other tissues for long periods of time. Its most severe manifestations are found in congenital infections, occurring during the acute infection of the mother. There is no adequate proof that full-term or near-term infants are infected congenitally by mothers with chronic toxoplasma infection prior to conception.

The question of habitual abortion was discussed and it was agreed that treatment of women with chronic infection is not justified at this time because
the drugs are teratogenic. There is little evidence to support the claims that there is an association between chronic toxoplasmosis and abortion.

It can be stated that the infection is highly prevalent but the disease, fortunately, is rare. One can estimate the possibility that one out of every 5,000 births in some areas of the world has congenital toxoplasmosis and that one per cent of all persons legally blind have as the cause posterior uveitis. One third of these cases of uveitis may be due to toxoplasma, either congenital or acquired. Because toxoplasmosis seems to be one of the more prevalent human infections, further research, both at laboratory and epidemiological levels, is required to elucidate its natural history and its future control.

16. Influence of Infections and Deficient Diet on Child Growth Early in Life

A report was presented of studies in INCAP* in which a cohort of children was followed from birth to age two years with observation of their diet, clinical experiences, and colonization by viruses, bacteria and parasites.

The growth rate was adequate during the first few months in spite of an initially low birth weight. Weight deterioration was apparent after 3 to 6 months associated with a progressively deficient diet and an increasing frequency of infections and infectious diseases. The effect of infection was determined by comparing observed with expected weight increments and by correlating days of illness with weight gain. An association between infectious diseases, low calorie intake, and failure to gain weight was demonstrated.

The two factors mentioned (deficient diet and infection) are responsible in part for the stunting of children evident in the second year of life. The time at which nutritional deficiencies, infections, and their interaction result in irreversible damage and the magnitude of the result necessary to induce that damage has not been established for the human host. Studies in animals show that early influences cause permanent stunting even if animals are placed under adequate conditions at a later date. From this study it appears that children living under the conditions described are affected within the first few months of life.

*Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala.
Further investigations to understand some of these phenomena in the very young are recommended by the Committee. Studies are under consideration at INCAP to determine how the intestine is colonized by bacteria and other agents and how this relates to general health and growth and development in the host. Furthermore, it would appear that this is an area of research in which animal models may be of great usefulness in exploring questions pertaining to the relationship between the characteristics of the intestinal biota, the amount and quality of the food, and a variety of parameters of development.

More physiological studies are also needed in the perinatal ages. The phenomena of contamination and of other stimuli in early life are of paramount importance and deserve more study in the human host.

17. Endemic Goiter

Reports were presented on the study of the treatment and prophylaxis of goiter and cretinism with iodinated oil in remote areas of Ecuador and Peru. The treatment appears to be effective in reducing the size of goiter, but no information is yet available on whether the incidence of cretinism can be reduced. The program has developed well in Ecuador through the excellent cooperation of local personnel. Work in Peru has been hampered by shortages of both personnel and funds.

Mention was made of goiter surveys in Mexico and of studies in southern Chile which indicate the possibility of goitrogenous substances in the diet. Some evidence was presented of possible disorders of iodine metabolism as a contributory cause of goiter.

It was noted that the PAHO Reference Laboratory and Training Center for Iodine Determinations in Endemic Goiter Research had been set up and is now in operation.

The Committee felt that the work done so far represented an excellent example of collaborative research but that much remains to be done in this field. Additional support is needed for the Scientific Group on Research in Endemic Goiter, both for field and laboratory research and for the training of personnel.
18. Inter-American Investigation of Mortality

The report of this large collaborative research project designed to give an accurate and comprehensive account of mortality is now in its final phases.*

For a two year period, records with clinical, laboratory and pathological information were collected regarding 43,298 deaths of residents of 12 widely scattered cities in 10 countries. Two medical referees assigned the underlying cause of death using a weighting system. Age-specific and age-adjusted death rates from specific causes for these cities may now be compared with confidence.

