

**Special Programme of Research, Development
and Research Training in Human Reproduction**

Co-sponsored by UNDP, UNFPA, WHO and the World Bank

Research in Human Reproduction

Biennial Report 1988-1989



World Health Organization
Geneva 1990

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This Biennial Progress Report for 1988-1989 of the Special Programme of Research, Development and Research Training in Human Reproduction differs in format and in content from its predecessors. It has been made less technical in the hope that it will reach and benefit a wider audience including, in addition to the scientific community, policy-makers, health care providers and "consumers" at large.

For this reason, the Report is not an exhaustive review of all that the Programme has done in the past two years. Certain activities which are not yet of major relevance to this larger audience have been omitted.

It would be inaccurate to see this Report as just an account of two years' work by the director and staff of the Programme. On the contrary, it is a record of a global partnership between scientists and scientific institutions in 54 developing and 26 developed countries, who have pooled their resources for the common good.

This global effort has been made possible only by the voluntary financial contributions of WHO Member States and the co-sponsoring agencies and other donors, which share the conviction that an investment in reproductive health research is an investment for a better future for the whole of mankind ■

Dr Mahmoud Fathalla, Director

The Special Programme of Research, Development and Research Training in Human Reproduction (HRP) was established by WHO in 1972 in response to the expanding demands for human reproduction research and in recognition of the fact that the resources needed for such research can only be effectively mobilized and managed through a worldwide, collaborative effort. In May 1988, the Forty-first World Health Assembly approved the Programme's co-sponsorship by the United Nations Development Programme, the United Nations Population Fund and the World Bank. The co-sponsorship reflects confidence in the Programme as the main instrument for human reproduction research within the United Nations system. But it also reflects the increasing realization that human reproduction has a wide-ranging impact on the health of women and children, on population, on

socio-economic development, on the status of women and on the global environment.

The Programme is financed by voluntary contributions from developed as well as developing Member States of WHO, from its co-sponsors and from other organizations. Apart from this direct financing, which amounted to US\$ 43.4 million during the biennium 1988-1989, contributions in kind are made by collaborating research institutions in 26 developed and 54 developing countries, and by scientists worldwide who volunteer to devote their time and effort to the Programme's activities. This global partnership between countries and scientists pooling their expertise and resources for the common good is the Programme's main *modus operandi* and is reflected also in its mechanisms for policy setting and scientific direction.

Policy and budgetary decisions are made by the Policy and Coordination Committee of 32 members, most of whom represent developing country governments. Scientific committees and *ad hoc* expert consultations involving men and women from a wide variety of professional and cultural backgrounds guide the Programme's work. By the end of 1989, 293 scientists from 25 developed countries and 265 scientists from 39 developing countries had participated in the scientific direction of the Programme.

In order to fulfil its mandate, which is "to promote, coordinate, support, conduct and evaluate research on human reproduction, with particular reference to the needs of developing countries", the Programme carries out two types of operation. The first is the mobilization and coordination of a worldwide effort to develop the appropriate technologies and generate information in selected

areas of reproductive health that are of high priority to developing countries. This is the thrust of the Research and Development component of the Programme. The second type of operation, equally important, is the strengthening of human and material resources for research in order to enable developing countries to address their own research needs and also participate in the global effort. This building of self-reliance in reproductive health research is the goal of the Resources for Research component of the Programme.

The Research and Development component is organized into eight Task Forces covering three main topics: improving the performance of current methods of fertility regulation, development of new and improved methods, and infertility. Highlights of the biennium included the publication of the first series of results from the large, multicentre study on oral contraceptive use and cancer, and the successful completion of the clinical development of two contraceptive modalities: the once-a-month injectables,

Cyclofem and Mesigyna, and the levonorgestrel-releasing vaginal ring. Introductory trials with Cyclofem have started - or are about to start - in several countries, and a licence agreement has been concluded with a commercial company for the manufacture and distribution of the vaginal ring. Research has continued to assess the safety and efficacy of the non-surgical approach to early pregnancy termination involving the use of a combination regimen of an antiprogesterin and prostaglandin. Significant progress has been made also in the development of a hormonal contraceptive for men and of a birth-control vaccine for women.

