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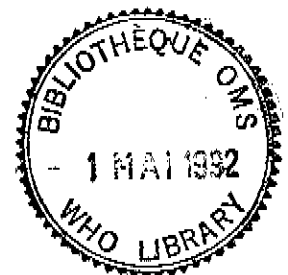
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TUBERCULOSIS CONTROL PROGRAMME

*REPORT OF THE SECOND MEETING OF THE
COORDINATION, ADVISORY AND REVIEW GROUP*

(Geneva, 22-23 November 1991)



*Tuberculosis Programme
WHO, 20 Avenue Appia, CH-1211-Geneva 27*

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1. CONCLUSIONS AND RECOMMENDATIONS

1.1 General

The CARG noted with great appreciation and pleasure that the World Health Assembly endorsed resolution WHA 44.8 which requests the Director-General to strengthen global tuberculosis control efforts. The CARG was also delighted to learn that WHO has identified the Tuberculosis Programme as a high priority of the Organization and has increased the level of the Global and Interregional regular budget of this Programme by more than one-third for 1992-1993, as compared to 1990-1991. Further increases in the regular budget for the Programme are expected in 1994-1995.

1.2 China TB Control Project

WHO and the World Bank have closely cooperated to successfully bring this US\$ 130 million project to implementation in only 16 months. With the help of their Chinese counterparts, the World Bank/WHO team designed a project which supports the National Tuberculosis Control Programme (NTP) through investments in 12 provincial tuberculosis programmes and for essential operational research and capacity building at the central and provincial level. Investments have been made for improving diagnostic services, chemotherapy, case management, and capacity building. Capacity building investments include the establishment of a national Tuberculosis Project Office and Tuberculosis Control Centre, provincial tuberculosis programmes (including dispensaries), a health education programme, training, vehicles and operational research capabilities.

The early success is encouraging and suggests that this model has the potential for furthering effective collaboration in support of revitalized NTPs. The CARG was very pleased to learn that similar projects are being planned for Bangladesh and India.

1.3 TB Control in the Face of the HIV Epidemic

The CARG noted with great concern the deterioration in the tuberculosis situation in Malawi and other African countries. Since 1985, the annual number of reported cases in Malawi has increased by 120%! This increase is thought to be due primarily to the occurrence of TB in HIV-infected persons, although cases among Mozambican refugees and increased case detection efforts by the successful NTP now in place may also have contributed.

The increase in the number of cases has created several problems for NTPs including crowding of tuberculosis wards and clinics, an increased risk of HIV transmission through streptomycin injections, an increased frequency of adverse drug reactions (especially to thioacetazone), and an increased case fatality ratio that undermines programme credibility.

The CARG urges the Programme, in cooperation with the Global Programme on AIDS, to address these issues as quickly as possible.

1.4 TB in Eastern Europe

TB continues to be a public health problem in many Eastern European countries. The situation in Romania was presented as an example. On the average, the annual incidence is 65 per 100 000 population, but wide variations have occurred among districts and populations groups, with very high rates among disfavoured minorities. Although short-course chemotherapy is used and the failure and relapse rates among new patients are not alarmingly high, there is

a large pool of chronic cases estimated to be responsible for 13-15% of all new infections in children. More than half of treatment failure is due to default from treatment, but drug resistance may be another major factor. Among retreated patients the failure rate is 24%. Only about 20% of patients who have failed on a retreatment regimen are later cured; 80% remain patients until they die -- on the average, 7 years after they failed on the first course of retreatment.

1.5 Drug Resistance

The CARG expressed great concern about the problem of resistance to antituberculosis drugs. It urges the Programme to institute surveillance of drug resistance at the global level and to take all possible measures to prevent a further increase in drug resistance through appropriate training in the use of antituberculosis drugs and in supervision of therapy. It was recommended that an expert group meeting be held to specifically address these issues and to devise programme activities in this area.

1.6 Drug Supplies

Adequate supply of anti-TB drugs of assured quality is crucial for implementing the Programme on a global scale. A number of problems related to the availability of antituberculosis drug supplies have been identified. The CARG endorses the activities of the Programme to date directed toward solving these problems and strongly urges the Programme to continue its important work in this area, including following up on Dr Velayati's offer to have drug producers in the Islamic Republic of Iran supply drugs to low income countries.