The apparent wide variation in death rates from cancer of the stomach, cancer of the lung, diabetes mellitus, cardiovascular diseases - particularly arteriosclerotic heart disease - and cirrhosis of the liver were given as illustration. The Investigation has made significant contribution by identifying with certainty populations where risks are high and others where risks are low. These data indicate that environmental determinants probably operate at varying levels of intensity in different cities.

The Committee commented on the apparent increase in diabetes in certain cities and the complex interactions of environmental and genetic factors. Further research is needed to elucidate the etiological factors responsible for the marked contrasts in mortality in these cities in the categories of cardiovascular disease, cancer of certain sites and several other causes of death. The Committee commented favorably on the quality, volume and significance of the results of this research.

Such studies should be extended to all Latin American countries, including urban and rural areas, and on a continuing basis. The next step would be to establish continuing morbidity surveys to provide exact data on the extent and characteristics of the principal problems in community health. This, in turn, would lead to more accurate and comprehensive health planning to make the best use of limited resources. A network of Panamerican health centers for biostatistics and epidemiology would provide basic information for all other health activities in Latin America. Such centers would be invaluable to all the ministries of health

in service, research, education and training and to the other multinational centers proposed to the Committee.

19. **Selection of the Topic for the Special Session of the Seventh PAHO/ACMR**

The Committee discussed the selection of a topic for the special session next year and proposed that it be entitled "Some Biomedical Challenges Presented by the American Indian." It also considered highly desirable that a half-day session be presented on some aspect of nutrition in view of the dimension of the problem in Latin America.

The Committee found the topic dealing with factors affecting the fetus and neonate which may have long-term consequences in the individual to be of considerable importance and deserving of the Committee's attention at a future date.

20. **Other Matters**

20.1 The need for improvement in primary research journal distribution in Latin America is recognized. A study of the current situation is recommended through consultation with responsible persons in libraries, universities and documentation centers and with airline, customs and postal authorities. Implementation of survey findings would depend on their nature and on the availability of sufficient funds for an adequate experiment in jet age distribution of primary scientific journals. Biomedical journals in the Americas would provide a representative trial area in a problem that is worldwide and affects all disciplines.

20.2 The Committee recommended that for the Seventh Meeting of the PAHO/ACMR a report on a multinational center in nutrition be presented based on a survey of needs and potential in Latin America and on an inventory of available resources.

20.3 The date of the Seventh PAHO/ACMR Meeting was set for 27-31 May 1968 with a locale within the Western Hemisphere to be determined by the Director.
COOPERATIVE PROGRAMS

TO STRENGTHEN MULTINATIONAL ACTIVITIES FOR
ADVANCED TRAINING AND RESEARCH
IN THE HEALTH SCIENCES
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1 August 1967

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau Regional Office of the
WORLD HEALTH ORGANIZATION
Washington, D.C.
FOREWORD

This report is a working document prepared for the information and guidance of the Directing Council of the Pan American Health Organization at its meeting on 2-13 October 1967. A preliminary version was presented to and discussed by the PAHO Advisory Committee on Medical Research at its Sixth Meeting, 12-16 June 1967. The document summarizes the development of PAHO cooperative programs involving multinational efforts, incorporates the recommendations of the PAHO/ACMR towards such programs, and reviews the effects of the Declaration of the Heads of American States at Punta del Este in April, 1967.
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COOPERATIVE PROGRAMS
TO STRENGTHEN MULTINATIONAL ACTIVITIES FOR
ADVANCED TRAINING AND RESEARCH
IN THE HEALTH SCIENCES

1. Introduction

The Pan American Health Organization has for several years advocated the strengthening of existing centers of research and advanced teaching in biology, medicine and health as a means of strengthening these fields and of improving their capacity to contribute to economic and social development (see Annex A). The Organization has studied the principles that should govern such efforts. It has also applied these principles to the development of specific proposals by requesting outstanding groups of scientists from Latin America and the United States to draw up plans for action. In accordance with Resolution XVI adopted by the XVII Pan American Sanitary Conference in September, 1966, the Organization has brought both the general study and specific proposals up to date. The present document summarizes the results of the study and recounts significant steps towards the development of a general plan.

As a consequence of completed work, the Organization is prepared to make detailed recommendations for multinational consortia of outstanding laboratories in several fields of biology and medicine in Latin America.