Several major multinational trials and research initiatives were launched during the biennium. Amongst them are a 20-centre, four-year study on the risk of cardiovascular disease from the use of lower dose hormonal contraceptive pills, a post-registration surveillance project of the

contraceptive implant NORPLANT® a seven-centre study on breast-feeding practices and their inhibitory effect on ovarian function, and a multinational project to study the prevalence of past chlamydial and gonococcal diseases as a cause of male and female infertility. In the area of behavioural and social determinants of fertility regulation, research initiatives were launched on the dynamics of contraceptive use and on the determinants and consequences of induced abortion.

To solve the reproductive health problems of their fast-increasing populations, developing countries need a strong, national research capacity. Building up this self-reliance in research is the driving force behind the work of the Resources for Research component of the Programme. During the biennium, 27 developing countries were given assistance with the planning and implementation of long-term development projects specifically designed to strengthen institutional research capability. This assistance included support for training of 146 researchers, while a

similar number returned home after training abroad to put their newly acquired knowledge and skills into practice.

In developing the human and material resources for research, increasing emphasis is being placed on fostering cooperation between the developing countries themselves in the areas of training, research planning and institutional development, the development of technical facilities for research, and collaboration in research projects. Apart from the direct benefits to the countries themselves, this strategy of promoting South-to-South cooperation ensures optimal use of the limited, and invariably inadequate, resources available. Although one third of the Programme's biennial budget is earmarked for the strengthening of research capability in developing countries, the demand for support during the biennium was such that the Programme was forced to decline, or to fund at a lower level, many worthwhile research projects.

As the main instrument within the United Nations for human reproduction research, and as a WHO-

executed activity, the Programme has three special roles: it coordinates research; it advises Member States; and it sets standards and develops guidelines.

The conflict between the increasing need and demand for research in reproductive health on the one hand and static or diminishing financial resources worldwide on the other, makes coordination of the activities supported by national and international agencies essential if efficient use is to be made of the limited resources. During the biennium, the Programme has continued coordination of research in reproductive health issues within WHO, in the United Nations system, and in collaboration with national and international research programmes, non-governmental organizations and industry. Examples of such collaboration, and of the benefits it entails, are the fruitful cooperative activities between the United Nations Population Fund and the Programme in strengthening research capabilities in the People's Republic of China, Indonesia and Viet Nam.

Advice to Member States, enabling them to make sound policy decisions on technical issues, is provided by the Programme in a variety of ways. Apart from responding to specific requests for information, the Programme publishes a quarterly newsletter, *Progress*, convenes expert meetings such as the symposium on the Assessment of the Safety and Efficacy of Vaccines to Regulate Fertility held in June 1989, and ensures wide dissemination of the reports of such meetings.

The Programme also plays a leading role in setting standards and in developing and promoting guidelines that ensure that sound, rational and ethically acceptable approaches are employed in research and development of new methods of fertility regulation and in their subsequent introduction and use in health care systems. In recognition of its work in this area, specifically the development of guidelines for the toxicological assessment of steroidal contraceptive drugs which reduce the number of laboratory animals required for toxicological testing, the Programme

received in 1988 an award from the Hildegard Doerenkamp-Gerhard Zbinden Foundation for Realistic Animal Protection. Also in 1988, a major international conference was organized, in collaboration with the Council for International Organizations of Medical Sciences, to promote intercultural dialogue on ethical issues and human values in family planning.

Women are at the heart of development. They are also the main victims of unregulated fertility and it is imperative, therefore, that any organization concerned with reproductive health issues involves women in all aspects of its operations from policy setting through planning and implementation of activities to disseminating

information. In this last respect the Programme has taken an active role during the biennium in seeking to expand its links with women's groups, which are important sources of information to women in many parts of the world.

“(That) HRP (should) be retained as a Special Programme within the United Nations system, and that the sponsoring agencies and the donors increase the financial resources in order that the Programme may continue to develop the research capability and coordinate activities to meet the challenges of protecting and improving

reproductive health and family wellbeing in the 21st century”. Such was the firm recommendation of the team of six independent experts commissioned by the Policy and Coordination Committee to carry out an in-depth assessment of the impact of the Programme's activities in developing countries. Striving to continue and improve upon its work in a global partnership with organizations, programmes and individuals dedicated to improving the level of reproductive health and hence the lives of women, the Programme enters the last decade of this century with confidence in its ability to make a significant contribution to our common goal of “Health for All by the Year 2000” ■

- Co-sponsorship
- Finance
- Policy-setting
- Scientific direction
- Operations
- Research and development
- Resource development
- Special roles
- Programme evaluation

The Special Programme of Research, Development and Research Training in Human Reproduction (HRP) was formed by WHO in 1972. It is a global programme of technical cooperation, designed to promote, coordinate, support, conduct and evaluate research on human reproduction, with particular reference to the needs of developing countries.