1.7 Progress of the Programme to Date

The CARG was very pleased with the performance of the Programme in the last 6 months and also commends the Secretariat on the reports it prepared and distributed at this meeting.

1.8 Management Structure

Recognizing the difficulty in developing a management structure that satisfies the desires of all interested parties, the CARG approved in concept the management structure proposal of the Secretariat. However, the CARG does request that the Secretariat reconsider some of the specific aspects of the proposal, such as the inclusion of NGOs within each management body, the exact size of the reconstituted CARG and the exact number of representatives from each group, the method of selecting CARG members by lot, the exclusion of developed countries from the CARG (unless they represented donor agencies), and the need to have the Technical and Research Advisory sub-Committee review operational, as well as research, activities of the Programme.

1.9 Workplan and Budget

The CARG was very pleased with the proposed workplan and budget and wholeheartedly approved proceeding with their implementation. Several donors, such as the Netherlands and Japan, expressed their intention to increase their financial support, others expressed their intention of at least maintaining their current level of financial support, and others hoped that financial support would soon be forthcoming. All participants indicated their moral support and interest in continuing their participation at whatever level was feasible for their organizations.

1.10 Recognition of Dr Rouillon

The CARG recognized the outstanding career achievements of Dr A. Rouillon, Executive Director of the International Union against Tuberculosis and Lung Disease, and wished her well on her retirement.

1.11 Next CARG Meeting

The next meeting date will be established by the Secretariat, taking into account the dates of the next IUATLD meeting and the World Congress on Tuberculosis.

2. INTRODUCTION

The second meeting of the Coordination, Advisory and Review Group (CARG) of the Tuberculosis Programme was held in Geneva from 22-23 November 1991. In addition to CARG members, participants included temporary advisors and representatives of various government agencies, United Nations organizations and specialized agencies, nongovernmental organizations, foundations, and private industry (Annex A). The meeting agenda (Annex B) was approved by all participants. The chairman of the meeting was Dr T. Shimao and Dr A. Salomao served as vice-chair. Dr D. Snider served as rapporteur.

The meeting was opened on behalf of the Director-General by Dr R.H. Henderson, Assistant Director-General, who noted that during the last six months since the first CARG meeting, both positive and negative events related to tuberculosis had occurred. On the negative side, during this period 1.5 million people died from tuberculosis and 4 million new cases occurred, unfortunately without drawing much attention from the world. Considering the rapid spread of the HIV pandemic, particularly to Asia, a "silent" escalation of the tuberculosis problem will inevitably occur unless urgent, coordinated and effective action is taken.

The positive aspects are that important progress has been made over the last six months at both global and country levels. Immediately after the first CARG meeting, the World Health Assembly (WHA) endorsed resolution WHA 44.8 which set clear global targets for the Tuberculosis Programme; namely to cure 85% of all detected sputum positive cases and detect 70% of such cases by the year 2000. To achieve this target, the WHA endorsed three basic strategies to be pursued:

- i) The Programme should effectively assist Member States in implementing the new TB control strategy -- emphasizing short course chemotherapy and the improvement of the treatment management system -- through primary health care services. This is based on the resourceful application of very cost-effective existing technologies.
- ii) In addition to control activities, the Programme should undertake operational research to improve TB service delivery as well as more basic research to develop new technologies.
- iii) The Programme should build a global coalition of all interested parties. This is essential to mobilize needed resources, and to effectively and efficiently use these resources to achieve the global targets.

Dr Henderson noted that, with the help of the Programme, more than 10 countries have started implementing the new strategy or are preparing plans for

a new strategy. One of these countries is China, where a US\$ 130 million TB project was started with a loan from the World Bank and with WHO's technical assistance. Another large project under preparation is a US\$ 30 million project for tuberculosis and leprosy control in Bangladesh which is supported by the World Bank and the Netherlands, with WHO providing technical and some financial assistance.