The earlier work of PAHO was followed by a particularly significant international development relevant to all fields of science and technology. For the first time in the history of meetings of Heads
of States in the Western Hemisphere, the Declaration of the Presidents of the Americas at Punta del Este, 12-14 April 1967, contained a strong statement on the place of science and technology in development:

"Science and technology offer genuine instruments for Latin American progress and must be given unprecedented impetus at this time. This effort calls for inter-American cooperation, in view of the magnitude of the investments required and the level attained in such knowledge."*

This general declaration was followed by the specifications of a plan** that called both for intensified internal efforts - which are the responsibility of each member nation - and for multinational efforts in the form of a Regional Scientific and Technological Development Program.

The Regional Program to which the Presidents committed themselves contains the following seven elements:

The Program should be related to economic development and to the characteristics of each country.

The Program should encompass scientific and technological research, training of research personnel and transfer of technology to Latin America.

The Program should be conducted through national agencies responsible for scientific and technological policy, and through national or international agencies (public or private) which exist or which may be created.

Multinational technological and scientific training and research institutions at the post-graduate level should be established, and institutions of this nature already existing in Latin America should be strengthened.

A group of high ranking, well-qualified persons should be established to recommend to the Inter-American Cultural Council such matters as organization, administration, financing, location, etc.

* OEA Documents Oficiales, OEA/Ser. K/XIV/1.1 Doc.4 (English, 14 April 1967)
** Part V, B, of the Declaration.
An Inter-American Fund for training of scientific and technological personnel at high levels should be established.

The Program should be promoted by the Inter-American Cultural Council, in cooperation with CIAP (Inter-American Committee on the Alliance for Progress).

The Program may be financed by contributions of Member States, inter-American or international institutions, technologically advanced countries, universities, foundations and private individuals.

Acceptance of these principles by the Heads of States promised to provide a broad base of support for a broad scientific and technological effort which would include the biomedical sciences.

2. Meeting of the PAHO Advisory Committee on Medical Research, 12-16 June 1967

A major item on the agenda of the Advisory Committee on Medical Research at its meeting in Washington in June, 1967, was consideration of cooperative programs among institutions in different countries. This led to a full discussion which is summarized below. (The full report of this meeting has been made available to the Directing Council).

2.1 Statement of the Director

The Director outlined the goals that he thought could be achieved through more extensive collaboration among laboratories in different countries. He summarized the staff analyses of the potential gains through such collaboration, of mechanisms for collaboration, and of specific areas for collaboration. He pointed out the general desirability of supporting existing centers as contrasted with the establishment of new centers (see Annexes B, C, and D for background).
Finally, the Director suggested that four areas representative of basic science, applied science, clinical science and scientific communications be selected for initial development. He summarized consultant reports dealing with biochemical sciences, arbovirology, pathology and a Regional Library of Medicine (see Annex E).

2.1.1 Organization

The Director pointed out that the general policy to be followed in organizing collaboration will be to amalgamate into centers under the auspices of PAHO a number of institutions of recognized standing in a given field of science. The component institutions of the centers will usually be situated in different countries, although they may all be in a single country. The directors of the centers will constitute a "board of directors" and will be responsible for making proposals on such matters as joint curriculum construction, visits by outstanding investigators and teachers, collaborative research, exchange of students, and use of expensive equipment.

The PAHO Advisory Committee on Medical Research would be asked to review plans and assess their execution. The precise relationships between PAHO and its Advisory Committee on Medical Research, and OAS and its research structure would have to be worked out as planning proceeds.

2.1.2 Financing

The Director noted that financing would primarily be by the countries concerned, through their basic support of the collaborating institutions. In the life sciences most of the investment for effective multinational collaboration is already being made by the countries
themselves in the form of salaries of professors, support of students, provision of research and teaching space, and supply of basic equipment. The supplementary funds required from external sources to realize the potentialities of international collaboration would be relatively small. PAHO would make funds available to selected centers on the basis of approved plans.