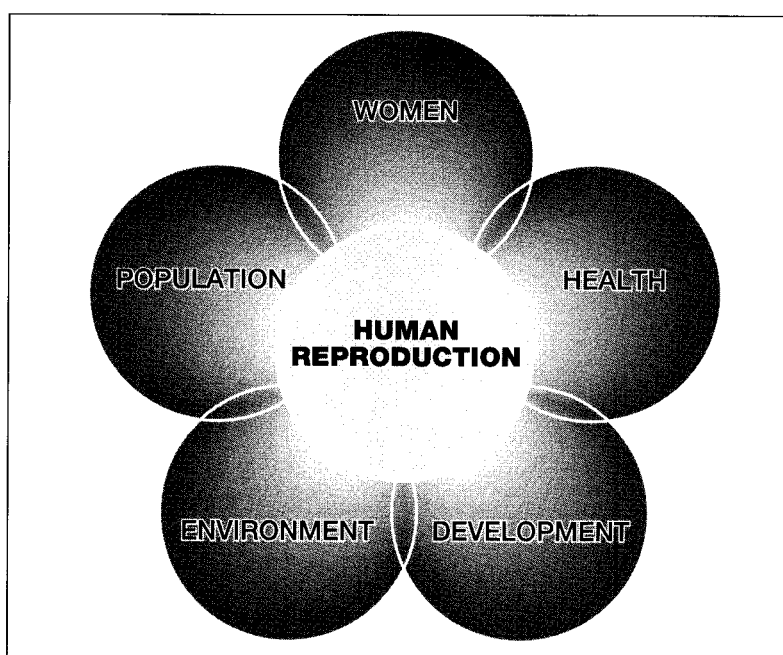
investment by Member States, over and above their contributions to the WHO regular budget.

This co-sponsorship reflects confidence in the Programme as the UN system's main instrument for human reproduction research. It also reflects an increasing realization that human reproduction has a wide-ranging impact on the health of women and children, on population, on socioeconomic development, on the status of women and on the global environment.

Co-sponsorship

The Programme's co-sponsorship by the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA) and the World Bank, as approved by the Forty-first World Health Assembly, was a major policy event of 1988-1989.

WHO established the Programme in response to the expanding demands for human reproduction research and in recognition of the fact that the resources needed for such research can only be effectively mobilized and managed through a global, collaborative effort, organized in the spirit of the Declaration of Alma-Ata, which says that "the attainment of health by people in any one country directly concerns and benefits every other country". This situation called for a globally coordinated effort, and an extra



The Special Programme operates on the principle of a global partnership. This is reflected in its mechanisms for finance, policy setting and scientific directions.

from governments, its co-sponsors and other organizations. Although the major contributions come from developed-country governments, several developing countries also give financial support to the Programme. In 1988-1989, two of the eleven larger contributions were provided by governments of developing countries.

and by scientists worldwide who volunteer to devote their time and effort to the Programme's activities.

In a spirit of partnership, financial contributors to the Programme do not earmark their funds for any specific activity or geographical area, but leave decisions about allocation of funds to the Programme's collective policy-makers.

Finance

The Programme continues to be financed by voluntary contributions

Apart from direct financing, contributions in kind are made by collaborating research institutions in developed and developing countries,