To implement the WHA resolution, the Programme Secretariat was asked at the first CARG meeting to develop the options for an appropriate management structure of the Programme and to propose a workplan and budget for the Programme. The CARG Task Force on Management Structure met this August and prepared the proposal and options for the management of the Programme. As requested by the Task Force, the Programme Secretariat prepared the more detailed proposals. WHO fully endorses the recommendations of the Task Force, which are as follows:

First, the main thrust of this Programme should be to assist Member States in their TB control activities. In support of this, WHO has identified the Tuberculosis Programme as a high priority of the Organization. For 1992-1993 WHO has increased the level of the Global and Interregional regular budget of this Programme by more than one-third, compared to the previous biennium. The Director-General has further identified this Programme as one of WHO's top priorities and has indicated a further increase of the regular budget for the Programme in 1994-1995.

Second, the Programme should be responsible for both control and research activities in order to ensure that research is maximally supportive of control activities. Finally, the Programme should actively collaborate with other relevant WHO programmes, in both control and research activities, to draw upon the broad experience already gained by a number of programmes.

Dr Henderson invited comments from all participants on the proposals that have been developed.

3. EXPERIENCE OF THE WORLD BANK/WHO ASSISTED CHINA TB CONTROL PROJECT

Mr. Richard Bungarner, World Bank, briefed the CARG on the background and progress made thus far in developing the TB control project for China. The WHO Tuberculosis Programme and the World Bank have cooperated closely and successfully in assisting China in bringing this large project to the stage of implementation in only 16 months. This model shows the potential for further effective international collaboration in support of revitalized national TB programmes.

China's Health Ministry had long acknowledged that TB was their most serious remaining infectious disease, but there was an absence of visible national action against TB.

The World Bank/WHO team found China's TB control system to be struggling under four broad categories of problems:

- (a) Case-finding problems
- (b) Chemotherapy and case management problems
- (c) Supervision problems
- (d) Recording, reporting and evaluation problems

The World Bank/WHO team assisted their Chinese counterparts in designing a project to deal with these problems. The project supports China's NTP through investments in 12 provincial tuberculosis programmes. Additional investment was made for essential operational research and capacity building at the central and provincial levels for programme implementation.

To provide an overall framework for the project, the teams had designed, and the Government has agreed to, a Tuberculosis Policy Package which addresses each of the main problems. The main features of the Policy Package provide:

- (a) Chemotherapy for eligible patients, all case-detection examinations and follow-up, free of charge to the patient.
- (b) Only approved short-course chemotherapy regimens will be stocked and prescribed by dispensaries.
- (c) All project provinces will use a new registry system and quarterly reporting system. Use of standardized forms will be enforced throughout all counties in project provinces.

The main subcomponents of the project are Tuberculosis Control investments, costing \$68.2 million, and capacity building investments, costing \$34.3 million.

The main elements for the tuberculosis control investments are:

- (a) Diagnostic Services.
- (b) Chemotherapy with five basic anti-tuberculosis drugs.
- (c) Case Management, including a new registry system and evaluation and supervision procedures and a patient and health care provider incentive system.

Capacity Building investments consist of five sub-components:

- (a) A Tuberculosis Project Office has been established in the Ministry of Public Health. A core group of full-time staff is responsible for implementation and supervision of the project at the national level. They will also provide training for provincial level supervisory staff, organize procurement of drugs and equipment, and monitor and evaluate overall progress of the project. The Project Office will be assisted by the Tuberculosis Control Centre which is responsible for coordinating the provinces in operational research, for the national reference laboratory and for national training programmes.
- (b) Provincial Tuberculosis Programmes will establish or reorganize dispensaries and be responsible for the overall programme. To improve bacteriological services and assure microscopy quality, a reference laboratory will be established in each province.
- (c) A Health Education Programme will support physician, patient and family commitment to complete the course of chemotherapy.
- (d) Programme Implementation. Regular, frequent supervision of the dispensaries at each level will be critical to ensuring implementation of the Policy Package. Vehicles, their operating costs, and incremental recurrent costs to undertake county-level supervision are provided in the project.

- (e) Training and Technical Assistance. Basic training equipment and space will be provided for each provincial training centre. The costs of conducting the training programmes and of materials are provided.
- (f) Operational Research will help improve management methods, TB control techniques and develop better control measures throughout project implementation. The WHO Tuberculosis Programme will provide guidance and support in this operational research programme.