2.1.3 Remaining Problems

In conclusion, the Director pointed out the following problems to be solved:

- Securing funds for the program, since the existing resources of PAHO are not adequate to finance a significant program. The Committee recommended that steps be taken to secure the necessary funds from whatever sources the Director might develop;

- Appropriate means for ensuring that the larger participating laboratories will actually receive students and scientists from other countries;

- Practical problems, such as the kinds of expenses which may be put in budgets; and

- Care must be exercised to ensure that the total program is not simply one to make strong centers still stronger at the expense of the development of other centers.

2.2 Advice of the Committee

The Committee gave advice to the Director which can be summarized as follows:

- Continue to encourage the development of cooperative programs to strengthen multinational activities in research and advanced training;

- Seek support for the programs from appropriate national and international sources;

- Give priority to strengthening existing centers but to consider seriously the possible establishment of new centers in selected areas;
- Proceed to develop the four programs presented to the Committee but ensure that they encompass all of the major points of strength in each field;

- Consider additional disciplines for cooperative programs, including population dynamics, health administration, social pediatrics, biophysics, nutrition, and the biology of reproduction;

- Give high priority to the application of research in biology and medicine to the improvement of health and social well-being, but simultaneously support an equally vigorous program of basic research;

- Take measures to strengthen the link between research and economic and social development through such measures as:

  More attention to research on the effective administration (organization and management) of health programs;

  Investigations of the process of planning, organizing and managing research itself; and

  A broad attack on the means by which all available knowledge - from the social and physical sciences and engineering as well as from biology and medicine - can be brought to bear most effectively on new means of solving both personal and environmental health problems (taking into account social, cultural, political and economic constraints) through changes in institutional forms as well as through applying specific technologies.

- Consider seriously the creation of a new institutional form - possibly a new and extensive multinational center - and appoint a subcommittee to elaborate the general idea into specific terms.

- Establish criteria such as the following for adding new programs:

  Priority should be given to areas of research which promise significant and rapid advances in levels of health;

  Support should be selective, and high priority should be given to centers capable of advanced training and high quality research; and

  Priority should be given to proposals which have the prospect of strengthening regional collaboration within Latin America.
3. Meeting of the OAS Group of Experts in Science and Technology, July 17-21, 1967

The Inter-American Cultural Council convened a special meeting on May 25, 1967, to set the terms of reference of the study called for by paragraph 4 of Part V (B) of the Punta del Este Declaration, and to select the members of the group of experts.

The terms of reference of the Group were broadened to cover the study of the entire program in science and technology, rather than simply the question of multinational institutes.

The Group of Experts convened on July 17, 1967, in Washington, and produced the general specifications of a program.

3.1 Scope

The Group of Experts observed that the program should encompass not only the physical sciences and engineering, but also the agricultural, medical, economic and social sciences. With respect to the medical sciences, the extent to which the new program would encompass the basic sciences, applied health sciences, clinical sciences and education in the health professions, and the role of existing health organizations - including the responsibility of PAHO in terms of planning, financing and administering - were not precisely worked out.

3.2 Multinational Efforts

The Group specified the conditions which make multinational efforts desirable (such as the need for expensive facilities that cannot be financed by one country or integration of the efforts of several centers to form parts of a total program in a single or related field of science).
3.3 Kinds of Multinational Institutions

The Group recognized several types of multinational institutions:

3.3.1 A local institution that offers its services to a region or group of countries.

3.3.2 A multinational institution in whose maintenance several countries participate and that is under multinational direction.

3.3.3 A consortium, in which a group of national or regional institutions agree to combine their resources in certain areas of knowledge and which is under the direction of the representatives of the participating institutions. Its headquarters may be either fixed or by rotation.

3.3.4 New multinational institutions organized for specific fields in accordance with regional or subregional needs, but preference should be given to proposals such as those above which involve the utilization of one or several existing institutions.

3.3.5 All multinational arrangements and institutions of the kinds outlined above should have priority over the establishment of new comprehensive multinational centers.

3.4 Supporting Activities

The Group recommended such measures as fellowships, exchange of professors, improvement of curricula, training of teachers, etc. be carefully studied.

