XXXI ACHR

Meeting of the Advisory Committee on Health Research of the Pan American Health Organization
15-17 July 1996
Washington, D.C.

TECHNICAL COOPERATION PLAN FOR THE DEVELOPMENT OF BIOTECHNOLOGY IN HEALTH

ACHR Biotechnology Subcommittee

Research Coordination
Division of Health and Human Development
Pan American Health Organization
Pan American Sanitary Bureau • Regional Office of the World Health Organization
Washington, D.C
1996
PLAN OF ACTION

TECHNICAL COOPERATION PLAN FOR THE DEVELOPMENT OF BIOTECHNOLOGY IN HEALTH

Dr. Elsa L. Segura
Dr. Bianca Zingales
Dr. Jorge E. Allende
Dr. Alberto J. Marcipar

MEETING OF THE BIOTECHNOLOGY SUBCOMMITTEE
ADVISORY COMMITTEE ON HEALTH RESEARCH
PAN AMERICAN HEALTH ORGANIZATION
Buenos Aires, Argentina
16-19 April 1996
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Introduction</td>
<td>1</td>
</tr>
<tr>
<td>II. Objectives for the Period 1996-1999</td>
<td>2</td>
</tr>
<tr>
<td>III. Subject Areas</td>
<td>2</td>
</tr>
<tr>
<td>IV. Development Needs</td>
<td>5</td>
</tr>
<tr>
<td>V. Specific Objectives</td>
<td>7</td>
</tr>
<tr>
<td>VI. General Recommendations</td>
<td>9</td>
</tr>
<tr>
<td>VII. Outlook</td>
<td>10</td>
</tr>
<tr>
<td>VIII. Budget</td>
<td>11</td>
</tr>
</tbody>
</table>
I. INTRODUCTION

Since 1987 the Regional Program for the Development of Biotechnology Applied to Health in Latin America, promoted by the Pan American Health Organization (PAHO), has attempted to deal with health problems in the Region through research and the generation of biotechnology products. In this context, emphasis has been placed on supporting research leading to the production of native synthetic and recombinant macromolecules and to the training of human resources in the Region.

As the Program developed, an attempt was made to balance distribution of this support while taking into account the differences in biotechnology development for the diagnosis and treatment of infectious diseases and the training of human resources capable of employing these techniques in addressing health problems in the countries of the Region.

Once the groups working in institutions in the Region were identified, support was given to 14 projects that addressed the following priorities:


b) Development and evaluation of an HIV diagnostic kit.

c) A PAHO-NIH project for the development of vaccines for priority pathologies in the Region.

Support was provided for 12 additional projects that were chosen on the basis of their scientific merit and design or related either to initiatives to halt transmission or to the SIREVA project, within the framework of the PAHO Research Grants Program.

Support was provided for 10 training courses in molecular biology techniques and other areas necessary for the development of biotechnology products. Five of these courses have received support under the UNESCO/UNDP/UNIDO Regional Program on
Biotechnology on topics of common interest, within the framework of the recommendation made by the Subcommittee at its III Meeting in November 1992.

In preparing this second Plan of Action for biotechnology activities being implemented by PAHO, due account was taken of the fact that the specter of infectious disease is changing in the Region. This is attributable on the one hand to the impact of the control activities being carried out under the immunization plans and the initiatives for the elimination of transmission of certain diseases, such as Chagas (PAHO Directing Council 1991) and, on the other, to the social and environmental changes occurring globally as a result of human migrations and the spread of poverty. These, in turn, have led to the reemergence of certain previously controlled infections in some regions or even worldwide and the emergence of new diseases.

II. OBJECTIVES FOR THE PERIOD 1996-1999

To contribute to the training of health researchers and technicians and the creation of the conditions necessary for developing and utilizing biotechnology products and molecular biology methods to improve the health conditions of the Region's population.

III. SUBJECT AREAS

As noted in the Introduction to the present document, the Plan of Action proposed to the ACHR for the period 1996-1999 assigns priority to the diseases that affect large populations, those responsible for neonatal and perinatal mortality, those included in the elimination initiative, and emerging and reemerging diseases in the Region (Table 1).

This stage seeks to disseminate direct or amplified techniques for the detection of the nucleic acids of microorganisms and to disseminate or develop ELISA systems for the detection of antigens or antibodies. At the present time these techniques are poorly distributed, since they are confined to more developed urban centers, and particularly to the centers of excellence, where they are employed for biological research purposes. This situation creates great disparities between the institutions that either possess these technologies or can gain access to them indirectly and those that provide care to patients in disadvantaged areas where the technologies are inaccessible.
Most of the vaccines used for human disease prevention have been based on the use of attenuated pathogens. Biotechnologies currently provide the means to afford immediate protection to populations through the use of safe, more specific antigens and to extend immunoprotection against new diseases. This second stage of the Program is intended to support the generation of immunological knowledge and the use of molecular biology to develop vaccines for priority diseases (Table 1), especially those associated with perinatal pathologies, notably cholera, malaria, and leishmaniasis.