Since 1 April, 1991 pilot programmes to develop and field-test chemotherapy, registry materials, supervision methods and operational procedures have been underway in five counties in Hebei province. Dr Spinaci summarized the encouraging early results achieved in these pilot counties as follows:

Among 165 new patients placed on short-course chemotherapy, 77% had sputum conversion after 2 months of therapy and 85% had converted after 3 months of therapy.

Among 298 retreatment cases, 62% had converted after 2 months of therapy and 66% had converted after 4 months of therapy.

Mr. Bumgarner said a number of lessons have been learned from this process:

- (a) External support to NTPs in developing countries is catalytic.
- (b) Tuberculosis seems to be a very important element in causing and perpetuating poverty. This is not well documented however, and more work is needed in this area.
- (c) Government support, even for difficult changes, can be forthcoming. Local governments and national level leaders are quick to lend support to needed programme changes and policy reforms once the whole picture is clear to them and the potential for progress becomes obvious.
- (d) Cooperation and coordination among the international agencies is important and possible.
- (e) National TB programmes need external cooperation and advocacy:
- to articulate the interests of developing countries;
 - to explain what can be achieved with existing tools;
 - to overcome a lack of consensus among health professionals and among public leaders about TB's importance and potential for control;
 - to support the development of a policy framework appropriate for an efficient and economic programme;
 - to coordinate and make available the best external assistance in a consistent way; and,
 - to mobilize and allocate the resources needed for TB control.

CARG members and participants were very pleased and encouraged by this collaborative effort. There was some concern about how this project will be expanded to the whole country. Success in a small number of areas is easier to achieve than on a larger scale. Concern was also expressed about the large number of retreatment cases and the possibility that drug resistance might be a significant problem in China. It will be important to monitor drug resistance in China at the provincial or central level, although the CARG agreed with the Secretariat that the first laboratory priority should be to improve microscopy in the periphery.

In response to questions, Mr. Bumgarner said that 12 provinces with a total population of over 550 million people could scarcely be considered a small area and that if the project is successful in those provinces, where the tuberculosis problem is the largest, it certainly will be expanded to the rest of the country.

4. TUBERCULOSIS CONTROL IN THE FACE OF THE HIV EPIDEMIC: MALAWI

Mr W. Nkhoma informed the meeting that reported cases of tuberculosis in Malawi had increased by 120% since 1985. Almost 12 000 new cases were reported in 1990 as compared to 5 000 in 1985. The largest rises have been seen in smear-negative and extra-pulmonary cases. There has, however, been a continued decline in the number of retreatment cases.

The upsurge in reported cases in recent years is in a large part related to dual HIV/TB infection. However, TB cases from an influx of 1 million Mozambican refugees and the favourable influence of the successful programme in attracting new patients may also be contributing to the increase. A few reports indicate that HIV infection among TB patients ranges between 25% and 50%. Most patients are young, economically productive and sexually active men and women.

The major consequences of this epidemic for the tuberculosis programme have been:

- i) overcrowding of tuberculosis wards;
- ii) an increased risk of HIV transmission through streptomycin injections;
- iii) an increased frequency of adverse reactions to antituberculosis drugs, especially thioacetazone; and
- iv) an increased case fatality ratio among tuberculosis patients that may undermine programme credibility.

To address these problems, the following measures have been recommended or implemented:

- i) ambulatory care of smear-negative and extra-pulmonary cases of tuberculosis, and staff education about the diagnosis of TB among HIV infected individuals;
- ii) limitation of the use of streptomycin to the greatest extent possible and the improvement of sterilization practices;
- iii) the replacement of thioacetazone by ethambutol for persons suspected of having HIV infection and increased emphasis on the prevention and early identification of adverse drug reactions;
- iv) staff, patient and community education and counselling on HIV/AIDS and the introduction of blinded HIV surveillance among TB patients.