3.5 Further Steps

The Group of Experts established two sub-groups whose function is to prepare specific proposals for presentation to the Inter-American
Council for Education, Science and Culture at its next meeting, probably in January 1968.

3.5.1 Working Group I for Mechanisms and Financing.

3.5.2 Working Group II for Program and Budget.

3.6 Timing of Further Steps

3.6.1 Working Group I on Mechanisms and Financing to prepare a final version of its proposals at a meeting on November 6-12, 1967, in Washington.

3.6.2 Working Group II on Program and Budget to contact all organizations concerned (including international organizations) over the period August 7 - September 15, and to recommend actions and programs considered most promising and which are to be prepared in greater detail at a meeting September 18-22 in Washington.

3.6.3 The Group of Experts will meet in Washington, December 4-9, 1967, to approve a program and budget.

3.6.4 The program approved by the Group of Experts to be placed before the Inter-American Cultural Council for approval, probably in January, 1968.

4. Position of the Director of PAHO at the July 17, 1967, Meeting of the OAS Group of Experts in Science and Technology

Based upon the advice provided by the PAHO Advisory Committee on Medical Research, the Director of PAHO indicated to the Secretary General of the Organization of American States, and to the Group of Experts at the July, 1967, meeting the strong interest of PAHO in participating in the
medical and biological aspects of the total Regional Scientific and Technological Development Program. The rationale of that position was basically that a well-designed program for the development of scientific and technological research in Latin America would include a strong biological-medical component for the following reasons:

4.1 Biomedical science and technology, including preventive medicine and public health, play a central role in increasing the productive capacity of the population and in achieving a better balance between the expansion of population and the expansion of food supplies.

4.2 The biomedical sciences deal essentially with the phenomena of life. It is generally agreed that the next decades will witness developments in these sciences whose significance for mankind may well transcend that of the exploration of the atomic nucleus during the past two decades. Any region of the world that cannot understand and participate in these developments will not be able to benefit fully from them.

4.3 There exist centers of excellence in the biomedical sciences in Latin America which have the stability, demonstrated scientific productivity on an international scale, proven ability to train students at the doctoral and post doctoral level, and ability to contribute to the solution of important disease problems. However, these centers have varied handicaps, including inadequate equipment, inadequate scientific contacts, inadequate cooperative relationship with other Latin American laboratories, inadequate technical support and inadequate access to current literature. The specific needs of each center vary. With carefully planned programs of development, the contributions of these centers could be markedly increased.
4.4 Some important health research needs are not met by existing centers, and of primary importance among these is an ecological approach to the health of man which would encompass the effects of such factors as education, housing, social and geographical mobility, family structure, traditions and transportation on health.

4.5 It is important to recognize that biomedical research is not well financed in Latin America. The Pan American Health Organization has limited funds for research. The Latin American countries have concentrated their expenditures on promotion of public health and support of medical education, with very little support for medical research.

4.6 PAHO is prepared to make its experience and resources available to assist the new program, and to propose new activities which might be supported in whole or in part by the new program with the understanding that PAHO would (i) fully coordinate its activities with the new program, and (ii) be bound by the policies and regulations of the new program.
PAHO Planning for Multinational Collaboration in the Health Sciences
(1962 - 1966)

The Pan American Health Organization has carried on both general
and specific studies on multinational collaboration in the health sci-
ences. Earlier specific studies led to these general findings and
recommendations:

Migration of Health Personnel, Scientists and Engineers from Latin America
118 pages.

"High priority should be given to the reinforcement of existing
strength ... medicine. In general, investments in selected existing
centers of high quality - organizations already in being that have good
leadership, facilities, equipment, and students - will yield a greater
return in terms of the training and quality of research than invest-
ments in new centers.

