WORLD HEALTH ORGANIZATION

EXPANDED PROGRAMME OF RESEARCH, DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION

REPORT OF A FEASIBILITY PROJECT

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INTRODUCTION

In June 1970 the World Health Organization convened a meeting of agencies interested in the promotion of research in reproductive biomedicine including fertility regulation. The meeting considered ways in which research and development and research training in human reproduction could best be accelerated and expanded. It was recommended that WHO should undertake a Feasibility Project to provide substantive answers to these questions and to suggest a specific course of action.

During the period November 1970 through April 1971 WHO carried out such a Feasibility Project. Teams of experts have visited more than 69 institutions in 23 countries (Appendix A). Scientists, research administrators and research strategists in several countries have been consulted. The Feasibility Project has led to the development of an Expanded Programme of Research, Development and Research Training in Human Reproduction. The Five Tracks described on the following pages present a comprehensive action programme that would implement WHO's mandate to stimulate and expand research in human reproduction including fertility control. Specific proposals illustrative of the type of activity that would be undertaken are appended to the report.

The World Health Organization believes it can make a unique contribution to this field. WHO operates in the world context and is well placed to promote scientific collaboration across national frontiers. Research in human reproduction and fertility control has yet to benefit from the kind of purposive approach successful in other fields. WHO believes its Expanded Programme in Human Reproduction will mobilize the talents of scientists in many countries towards a significant expansion of research and development and research training. The components of the Expanded Programme are areas in which WHO can act quickly and effectively. These activities are seen as complementing the programmes of other agencies and institutions engaged in this field. Greatly increased support for a number of different approaches to expanding research in human reproduction would appear both necessary and desirable. WHO is prepared to play an important role in this expanded world effort.

SECTION I

EXPANDED PROGRAMME OF RESEARCH, DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION

TRACK 1 WHO RESEARCH AND TRAINING CENTRES (Appendix B)

It is proposed to designate at least four major existing centres as WHO Research and Training Centres in Human Reproduction. This strategy will have the double objective of expanding multi-disciplinary research and development, and research training in human reproduction as well as providing a focus to stimulate research in the regions in which these centres are located. Facilitating the rapid expansion of a number of existing centres is viewed as a most expedient way of producing a significant qualitative and quantitative expansion of research in human reproduction on a global basis.

Criteria for the selection of Research and Training Centres include: relevance and breadth of existing programme; potential for a significant expansion of the research and/or training programme; capacity for regional or international leadership; interest in increased international collaboration and willingness to provide technical assistance to other centres in the region.

The functions of each of the Research and Training Centres will include some or all of the following:

(a) to carry out research in human reproduction with particular emphasis on those processes which may be subject to regulation;

(b) to initiate or participate in collaborative research and development efforts involving a number of institutions;

(c) to provide research training in reproductive biomedicine for scientists and clinicians and to encourage and assist them in developing active research programmes in their own centres;

(d) to organize conferences, symposia and seminars and to participate in the exchange of scientists with other collaborating institutions;

(e) to serve as regional documentation centres;

(f) to develop and maintain regional inventories of scientists and projects in the field of human reproduction;

(g) to advise WHO on matters related to research and training in human reproduction.

Research and Training Centres would be encouraged to formulate detailed proposals for an expanded five year research and training programme. (Appendix B). To assure an acceleration and expansion of the research, training and development programmes at these institutions financial assistance provided by WHO would be additive and complementary rather than replacing existing support from other sources.

TRACK 2 WHO COLLABORATING CLINICAL CENTRES (Appendix C)

To facilitate the rapid clinical evaluation of new fertility regulating agents as well as comparative trials of existing agents on an international basis it is proposed to establish a global network of Collaborating Clinical Centres. During the past few months teams of experts have visited institutions in each of the six WHO regions. It is apparent that as many as 34 centres in 25 countries would qualify as Collaborating Clinical Centres as defined in Appendix C. The creation of such a network would provide a mechanism for the clinical study of new agents affecting fertility, simultaneously, in a number of countries, under a variety of field situations. The WHO designation given to these Centres would facilitate their collaboration and would create a truly international network for clinical trials.