5. TUBERCULOSIS IN AFRICA

Dr P. Eriki pointed out that, of the 650 million population in Africa, 171 million are estimated to be TB infected and 7 million HIV-infected, and 2.8 million may have dual infection with both TB and HIV. By the year 2000, it is estimated that 20 million people will be HIV infected. Steep increases in the incidence of tuberculosis have already been reported in several countries, including Mozambique, Zambia, Malawi, Tanzania, and Burundi. Even in Kenya where the total number of cases has not substantially increased, increases in cases in the 15-34 year age group are being seen. Thus, there is an urgent need to address the TB problem in Africa.

In response to questions, Dr Eriki said that there is no evidence that BCG vaccination is harmful to infants born to HIV-infected mothers. Thus, the WHO BCG vaccination policy should remain unchanged.

6. TB CONTROL IN EASTERN EUROPE: ROMANIA

The Problem: Dr P. Mihailescu reported that tuberculosis morbidity had decreased in Romania since 1949, but, in the past 10 years, TB incidence increased up to 64.6 per 100 000 in 1990. In some districts, an incidence of up to 100 per 100 000 has been reported. The total prevalence of infectious patients (new cases, relapses and chronics) increased by 17.1% between 1981 and 1990, reaching 79.9 per 100 000. This was associated with a 55.6% increase in tuberculosis among children.

Factors which contributed to the deteriorating situation include social and economic factors and an increase in the population of some minority groups, such as gypsies. There was a 3-fold increase in the number of gypsy children with TB within a 4-year period. Medical factors which contributed included a decreasing number of tuberculosis specialists, a lack of antituberculosis drugs, incorrect administration of treatment, and inadequate equipment and supplies for TB case-finding and diagnosis.

The NTP: Romania's NTP was implemented in 1977. There are 199 out-patient clinics (one clinic per 115 000 inhabitants), each clinic covering an area not exceeding 100 km in diameter. There are 11 578 beds for tuberculosis, which is excessive. Of the total tuberculosis budget, 85% to 88% is allotted these beds; only 12-15% remains for the out-patient activities. Short-course chemotherapy is used in Romania: HRSZ for 3 months, followed by HR for another 3 months, given twice weekly from the very beginning.

Recent evaluations (1986-1987) revealed low rates of therapeutic failures (4.9-5.2%), and of bacteriological relapses (2.7-2.8%), but failures in re-treated cases occur in up to 24%. The main cause of failures, present in more than 50% of cases, was drug default; 14.7% of patients did not follow their out-patient treatment after discharge from hospital, 21.3% gave up their treatment before the sixth month, and 17.3% had irregular drug intake. Drug resistance was found in 18.9% of investigated failure cases. The presence of TB-associated diseases such as diabetes mellitus, silicosis, psychiatric diseases and alcoholism was also associated with treatment failure.

The large majority of chronic patients are unemployed, homeless, and suffer from alcoholism. Their treatment is difficult, and cure is only obtained in about 20% of cases. Most of them die of TB or other diseases. The average duration of survival (from chronicity to death) is 7.3 years. Chronic cases are long-lasting sources of infection and responsible for the infections in 13-14% of all children with primary tuberculosis registered yearly.

Recommendations: To improve the present situation, it will be necessary to elaborate a new NTP which includes the following measures:

- i) A reduction in the number of beds in TB hospitals and sanatoria. Money, equipment and staff becoming available should be used for the reorganization and consolidation of TB clinic out-patient activities.
- ii) The provision of all TB units with modern equipment (for X-ray, MMR, microscopy and culture) and the re-organization of bacteriological

laboratory services for M. tuberculosis, providing them with the necessary reagents and re-training of the personnel.

- iii) The standardization of TB treatment which is to be applied uniformly all over the country. The quantities of drugs necessary should be guaranteed at national level and optimally distributed in all districts. In this respect, a central stock of TB drugs should be constituted, for all the requirements of the field.
- iv) The provision of single-use syringes and needles for streptomycin injections and BCG vaccinations.
- v) The development of operational research capabilities and a research plan for the Pneumophtisiology Institute, Bucharest, to identify better solutions to the present problems in tuberculosis.

In response to questions, Dr Mihailescu said that HIV infection was not playing a major role in causing the increase in tuberculosis in Romania, although tuberculosis has occurred in association with AIDS in 58 children.