"In general, and as a long-range objective, emphasis should be
on strengthening the areas of excellence - departments, faculties,
research groups institutes, or whatever they may be - that have a
strong educational component. This, as a rule, means areas associated
with universities. Some universities are so archaic, badly organized,
and poorly staffed, however, that they fall far short of the ideal
institution combining teaching and research. In such cases, it is
necessary to consider the strengthening of nonuniversity points of
excellence." (p. 48)
"The principle of the intellectual common market has been recognized and enunciated by informed and influential groups. It was, for example, the subject of a specific recommendation by the OAS Science Advisory Committee at its first meeting in 1958. The Committee proposed the 'expansion of the support and activities of a relatively modest number of existing research institutes, with a view to using them as Regional Centers of research on an increasingly international basis.'* In 1959 the U.S. National Commission for UNESCO proposed that at least six regional research centers should be established including centers for biophysics, biochemistry, and microbiology.** First steps have been taken in the direction recommended by these reports. For example, the Latin American Society for the Physiological Sciences has served as the agent to coordinate ten laboratories, and the Pan American Federation of Associations of Medical Schools has strongly urged this approach. In fact, all the strong centers of research in Latin America attract and welcome students and mature scientists." (p. 45).


Seven specific surveys leading to the general recommendations were:

9.3 Program for Advanced Education and Research in Pathology. (PAHO internal document) 1966.


Reasons for Cooperative Programs to Strengthen Multinational Activities in the Health Sciences.

Multinational and international efforts in science and technology should always be planned on the assumption that the great bulk of research and training will be done in national laboratories and with national financing.

Most of the answers to the problems facing medical science and education will be found in the countries themselves. Most of the resources will be national. Most of the decisions affecting the contributions which medicine can make to development will be taken by national governments.

The underlying significance of national efforts does not mean that multinational efforts are not important. It simply provides guides to the primary needs and to the kinds of efforts which are likely to be most significant.

The major reasons why international collaboration is needed are as follows:

1. In most countries resources are inadequate and must therefore be supplemented. The enhancement of material resources often requires the investment of funds from outside sources; the human resources in a given country must often be supplemented by the help of outstanding leaders from other countries.

   Most institutions for advanced teaching and research in individual countries are specialized and relatively small. International
collaboration is needed to help them become more effective. This collaboration can be helpful in several ways:

- Less than full understanding in the higher levels of government of the indispensable role of science and technology in economic and social development.

- Not enough adequately remunerated full-time university positions combining research and teaching.

- An atmosphere inimical to investigation in many universities.

- Inadequate attention by scientists to important social and national problems.

- Incomplete communication between Latin American educators and scientists, between scientists and engineers, and between scientists and national policy makers.

- A general tendency to produce too many poorly trained persons in the professions (law, engineering, and medicine, for example) and too few highly trained persons.

- Advanced teaching and research are sometimes carried on in an atmosphere characterized by instability of leadership and of support.

All of the problems of developing science and technology in individual countries cannot be solved by wider international efforts, but the exposure of national practices and customs to scrutiny and comment by scientists from other countries should exercise useful pressures.

- International collaboration can enhance the prestige of national institutions by recognizing them and by calling the quality of their teachers and scientists to the attention of national authorities.

- International collaboration can help give institutional stability to a field of teaching and research and thus offset the instability of individual departments and laboratories.

- The nature of many research problems is such that they can be carried out effectively only through collaboration among a number of
laboratories, which are often located in different countries.

- The efficiency of the use of expensive facilities for research and training can often be enhanced by collaboration.
Aims of Multinational Collaboration in the Health Sciences

Over the last five years the PAHO Advisory Committee on Medical Research and special study groups have examined the characteristics and needs of the health sciences. In the light of these studies PAHO has developed a plan covering the aims, functions, organization and financing of multinational efforts in health research and education. It proposes that, in each discipline related to health, the outstanding centers for advanced teaching and research in Latin America become formally associated so as to attain the following aims:

1. Increase the number of highly trained teachers and investigators by linking research and training at the graduate level. Enable teachers and scientists to pursue their work at an advanced level in Latin America and thus reduce incentives to migration.

2. Ensure that effective use is made of the existing material and human resources by assessing the capability of different laboratories, departments, and institutes, planning the specialization of function and equipment, and rotating advanced students and senior investigators among laboratories.

3. Secure international recognition of the quality of selected centers and thus enlist national support for research and training; stimulate Latin American scientists to plan for the development of science and technology in Latin America.