The availability of human resources continues to be one of the constraints in applying biotechnology to health problems. It is consequently proposed that training continue to be provided through intensive courses on topics related to selected pathologies.
Table 1. PRIORITY PATHOLOGIES CONSIDERED FOR INVESTIGATING OR DEVELOPING BIOTECHNOLOGICAL PRODUCTS AND FOR TRAINING HUMAN RESOURCES IN DIAGNOSIS, TREATMENT, AND THE USE OF VACCINES, 1996-1999.

<table>
<thead>
<tr>
<th>1. Diseases included in the Initiative for the Elimination of Transmission by the Year 2000:</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Chagas' disease</td>
</tr>
<tr>
<td>* Leprosy</td>
</tr>
<tr>
<td>* Onchocercosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Reemerging diseases:</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Tuberculosis</td>
</tr>
<tr>
<td>* Cholera</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Emerging diseases:</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Hantavirus lung syndrome</td>
</tr>
<tr>
<td>* HIV/AIDS infection produced by HIV and AIDS</td>
</tr>
<tr>
<td>* Bacterial diseases resistant to treatment with antibiotics</td>
</tr>
<tr>
<td>* Hemorrhagic fevers, when concentrated in certain geographical areas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Diseases that affect large populations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Acute respiratory diseases and infant diarrheal diseases</td>
</tr>
<tr>
<td>* Chagas' disease</td>
</tr>
<tr>
<td>* Malaria</td>
</tr>
<tr>
<td>* HIV/AIDS</td>
</tr>
<tr>
<td>* Leishmaniasis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Leading causes of infant mortality:</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Infant diarrheal diseases</td>
</tr>
<tr>
<td>* Acute respiratory diseases</td>
</tr>
</tbody>
</table>
IV. SOME DEVELOPMENT NEEDS

Some biotechnology development needs are described below.

Chagas’ Disease:

Polymerase chain reaction (PCR) to determine *Trypanosoma cruzi* infection is yielding interesting results in laboratories in the Region through the detection of specific target sequences, both in the nuclear genome and in the DNA of the kinetoplast. Studies on infected populations are relatively limited but nevertheless demonstrate a sensitivity that in some instances reaches values equivalent to those obtained through serology and are in all cases higher than those obtained through xenodiagnosis.

Consequently, the diagnostic value of PCR reaction must be validated in different populations and regions of the American subcontinent. Validation of this reaction could, furthermore, resolve current problems that cannot be addressed by conventional serology.

These cases include:

* Diagnosis of Chagas’ disease in neonatal infections
* Monitoring and evaluation of the efficiency of chemotherapy treatment
* Immunodeficiency situations

Tuberculosis:

Recent publications have shown that several PCR techniques--mainly those that use the IS6110 insert as a DNA marker for the *M. tuberculosis* complex--have a more than 90% sensitivity and specificity for detecting tuberculosis of the lungs in adults. Nevertheless, the sensitivity of the technique must be tested in more comprehensive studies, and its application must be standardized.
Malaria:

Among tropical diseases, malaria is responsible for the greatest infant morbidity and mortality. One million new cases a year are reported in the Region of the Americas alone.

Progress of clinical and epidemiological importance has been made in the development of genetic diagnostic techniques. These techniques have made it possible to differentiate between infection from *Plasmodium vivax* and *Plasmodium falciparum*.

There is also a need for molecular markers for the monitoring of vaccination or chemotherapy protocols. This demonstrates the need for developing methods for detecting and quantifying the presence of parasites and also for adapting these techniques to working conditions in the field.

In view of the potential of the PCR technique for detecting nucleic acid sequences specific to the infectious agent, it would be of great importance to have molecular markers that would make it possible to type these organisms and determine their possible association with biological or pathogenic characteristics.

As a work strategy for achieving these objectives, we suggest close cooperation between the health services in endemic areas and the research laboratories.

All efforts to consolidate and improve PCR technology should be continued without interrupting studies aimed at developing ELISA systems for the detection of specific antigens or antibodies or any other alternative proposals geared toward solving problems of this nature.
V. SPECIFIC OBJECTIVES

1. Development, evaluation, and transfer of molecular techniques for the diagnosis of priority diseases:

   1.1. Validation of the diagnostic value of existing PCR or ELISA techniques.
   1.2. Study of the usefulness of PCR for the control and monitoring of therapy protocols.
   1.3. Development and validation of ELISA techniques with prognostic value and value for the monitoring of treatment and vaccination.
   1.4. Adaptation of the scale and methods for visualization of PCR and ELISA reactions to local conditions.
   1.5. Characterization of molecular markers for the typing of pathogenic agents.

Specific actions:

* Support for projects to validate existing PCR techniques.
* Support for basic research projects for the identification of molecular markers and quantification of products of PCR.
* Support for projects to simplify PCR technology for application in field and scaling situations.

In order to realize the actions outlined above, support is proposed for 12 projects, at an average cost of US$ 25,000/project/biennium.