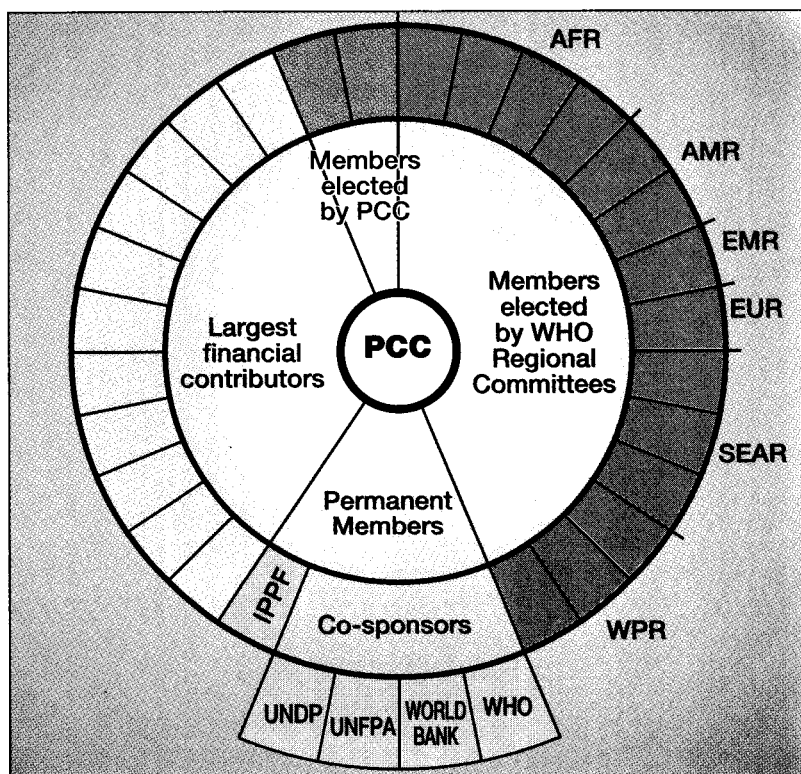
Policy-setting

Policies and decisions on budgetary allocations within the Programme are made by the *Policy and Coordination Committee (PCC)*. Its 32 members, most of whom represent developing country governments, meet at least once a year.

A *Standing Committee* of the four co-sponsors meets at least twice a year, between the meetings of the PCC, to review progress, plans of action and the budget.

Scientific direction

The *Scientific and Technical Advisory Group (STAG)* gives overall scientific direction to the Programme. The STAG has 15-18 members



Policy and Coordination Committee (PCC)

appointed by the PCC. They serve in a personal capacity, representing the broad range of biomedical and other disciplines needed to guide the Programme's activities. To make sure that the STAG is independent, its members cannot sit on the Programme's other committees, may not be principal investigators in studies undertaken by the Programme, and may not be Programme grantees. STAG members are appointed to serve for a period of three years, and are eligible for immediate reappointment only once.

The work of the Programme is guided by scientific committees and by experts called in for *ad hoc* consultations. The need to have a balanced geographical representation is kept in mind, and a special effort is made to include scientists from developing countries as well as women scientists. Members are appointed for three years, and can be reappointed immediately for a maximum of a further three years. With this rotation mechanism, the Programme obtains the maximum involvement of scientists from all over the world in the global effort to serve developing-country needs.

By the end of 1989, 293 scientists from 25 developed countries and 265 scientists from 39 developing countries had participated in the scientific direction of the Programme.

Operations

The Programme's operational objective is to promote the development of appropriate technologies and the generation of information that developing countries need to improve the reproductive health of their populations. Two types of operation are needed. The first is the mobilization and coordination of a

Task Forces in 1988-1989

- Task Force on Safety and Efficacy of Fertility-regulating Methods
- Task Force on Behavioural and Social Determinants of Fertility Regulation
- Task Force on Long-acting Systemic Agents for Fertility Regulation
- Task Force on Post-ovulatory Methods of Fertility Regulation
- Task Force on Vaccines for Fertility Regulation
- Task Force on Methods for the Regulation of Male Fertility
- Task Force on Methods for the Natural Regulation of Fertility
- Task Force on the Prevention and Management of Infertility

global effort to develop the appropriate technologies and to generate information in selected areas of high priority to developing countries. This is the thrust of the *Research and Development* component of the Programme. The second type of operation, equally important, is the strengthening of the developing countries' research capabilities so that they can tackle their own national research needs and also participate in the global effort. This is the purpose of the *Resources for Research* component of the Programme.

Research and development

The Programme's research and development activities are conducted through *Task Forces*, scientific groups with specific research objectives. The Task Force mechanism allows the Programme to channel its resources into certain relatively narrow priority areas, to make the maximum impact. Task Forces are composed of multidisciplinary, multinational teams selected from the scientific community in developed and developing countries. Each is managed by one or more scientists on the Programme's staff. As

priorities change, Task Forces are phased out and new ones are set up. The Programme's emphasis on the development of new methods of birth control is in response to the expanding worldwide need for fertility regulation, the inadequacy of present methods and their delivery systems, and the increasing withdrawal of private industry from research and development in this field for reasons of cost, profit, litigation and the political climate.