4. Establish wider collaborative research using both the specialized talents of individuals and the resources of institutions.
5. Provide, ultimately, for every center that aspires to excellence, organized assistance including a system for the exchange of teachers and investigators so that outstanding talent is made available to an entire discipline in Latin America.
Strengthening Existing Institutions and Creating New Institutions

A critical policy question in the field of medicine and biology is the relative emphasis, priority and timing of efforts to use and strengthen existing institutions as contrasted with establishing new institutions. Whether action should be taken to strengthen existing institutions or to establish new ones is a question to be decided on a pragmatic basis. The essential question is the return to be expected from a given investment.

For the most part, the return on investment in the health sciences is greater through strengthening existing centers. The major considerations are as follows:

1. In many biomedical fields, the level of excellence achieved in one or more centers is such that a new institution is not needed to establish standards of excellence.

2. Indigenous growth of national centers in the biomedical sciences can be promoted most economically and effectively by putting these centers more solidly in an international context rather than by establishing a new supra-national center.

3. Despite the relative strength of the biomedical sciences in Latin America, the establishment of a large new center would either draw a large proportion of the best investigators from their own laboratories, or result in second-rate staffing of a new laboratory.
4. While there may be in the United States as many as 100 excellently trained Latin American investigator-teachers in biomedical fields, it is not certain that they would be any more interested in going to a multi-national center than they would be in returning to laboratories in their native lands.

5. If salaries and working conditions at a new center are set at levels designed to draw people from either national laboratories or from the United States, the existence of a new center may retard the growth of national laboratories in the biomedical sciences. The "brain drain" is best moderated by strengthening national centers.

6. The investment required to establish a new biomedical research and training center could be spent more effectively to up-grade existing departments, institutes or centers. Money spent on additional space in Latin America is wasted because adequate space already exists in national institutions.

7. Effective research and advanced teaching in biology and medicine does not require such a large investment in large equipment that no single country can afford the expenditure.

8. The viability of an institution and its productivity depend heavily upon the enthusiasm of people who guide it, who staff it, who set its goals and who secure resources for it. Such enthusiasm exists for strengthening existing centers in the health sciences; it is almost non-existent for the establishment of new centers.

9. The important goal of bringing more good Latin American biomedical laboratories more closely and actively into the main stream of scientific development is more likely to be achieved by making them
active, responsible participants than by removing the best people from existing laboratories to a new one.

10. The important goal of securing more active and widespread participation of scientists from the United States in biomedical research with Latin American collaborators will be achieved more effectively by using stronger national institutions than by establishing a new multinational institution.

11. The term "Latin American" is in a sense an abstraction. A new "Latin American" center for health research (or for tropical medicine, or for any other specialized field) is not likely to be thought of as closer to any Latin American country than are the important U.S. universities - except for the fact that the common language might be for the most part Spanish. But a new institute which did not teach fluent English would not be attractive to many younger investigators.

12. The difficult practical problem of deciding where to locate a new biomedical center is avoided by relying on existing ones, but this is not an important consideration.

13. Reliance on a number of centers provides flexibility to deal with changing effectiveness of leadership, and for shifts in relative scientific urgency. A single organization under international auspices is likely to be less flexible.

14. Reliance on a number of centers provides a flexible approach to teaching.

These considerations do not rule out the possibility that new multinational institutes may be called for. In fact, such a new entity is proposed by PAHO - a new South American Regional Library of Medicine. In this field, the conditions generally found in the biological and medical
sciences do not apply:

- There are no existing strong medical library centers;

- A single strong entity is needed to link with the world's biological and medical system;

- The technology involved must be developed at a single point;

- The effort is so expensive that multinational efforts are indicated.

Further study may develop other specific areas where a new entity is called, but for the immediate future the greatest gains are to be made through linking together and strengthening existing centers.
Four Cooperative Programs to Strengthen the Biomedical Sciences Through Multinational Activities in Research and Advanced Training

A. Biochemical Sciences

The Ad Hoc Committee of Latin American Scientists for the Biochemical Sciences, an independently elected Committee more or less regionally representative of biochemical and related sciences in Latin America, had been asked by PAHO to accept the responsibility for making a study and recommendations for the development of multinational institutes in the biochemical sciences in Latin America. A preliminary proposal presented to the Committee for a multinational institute to be developed in Mexico was an example of what might be developed.