7. DRUG RESISTANCE, DRUG SHORTAGES, AND DRUG DEVELOPMENT IN THE UNITED STATES

Dr D. Snider reported that the number of tuberculosis cases reported annually in the United States has increased by 16% since 1985. The largest increases have occurred in the 25-44 year age group, the age group in which the largest number of AIDS cases have occurred. In addition, during the past two years, several outbreaks of multi-drug-resistant tuberculosis have occurred, especially among HIV-infected persons. Resistance to isoniazid and rifampin was most common. Increased risk of nosocomial transmission of drug-resistant organisms to patients and health care workers has been documented in facilities where HIV-infected persons receive care. Mortality from multi-drug-resistant TB has been high. Preliminary data indicate that about 34% of TB patients in New York City are excreting drug resistant organisms; 19% with organisms resistant to isoniazid and rifampin (30% of previously treated patients and 8% of new cases). Preliminary data from national drug resistance surveillance indicates that 13% of all cases tested have drug resistant organisms -- 3.5% resistant to isoniazid and rifampin. Drug resistance is seriously compromising TB control efforts in several areas of the country.

Concurrently with the increase in cases and the increase in drug resistance, there have been shortages of antituberculosis drugs including isoniazid, ethionamide, cycloserine, capreomycin, streptomycin, and PAS. The non-availability of these drugs in the U.S. has been attributed to several factors:

- 1) sole suppliers of bulk product,
- ii) sole suppliers of finished drug product,
- iii) no national surveillance of drug supplies,
- iv) a failure of some manufacturers to meet U.S. Food and Drug Administration requirements,
- v) limited financial incentives for drug companies to continue production of anti-TB drugs.

Because drug companies see little financial incentive to produce anti-TB drugs, new drug development has not occurred. Several methods for promoting new drug development have been proposed. These will be discussed at a meeting planned for 1992 and co-sponsored by the American Thoracic Society and the

Pittsfield Antituberculosis Association. Dr Snider invited WHO to join in this meeting.

8. ISSUES IN ANTI-TUBERCULOSIS DRUG SUPPLY

Ms D. Weil discussed issues in anti-tuberculosis drug supply. The WHO global strategy for tuberculosis control is based on the ability of NTPs to quickly identify and cure infectious TB patients using short-course chemotherapy (SCC). This requires the uninterrupted supply of four or more anti-TB drugs of assured quality at affordable prices and the distribution of these drugs on time to patients in need. Drug costs represent 20-40% of the budget of most NTPs.

Drug shortages can be caused by: (i) unexpected variations in consumption; (ii) the late purchasing of drugs; (iii) the unavailability of supplies in the pharmaceutical market; (iv) delays in the drug distribution chain. Each of these potential problems needs to be addressed by NTPs, with external technical assistance and financial support if required.

Three fundamental concerns relating to supply of anti-TB drugs need to be examined at the international level:

- i) accurate global forecasting of drug needs,
- ii) production of drugs of assured quality,
- iii) adequate financing for drug supply and low-cost drug procurement.

8.1 Global Drug Need Forecasting

WHO estimates that US\$ 93 million should have been spent in 1990 for drugs to treat the patients detected in developing countries, with 45% of these expenditures in WHO's South East Asia Region. More accurate drug forecasting models need to be developed to estimate quantities of drugs required, and their associated costs, to assist in global planning and national planning for tuberculosis control.

8.2. Drug Production, Cost, and Quality Assurance

Production: The Programme's Secretariat has made a first, but limited, attempt to compile a list of anti-TB drug producers. There are a very limited number of companies that regularly produce anti-TB drugs, and all rely on an even more restricted number of bulk product suppliers.

Anti-TB drug production is not generally looked on as a highly attractive area within the pharmaceutical field. It is not a big profit-maker. Limited demand for both first and second-line drugs in the last decade has meant that there are few incentives to maintain a major role in the market. As national TB control initiatives improve and expand, the expressed demand for drugs in the international market should grow, but still new strategies and mechanisms may be needed to assure continuous drug supplies.