The strategic plan for each Task Force is developed, monitored and evaluated by a *Steering Committee*, composed of scientists selected on the basis of their scientific knowledge and expertise in areas relevant to the Task Force's needs. A detailed strategic plan is prepared every two years for one biennium, with tentative projections for the next. Because of the nature of research and development, it is difficult to make precise predictions, with budgetary implications, over a longer term. Each Task Force's budget is set by the PCC, on advice from the STAG. In view of the urgency of the need for fertility regulation expressed by

developing countries, the Programme generally gives a higher priority to improving the performance of existing methods and to methods that are at an advanced stage of development, rather than to those at an early or exploratory stage of investigation.

An extensive network of *Collaborating Centres* in developing and developed countries forms the backbone of the Programme's research and development activities.

The Programme collaborates with a worldwide network of centres in 26 developed and 54 developing countries.

The Programme places a major emphasis on involving developing-country centres in the research effort, encouraging and supporting their participation in research relevant to their own needs. Technical cooperation is promoted between developed- and developing-country centres, and among developing countries. Much of the research is

done through large, collaborative *multicentre studies* involving many countries, an area in which the Programme has acquired a special expertise. These studies have several merits: the large number of subjects allows firmer scientific conclusions to be drawn; population differences can be taken into account in the evaluation of the results; and the studies are an effective exercise in technical cooperation. To help manage and coordinate such large studies, the Programme has set up a *Statistics and Data Processing Unit*, which also helps developing-country centres to achieve self-reliance in study design and analysis.

The Programme takes great care to maintain the highest attainable technical and ethical standards in the research it supports. A *Scientific and Ethical Review Group*, made up of independent scientists who are not members of other committees and are not principal investigators in studies supported by the Programme, must approve projects before they can be funded. Studies involving the use of new drugs or a new use of an existing drug, must be

approved by the Programme's *Toxicology Panel* which assesses all available information on the safety aspects of the proposed studies before approving experimentation on humans or animals.

The Programme emphasizes the importance of the *dissemination of information* resulting from its research, including publication in scientific journals, presentation at scientific meetings, and the communication of relevant findings to decision- and policy-makers and to service-providers.

The results of studies supported by the Programme have appeared in more than 6,000 publications. The proportion of these publications produced by developing-country scientists has gradually risen from about one third of the total in the 1970s to a half in the 1980s.

Resource development

The Programme helps national authorities and institutions in developing countries to improve and expand their research resources. The strengthening of these research capabilities has two objectives: to involve developing-country research institutions and scientists in the global research effort; and to help countries address their own specific research needs.

The number of countries and institutions collaborating with the Programme on research-capability strengthening is limited by the funds available. Rather than spread its limited resources too thin, the Programme concentrates its activities on a selected number of countries in which its investment can make a significant contribution. As capabilities are strengthened and institutions become more self-reliant, the support is gradually withdrawn and transferred to other countries. Priority is given to those countries with the greatest need and the strongest commitment on the part of the government and the institution. An additional consideration is

the institution's potential to support subsequent national and regional research-capability strengthening.

Priority research areas vary from one country to another, and can only be decided in and by the country. The Programme helps establish mechanisms for needs assessment in which policy-makers and research scientists participate, and matters of concern to women are taken into account.

A scientific committee, the *Committee on Resources for Research*, makes recommendations on how to improve the developing countries' research resources. To ensure effective management and coordination of activities, responsibility for certain geographical areas, e.g. Africa, China, rest of Asia, and Latin America, is assigned to individual Programme staff scientists.

The main instrument for research-capability strengthening is the *Long-Term Institutional Development Grant*. This support package includes the development of a nationally relevant research programme, strengthening of material resources, and strengthening of human

resources through *Research Training Grants*. This comprehensive package is meant to ensure that all elements are in place for the smooth development of the institution.

Since 1986, 38 institutions in 29 developing countries have received long-term institutional development grants.

Other grants are available for institutions that no longer need or qualify for institutional development support and for institutions that have relatively well developed research programmes: *Capital Grants*, to acquire a piece of equipment; *Small Grants*, to acquire journals or laboratory supplies; *Research Training Grants*, (followed by *Re-entry Grants* to help trainees apply their new knowledge and research skills in their home institution); and *Visiting Scientist Grants*, awarded to senior researchers to enable them to exchange research experience with scientists in other research institutes. In addition, the

Programme provides: *Grants for Short Group-Learning Activities*, such as holding workshops or seminars; and *Grants for Developing Master's Degree Level Courses*, with a research component for students from other developing countries.

A total of 1,122 scientists from 357 institutions in 67 countries have received Research Training Grants and Visiting Scientist Grants.