With the information on the present status of biochemical research and training obtained from the members of the Ad Hoc Committee and from other biochemists, an effort was made to identify, among the scientists engaged in biochemical work, those who might be considered productive and well established and those who are promising. It was readily apparent that high quality research nuclei have developed in Argentina, Brazil, Chile and Mexico. The reasons for the limitations in development and the unmet needs to achieve such developments were discussed.

The establishment of multinational centers - as defined by PAHO - for the biochemical sciences at least one in the north and at least one in the southern part of the Hemisphere was proposed. This proposal was developed at a meeting of the Ad Hoc Committee in Mexico City in August, 1967.
B. Virology with Emphasis on Arbovirology

Virology was selected by PAHO as one field of biomedical science and microbiology that deserved early consideration because of the importance of these diseases in Latin America in particular, arboviral diseases, e.g., yellow fever, many forms of encephalitis and dengue, are prime obstacles to development in many parts of Latin America. There is a current potential for rapid advancement of knowledge in this field.

The Ad Hoc PAHO Advisory Group on Multinational Collaboration for Research and Training in Arbovirology, convened at the Universidad del Valle in Cali, Colombia, 16-18 April 1967, recommended as first steps in a multinational program in arbovirology i) the formation of a Latin American Committee on Arboviruses (LACAV) and ii) multinational Latin American centers for training in three scientific fields basic to investigations of arboviruses and other viral zoonoses, namely, medical virology, medical entomology, and vertebrate ecology.

Possible functions of the LACAV would include training, research collaboration, enhancement of communication, a survey of arbovirologists and their facilities in Latin America, advice and assistance to governmental and other organizations, close affiliation with the PAHO/WHO Collaborating Center in Arboviruses in São Paulo, and coordination with the American Committee on Arboviruses in the USA.

C. Pathology

Research has priority in the development of pathology as a specialty in Latin America. A proposal was presented to the Committee as the collaborative effort of four departments of pathology in Colombia, Mexico, Peru and Venezuela.
The Committee considers that in the study of pathology, disturbances in function should be viewed together with alterations in structure. Consequently, pathological physiology and pathological biochemistry should be represented with pathological anatomy in the research and training activities of the multinational centers in pathology.

Multinational centers offer an opportunity to achieve a more productive balance between service and research. Some pathology departments in Latin America have had no alternative but to place emphasis on patient care rather than on disease processes. Such centers could broaden the opportunity of many departments to develop research while enhancing the quality of their service.

D. **Regional Library of Medicine**

In view of the serious deficiencies in biomedical communications in Latin America and of the interest of Latin American physicians and scientists in acquiring the literature of the biomedical sciences, recommendations were made during previous meetings of this Committee to develop a regional library of medicine strategically located in South America to improve documentation and library services throughout this area of the world.

With commitments from the National Library of Medicine to provide technical support as well as access to its book credits in the U.S. Book Exchange, the Pan American Health Organization agreed to serve as the agency to administer the Regional Library of Medicine.

A search for funds to implement the program has resulted in a series of agreements between the Government of Brazil, the Pan American Health Organization, the Commonwealth Fund and the National Library of Medicine which permitted the establishment of the Center at the Escola Paulista de Medicina of the Federal University of São Paulo.
It is believed that the Regional Library of Medicine should be considered an essential communications element for the multinational centers for advanced training and research in the health sciences currently being developed by PAHO and OAS. It is reasonable to expect that upon successful demonstration of the capabilities of the Regional Library of Medicine that long-range sustained funding should come either from the Pan American Health Organization itself or from some other stable funding source.

It was suggested that, in every Latin American country, local offices be established with professional personnel available to offer consultation to facilitate transmittal of library materials in both directions.

The method whereby experts visit all countries in Latin America and report back to PAHO, as has been done in developing this proposal, is commended by the Committee and is suggested as a guide for similar projects.