TRACK 3 WHO TASK FORCES FOR COLLABORATIVE RESEARCH AND DEVELOPMENT (Appendix D)

To promote collaborative research directed towards specific objectives, goal oriented task forces will be organized in a number of specific areas in the field of fertility regulation. The recommendation to convene a WHO Task Force on a specific topic might originate with the Advisory Group to the Expanded Programme (Section II, 1., page 7), a Research and Training Centre or with other investigators or institutions active in the field. Each Task Force would be made up of leading scientists in the specific field. The Task Force would identify priority research areas in which additional work is required. A collaborative research and development programme including standard protocols, timetable and budget estimates, would be planned and submitted to WHO for scientific review and funding. Task Forces might elect to submit a package of proposals for scientific review and support or could encourage collaborators to submit individual proposals. Each Task Force would monitor its collaborative research projects, publish results at appropriate intervals and meet sufficiently often to provide continuing direction to the Project. Collaborative projects organized by Task Forces would not necessarily be limited to the network of Research and Training Centres or Collaborating Clinical Centres but would also extend to other laboratories and investigators.

Each Task Force would report to WHO at regular intervals to enable the Advisory Group to assess progress towards the predefined objectives and to determine the amount of additional support required. The Task Force approach to collaborative research and development is designed to offer a flexible yet highly focused mechanism that can be expected to accelerate the development and critical assessment of new agents affecting fertility.

TRACK 4 WHO INTERNATIONAL DOCUMENTATION CENTRE ON THE BIOMEDICAL ASPECTS OF HUMAN REPRODUCTION (Appendix E)

It is estimated that some 20 000 publications related to the biomedical aspects of human reproduction are appearing in the world literature annually. Somewhat more than half of these publications are indexed by the National Library of Medicine's MEDLARS system. A significant part of the remainder are indexed by Chemical Abstracts and Biological Abstracts. There remain a considerable number of important publications that are not yet covered by the existing systems.

The Karolinska Institute proposes to create a special unit at its Biomedical Documentation Centre that would be responsible for compiling and maintaining as complete a file as possible of references to all published material related to the biomedical aspects of human reproduction. In addition to the medical literature it would include relevant publications from the fields of chemistry, biochemistry, biology, immunology and toxicology, as well as monographs, theses and relevant reports. Information from WHO Research and Training Centres, Collaborating Clinical Centres and International Reference Centres would be incorporated into the system. The aim is to create a special file for the entire field of human reproduction.

Using and building on the existing MEDLARS system would reduce the cost and enable the comprehensive file to be operational by 1 January 1972. The Documentation Centre would also expand the specialized vocabulary necessary for more complete coverage of the field of human reproduction. It would include a special effort to record data on toxicity and side effects reported from collaborative clinical studies and would contain a complete cross indexed file of authors and workers in the field.

Information distribution

The WHO International Documentation Centre would distribute profiles and retrospective searches on the biomedical aspects of human reproduction. These would be sent, without cost, to scientists in member countries who do not have access to this type of service. A need for such an information service was expressed by scientists in a number of the countries visited during the Feasibility Project. The service would tie the WHO Research and Training Centres more closely together through the two-way flow of scientific information that would be established. The files created in Stockholm would also be available by direct access or by distribution of tapes to other information centres throughout the world.

TRACK 5 OTHER WHO ACTIVITIES TO SUPPORT THE EXPANDED PROGRAMME IN HUMAN REPRODUCTION

A. Expanded Support to Scientists and Institutions

The Feasibility Project identified a substantial number of institutions qualifying for research grants and contracts. The Project also documented the fact that shortage of funds represents a major constraint to the expansion of research and research training in reproductive biomedicine at these institutions. Therefore, it is proposed to provide support to an increasing number of scientists and institutions, especially in countries where needs and opportunities for relevant research are greatest.

Support would include funds for specific research projects, for additional research personnel and for the purchase of essential equipment. Subject to the availability of funds, longer term (2-3 year) commitments would be provided whenever appropriate.

The means by which scientists and institutions would receive support is described in Appendix G.

B. Supplies for Collaborating Laboratories - "Spare Parts" Programme

The Feasibility Project provided evidence that research programmes in institutions in a number of countries are frequently delayed and often curtailed by a shortage of critical reagents or lack of spare parts for scientific equipment. These problems are most acute in countries where essential supplies and equipment are not available locally. WHO is in a unique position to contribute in this area. WHO may purchase essential supplies and equipment to be sent directly to scientists and scientific institutions. A pilot programme that is supplying essential spare parts and reagents to scientists in a number of countries has been implemented as part of the Feasibility Project. Initial experience confirms the need for such a programme and the desirability of its expansion. Modest support in this area appears likely to make a major contribution to expanded research in human reproduction.