Special roles

As the UN's main instrument for human reproduction research, and as a WHO-executed activity, the Programme has three special roles: it advises Member States; it sets standards and develops guidelines; and it coordinates research.

The Programme's advice to Member States enables them to make sound policy decisions on technical issues. The Programme responds to specific requests for information from Member States and publishes a quarterly newsletter, *Progress*. It convenes

meetings of consultants and experts to discuss important topics and ensures wide dissemination of their reports.

The *Programme of Standardization and Quality Control of Laboratory Procedures* provides matched reagents and external quality control services that enable reliable, valid and comparable hormonal and biochemical assays to be performed in research institutions. A scientific committee, the *Laboratory Methods Group*, directs this activity.

Guidelines are developed and distributed for studies, standard research protocols and, where necessary, new methodologies for dealing with research problems relevant to developing countries.

The Programme plays a leading role in developing regulatory requirements for new methods of fertility regulation. The objectives are to develop and promote sound and rational guidelines which ensure the safety of human subjects to the fullest extent possible during research and development and after products are in wide use, to protect animals from unnecessary

experimentation, and to avoid unnecessary delays in the research and development process.

In 1988, the Programme received an award from the Hildegard Doerenkamp-Gerhard Zbinden Foundation for Realistic Animal Protection in recognition of its work in developing guidelines for the toxicological assessment of steroidal contraceptive drugs, which reduced the number of laboratory animals required for toxicological testing.

The Programme also promotes ethical practices by formulating guidelines for the ethical review of research projects and by promoting the establishment of ethical review committees at research centres. It collaborates with the Council for International

Organizations of Medical Sciences (CIOMS) in supporting and promoting an intercultural dialogue on ethical issues and human values in family planning.

The Programme coordinates human reproduction research undertaken within WHO, in the UN System, and in collaboration with national and international research programmes, non-governmental organizations and industry. The main mechanism for this coordination is active participation in the meetings of the committees which give scientific direction to the Programme.

Programme evaluation

The Programme's internal evaluation mechanisms consist of regular evaluations of their respective activities by the scientific committees and periodic in-depth reviews carried out by the STAG of different Programme components.

The Director-General of WHO periodically submits a progress report on the Programme to the WHO Executive Board and to the World Health Assembly. Following a

major review in May 1988, the Assembly adopted Resolution WHA 41.9, endorsing the Programme's policy guidelines, reaffirming the

close relationship between family planning, health and development, emphasizing the importance of ensuring the rapid and widespread application of the results

of research, and urging Member States to contribute, or increase their contribution, to the Programme.

World Health Assembly Resolution WHA 41.9

The Forty-first World Health Assembly,

Having considered the Director-General's progress report on the Special Programme of Research, Development and Training in Human Reproduction;

1. ENDORSES the policy guidelines outlined by the Director-General, with particular attention to the role of the Programme in:

(1) the continued assessment of existing technologies and the acceleration of the development of new technologies in fertility regulation;

(2) the building-up of national self-reliance in research on all aspects of human reproduction in developing countries to meet their specific needs in primary health care;

(3) promoting scientific and technical cooperation between developed and developing countries, and between developing countries;

(4) coordination of the global research effort in the field of reproductive health;

(5) promoting ethical practices in the field of human reproduction research to protect the health and rights of individuals in different social and cultural settings;

2. REAFFIRMS the close relationship between family planning, health and development, and the need to integrate family planning activities with those of maternal and child health;

3. EMPHASIZES the importance of ensuring the rapid and widespread application of the results of research supported by the Programme in countries' national health strategies and programmes;

4. APPROVES the co-sponsorship of the Programme by the World Bank, the United Nations Development Programme and the United Nations Population Fund, as outlined in the report of the Director-General;

5. URGES Member States to contribute, or to increase their contributions, to the Programme in order to accelerate the achievement of its objectives at the approved level.

Three major external evaluations of the Programme have taken place. The most recent, in the biennium 1988-1989, focused on the Programme's impact, especially in developing

countries. The team of six high-level, independent experts came from different disciplines and different cultural backgrounds. The firm recommendation of the team's 200-page report was that:

"HRP be retained as a Special Programme within the United Nations system, and that the sponsoring agencies and the donors increase the financial resources in order that the Programme may continue to develop the research capability and coordinate activities to meet the challenges of protecting and improving reproductive health and family wellbeing in the 21st century".