2. Development and validation of vaccines for priority diseases:

   2.1. Promotion of research that utilizes recombinant DNA techniques and synthetic peptides in vaccine production.
   2.2. Promotion of studies to improve antigen presentation systems.
   2.3. Promotion of projects for field evaluation of vaccines developed.
Specific actions:

* Support for projects to develop vaccines through recombinant technology or synthetic peptides.
* Support for projects to develop immunogen presentation systems.
* Support for field studies to evaluate recently developed vaccines.

In order to realize the actions outlined above, support is proposed for four projects, at an average cost of US$ 50,000/project/biennium.

3. Human resources training in biotechnologies applied to health and to business enterprises.

3.1. Promotion of the transfer of molecular diagnostic technologies to health services and business enterprises through ongoing training of professional users at the local level.

3.2. Increase in the number of specialists with knowledge of molecular biology techniques in countries that are relatively less developed in this area.

Specific actions:

* Courses for health professionals.
  - The courses should concentrate on specific techniques and training.
  - Priority should be given to theoretical and practical training in new molecular diagnostic technologies.
  - The courses should be geared toward health professionals in the public or private sector, laboratories, clinical services, or business enterprises.
  - The courses should be given outside centers of excellence, preferably in local health institutions.
  - It is recommended that the courses include the participation of professors in the specialty from institutions in the Region.
  - The possibility should be considered of leaving the equipment and reagents for immediate use as a contribution to the services organizing the courses.

* Courses for investigators in relatively less developed countries.
  - The course content should include training in molecular biology.
- Priority will be given to theoretical and practical training in recombinant DNA technologies.
- The course should be directed toward young investigators from universities and institutes in the participating countries.

Support for 20 courses per biennium is proposed, at an average cost of US$ 15,000/course.

VI. GENERAL RECOMMENDATIONS

1) The Need for Continuing the PAHO Biotechnology Program

In recent years significant progress has been made through the PAHO Biotechnology Program. Nevertheless, the use of biotechnologies is not yet sufficiently widespread in the research on and diagnosis of the principal prevalent diseases in the Region, and it is therefore strongly recommended that the Program be continued with a plan of activities, as outlined in the present report.

In order to implement the Program it will be necessary to guarantee a budget for a minimum of four years. Budget disbursements and execution of the work plan should be monitored by the Subcommittee on Biotechnology in the interests of better coordination, evaluation, and complementation of the activities undertaken. Evaluation visits by experts to the principal participating centers are also highly recommended.

2) Promotion of National Biotechnology Plans in Health

PAHO should continue to promote the strengthening and establishment of national policies and plans in the health area in the countries of the Region. This could be achieved through regional or subregional meetings to discuss the various national priorities and programs that the Member States are carrying out in this field.

In addition, PAHO should urge the Member States to share efforts in this area by making their research infrastructure and human resources training systems available to investigators from neighboring countries. PAHO should also improve coordination and complementation of its activities with those of other international or subregional organizations that also work in this field, as it has done with UNDP, UNESCO, UNIDO, IICA, ICGEB, CABBIO, CYTED, etc.
3) Biosafety

PAHO should step up current efforts to reach a consensus on policies and supervision methods, disseminating information on international experiences, particularly in the field.

4) Generation of Products through Research

PAHO and the governments of the Member States should adopt policies and activities to stimulate the Region’s production system to utilize the results of this and other programs for the generation of products and services to benefit the health of the population of our Region.

VII. OUTLOOK

The rapid progress of biomedical science and technologies is opening new horizons for combating the numerous serious health problems faced by the Region. It is also necessary to bear in mind that the modern definition of health extends to nutrition, access to drinking water and waste disposal systems, and conservation of the environment. All these problems can also be dealt with through the diverse applications of biotechnology.

At the present time the immense Human Genome Project is generating information that will revolutionize medicine and our concept of susceptibility to disease. In the future, PAHO should consider the expansion of biotechnology fields on which to focus its activities, and in doing so, coordinate its actions with national programs and the activities of other international organizations.
VIII. BUDGET

Budget for the Plan of Action in Biotechnology for the biennium 1996-1997, to be repeated in the biennium 1998-1999*

<table>
<thead>
<tr>
<th>OBJECTIVE</th>
<th>AMOUNT NEEDED</th>
<th>AMOUNT ALREADY COMMITTED</th>
<th>INCREASE REQUESTED/BIENNium</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Diagnosis</td>
<td>300</td>
<td>0</td>
<td>300</td>
</tr>
<tr>
<td>2. Vaccines</td>
<td>200</td>
<td>150</td>
<td>50</td>
</tr>
<tr>
<td>3. Human Resources</td>
<td>300</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>4. Coord. Committee**</td>
<td>28</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>828</td>
<td>250</td>
<td>578</td>
</tr>
</tbody>
</table>

* Details justifying this request may be found under Specific Objectives.

** Budget requested for meetings of the Subcommittee on Biotechnology and the Executive Committee, in addition to coordination visits to the participating laboratories.