C. Research Training Grants

It is generally agreed that one of the constraints to an expanded world effort in human reproduction research is the shortage of trained scientists specialized in this field. An important objective of the Expanded Programme is to increase opportunities for advanced training in reproductive biology. Detailed plans for expanded research training at two major centres are presented in Appendix B. Additional research training grants for individuals will also be required and are included in the provisional budget.

The network of Research and Training Centres and Collaborating Clinical Centres will also provide a framework in which the international exchange of scientific workers can be significantly increased. Such an exchange programme can do much to overcome the scientific isolation reported by many of the scientists contacted during the Feasibility Project.

D. Seminars and Workshops

The network of WHO centres engaged in reproduction research offers a mechanism to increase the exchange of scientific information through a series of travelling seminars and workshops conducted under WHO sponsorship. WHO's ability to plan and conduct impartial, international meetings on specific scientific topics would offer further support to the Expanded Programme in Human Reproduction.

E. Consultant assistance

The site visits conducted as part of the Feasibility Project identified an urgent need to assist a number of developing laboratories to set up specific procedures and to provide advice on other aspects of their research programmes. In most cases, assignments of from one to three months would be adequate to accomplish the assigned task. Funds for an increase in consultant assistance are included in the provisional budget.

SECTION II

1. HEADQUARTERS TECHNICAL SUPPORT (Appendix G)

(a) Administration and technical staff

The Expanded Programme will be implemented within the framework of WHO policies and procedures. The technical staff of the Human Reproduction Unit will be increased to implement and administer the programme. Funds for the additional professional staff that will be needed are included under technical support costs in the provisional budget (page 8).

(b) Contracts and Grants

WHO presently commits some $5 000 000 annually from its regular budget for health related scientific research. The contract and grant programme in human reproduction has provided more than 40 investigators with some $700 000 during the past eight years.

The contract and grant mechanism would be used to channel support to the Research and Training Centres, to support the network of Collaborating Clinical Centres, to finance

the Task Forces and to support other collaborative research programmes. Individual scientists and institutions would also receive support through this mechanism. Contracts and grants would thus represent the principal funding mechanism of the Expanded Programme.

(c) Advisory Group

It is proposed to establish a scientific Advisory Group of up to 12 outstanding consultants to advise WHO on its Expanded Programme in Human Reproduction. The Advisory Group, appointed by the Director-General, would recommend strategy, plans and policy for the Expanded Programme. The Advisory Group would also advise on the allocation of available resources, both in general and in detail, and report on the progress of research and development in the field. An appropriate mechanism to assure the expeditious scientific review and processing of requests submitted to the Programme will be proposed by the Advisory Group. The composition, function and responsibilities of the Advisory Group are presented in more detail in Appendix G.

2. RELATIONSHIP TO PHARMACEUTICAL INDUSTRY

WHO recognizes the important role played by the pharmaceutical industry in drug development. Over the past ten years WHO, as part of its over-all research effort, has sponsored clinical studies of new vaccines, pesticides, anti-parasitic compounds and hypotensive agents developed by the pharmaceutical industry. Drawing on these precedents, the components of the Expanded Programme would be available to plan and undertake comparative trials or clinical studies of fertility regulating agents developed by industry. The results of collaborative studies would be published with the understanding that such articles do not constitute endorsement of a specific drug or device.

It may also prove advantageous to contract with pharmaceutical companies to undertake specific tasks related to one or more aspects of a collaborative research programme. There are precedents within WHO for such an undertaking.

3. PATENT RIGHTS

The disposition and administration of rights in any invention or patent resulting from or developed in the course of a WHO assisted project should:

(a) protect the public interest;

(b) give the invention the widest possible royalty free distribution.

WHO's legal department can advise on specific questions that may arise as a result of the Expanded Programme in Human Reproduction.

4. PROVISIONAL BUDGET

Table 1 reflects recommendations based on findings from the Feasibility Project as to the level of financial assistance required during the first five years of the Expanded Programme. Funds needed for the third, fourth and fifth year of the Programme are projected at two levels. A justification for the provisional budget is outlined in Appendix F.