Drug Costs: The estimated cost for a full course of SCC for one new sputum smear-positive patient with a WHO-recommended regimen is between US\$ 22 and US\$ 66, depending on the regimen used. However, there appears to be an important gap between these lower prices available in the international market and the prices actually paid by many countries. In some countries, drug costs are increasing. Major suppliers suggest that, without a great increase in demand, the prices of anti-TB drugs may rise with general inflationary

pressures. At the international level, UNICEF Supply Division and International Dispensary Association (IDA) prices since 1988 for rifampicin and pyrazinamide, two of the most costly drugs, have decreased in the last few years.

One factor that could increase the basic cost of drugs is a possible shift in drug packaging requested by NTPs. There is increasing interest in the use of blister-packaged anti-TB drugs in order to increase the ease of treatment administration both for the provider and for the patient, and to thereby increase compliance.

It is hoped that the increased demand for anti-TB drugs, that should accompany revitalized global control efforts, will lead to a decrease in the price of final products.

Quality Assurance: To ensure that drugs are safe and efficacious, the quality of bulk product and final drug formulations must be assured. Recent research suggests that the bioavailability of rifampicin in fixed combination tablets is probably the most important quality concern. The greatest problems, detected in serum bioavailability testing, have been associated with some of the isoniazid/rifampicin/pyrazinamide fixed combinations available in the international market. Because bioavailability testing is too expensive for most developing countries, independent research is needed to assess a wider range of the rifampicin formulations on the market to help determine whether some formulations must be avoided and where the greatest problems lie. In addition to drug bioavailability, the stability of drug formulations, especially in tropical climates, needs to be evaluated.

Over the last twenty-five years, WHO and other agencies have developed a number of measures to improve the capacity of developing countries to assess the quality of drugs imported or produced locally. One of the most important has been the development of standards of Good Manufacturing Practices (GMP), as adopted by the 28th World Health Assembly in resolution WHAT28.65. Countries can use GMP standards as one basic criteria in choosing from among suppliers. WHO has also developed a Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce, the most recent revisions of which are pending approval of the World Health Assembly. One hundred thirty countries have agreed to participate in the Scheme.

A number of programmes within WHO, in collaboration with representatives of the pharmaceutical industry and other institutions, are working to assist developing countries in improving local quality control facilities, including provision of training and equipment. With this assistance, more countries should become capable of carrying out some basic quality assurance tests on imported drugs, or drugs procured through contracts with local suppliers. There is also interest in the industry and in WHO to develop new lower cost, and less technology-intensive, methods of monitoring drug quality that may be applied in developing countries.

8.3 Drug Supply Financing and Procurement

Financing: One of the principal problems facing most NTPs, as well as essential drug programmes in general in developing countries, is the lack of available financing for drug procurement. There are a range of options for financing drug supplies:

- i) government covers all drug costs (with or without cost recovery from TB patients),
- ii) donor agencies and/or NGOs cover all costs,

- iii) governments and donor agencies/NGOs jointly cover costs,
- iv) state or provincial authorities are partially responsible for financing.

The Drug Procurement Process: There are a number of procurement approaches, used by governments, donors or independent agencies:

- i) direct procurement from local or international suppliers;
- ii) negotiated procurement with local or international suppliers;
- iii) open or restricted local tenders;
- iv) open or restricted international tenders.

Use of Procurement Agencies: There are a number of not-for-profit agencies that procure essential drugs, including anti-TB drugs, for sale at affordable prices to developing countries. These include the UNICEF Supply Division, IDA, as well as WHO and PAHO who both provide reimbursable procurement services for Member States. These agencies have the capacity to play a larger role in anti-TB drug procurement, and each has obtained relatively low prices for anti-TB drugs over the past few years. Another benefit of purchasing drugs through these procurement agencies is that they have adopted quality assurance measures suggested in the WHO Certification Scheme, and commission independent testing when necessary.

Although not acting as a formal procurement agency, the IUATLD has played a particularly important role in providing anti-TB drugs to NTPs with which it is working. Financing for these supplies is provided by bilateral agencies. Another organization that has purchased anti-TB drugs for a number of countries is the German Leprosy Relief Association (GLRA). These supplies have generally been targeted to TB control services in areas where leprosy control activities are very active and supported by the GLRA.