TABLE 1

PROVISIONAL BUDGET FIVE YEAR WHO EXPANDED PROGRAMME OF RESEARCH, DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION $000's

	71-72	72-73	73-76* (annual range of expenditure)
1. Research and Training Centres	2400	3000	4000 - 6000
2. Collaborating Clinical Centres	300	450	600 - 800
3. Task Forces	1000	1500	2000 - 4000
4. Documentation Centre	300	400	500 - 800
5. Expansion of other WHO activities			
(a) Expanded support to Scientists and Institutions	1500	3000	4000 - 8000
(b) Spare Parts	100	200	200 - 400
(c) Research Training Grants	150	150	200 - 400
(d) Seminars	100	200	300 - 600
(e) Consultant Assistance	100	100	200 - 400
Headquarters Technical Support	400	450	500 - 800
Additional two year commitment staff salaries	350		
TOTALS	6700	9450	12 500 - 22 200

* It is expected that the opportunities available to WHO to expand and accelerate research in human reproduction will continue to exceed available funds. It is also assumed that funds available during the third and subsequent years of the Expanded Programme will be determined, at least in part, by the performance of the Programme during the first two years. For these reasons the budget estimates in this column are only indicative of the order of magnitude of funds which could profitably be invested during this time period in human reproduction research using WHO mechanisms.

TABLE 2

HEADQUARTERS TECHNICAL SUPPORT BUDGET
FIRST TWO YEARS OF WHO EXPANDED PROGRAMME OF RESEARCH,
DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION

	71-72	72-73
1. Meetings		
(a) Advisory Group Study Panels	107 000	163 000
(b) Research and Training Centre Directors, Collaborating Clinical Centres	30 000	30 000
2. Site Visits	50 000	30 000
3. Headquarters Staff	166 400	170 000
4. Duty Travel	15 000	20 000
5. Supplies and Equipment	10 000	10 000
6. Consultants	21 600	27 000
	400 000	450 000

5. FUNDING

The Expanded Programme would be funded from contributions to WHO's Special Account for Medical Research. Contributions to this account would be earmarked for the Programme of Expanded Research and Development and Research Training in Human Reproduction. Contributions from a number of Member States, private foundations and multilateral assistance agencies will assure a broad range of support, thus strengthening the international character of the Programme.

6. TIMETABLE

Implementation of the Expanded Programme can begin as soon as funds become available. The specific proposals appended to this Report would also be implemented immediately after funding. The first phase of the Feasibility Project did not allow sufficient time to visit a number of countries with institutions actively engaged in reproductive research. It is

proposed to continue site visits to selected institutions as part of the continuing survey of research activities in this field. These visits are also necessary to identify additional Research and Training Centres, Collaborating Clinical Centres and International Reference Centres. The network of Collaborating Clinical Centres should be established before the end of 1971. It is expected that within twelve months of funding, each of the major programme components will be operational.

7. PROGRAMME RATIONALE AND JUSTIFICATION

The following conclusions from the Feasibility Project support the rationale for the Expanded Programme:

(1) Providing additional support to a number of major institutions actively involved in reproduction research is seen as an expedient way of promoting global collaboration and of rapidly expanding research and development and research training in this field.

(2) The need for new, improved methods of fertility regulation is widely accepted. The Task Force approach to collaborative research and development would provide an international mechanism that would focus the talents of experts from a number of countries on the development of new methods. The network of Research and Training Centres and Collaborating Clinical Centres would facilitate this effort.

(3) The need for a truly international mechanism to expedite clinical trials of new and existing methods of fertility regulation, simultaneously, in a number of countries is recognized. The WHO Collaborating Clinical Centre network would meet this need and would bring investigators from a number of countries together in a collaborative international effort. WHO is in a unique position to develop such a network of clinical centres.

(4) Reproduction research in a number of institutions could be substantially expanded and accelerated by the provision of additional equipment, project support and by the exchange of scientists between institutions. An expansion of WHO's contract and grant programme would make this possible.

(5) Scientists in many parts of the world experience great difficulty in obtaining current scientific information in a reasonable period of time. This problem enhances the scientific isolation in which they work. The proposed WHO International Documentation Centre would substantially reduce this obstacle.

(6) In a number of countries the lack of spare parts or reagents which are not available locally represents a serious constraint to ongoing research. This problem would be reduced by enlarging the WHO "spare parts" programme.

CONCLUSION

The WHO Expanded Programme of Research, Development and Research Training in Human Reproduction:

- identifies priority areas in which action is required
- presents a specific programme that would significantly expand and accelerate research, development and research training in human reproduction on a global basis
- proposes to establish a world-wide network of centres collaborating in a common research and development effort
- focuses on areas where WHO can and is prepared to contribute to the greatly expanded world effort required in this field.