Joint Drug Procurement: It has been frequently suggested that NTPs would benefit from opportunities for joint procurement of anti-TB drugs. Joint procurement means that a number of countries or institutions jointly develop drug supply orders and place unified tenders, or negotiate as a group with suppliers. There are a number of important benefits of joint procurement among countries:

- i) the choice of suppliers may improve because of the larger size of orders;
- ii) prices may be reduced, or volume bonuses provided with larger purchases;
- iii) quality assurance may be facilitated by group scrutiny of potential suppliers, and joint use of available quality control facilities;
- iv) longer term contracts with suppliers may be possible, further increasing opportunities for discounted or stabilized prices;
- v) delays in supply might also be reduced if suppliers receive more secure contracts and spaced delivery dates to make possible more regular production cycles.

There are several examples of successful joint drug procurement in North Africa, the Eastern Caribbean, and the IUATLD. Barriers to joint procurement may include the difficulty in obtaining government agreement for collaboration, or perceived difficulties in separating anti-TB drug purchases from other drug procurement. The major barrier to entrance into effective joint procurement arrangements, without external financing, is likely to be the lack of hard currency or secure financing to guarantee participation in joint orders, or to make possible longer-term contracts.

8.4 Proposed Programme Activities for Improved Anti-TB Drug Supply

The Programme is conducting and planning a range of activities to improve anti-TB drug supply as part of its National Programme Support activities: (a) developing a database on global anti-TB drug production capacity; (b) assessing current drug procurement and distribution practices in developing countries; (c) developing models for drug forecasting; (d) addressing drug supply and distribution issues in training, monitoring and programme review activities; (e) conducting relevant operational research; (f) facilitating drug financing and procurement; (g) assessing the feasibility and efficient approaches for joint procurement and/or revolving funds; (h) supporting bioavailability testing and improving low-cost methods of drug quality assurance in developing countries; and (i) coordinating with related programmes at the international level, especially the WHO Action Programme on Essential Drugs and Pharmaceuticals Programme.

In its Proposed Programme Budget for 1992-93, the Programme proposes the addition of one professional to the Secretariat staff to deal exclusively with drug issues.

8.5 CARG Reaction to Drug-Related Issues

CARG members expressed strong agreement with the Secretariat that ensuring adequate supplies of anti-TB drugs of assured quality at reasonable prices should be a high priority of the Programme. The lack of hard currency is a problem for many countries. However, countries sometimes use their hard currency to buy both essential and non-essential and useless drugs. It is important for the Programme to work with the Action Programme on Essential Drugs (DAF) to help countries develop a more rational drug procurement policy. CARG also supported the Programme's efforts to coordinate this work with other WHO programmes with experience and expertise in this area.

Participants were alarmed by the reports of significant levels of drug resistance in Member States. Monitoring for drug resistance must be implemented on a global scale. The available information would suggest there may be significant levels of drug resistance in Asia. Standardized and stable policies for treatment and case management should be developed and followed to prevent further increases in drug resistance. Proper supervision of therapy is crucial for a successful NTP. Strict control over anti-tuberculosis drug supplies to prevent their being used for other purposes or sold on the black market is also essential.

The Secretariat agreed with these recommendations from CARG members and assured CARG members that many of these issues are being addressed in WHO training modules and through collaboration with other relevant WHO programmes. Programme plans do include monitoring drug resistance in the coming years.

9. PROGRESS REPORT

Dr A. Kochi reported on the progress the Programme made over the last six months in the following programme areas: National Programme Support, Operational Research, Research and Development, and Management and Coordination.

9.1 National Programme Support

There are two principal elements of National Programme Support: basic support and intensified support.

Basic support offered to all Member States on request. Activities were undertaken in three categories of basic support:

- i) Development and provision of crucial tools for effective implementation of NTPs. The Programme has developed new treatment guidelines, completed two reports which were included in the background documents of this meeting, and developed the "Report on TB Elimination in the Countries of Europe and Other Industrialized Countries", in cooperation with the IUATLD.
- ii) Seminars and training courses. Training modules for mid-level managers were developed and will be reviewed by outside experts. The modules will be ready for field testing in April 1992.

Two seminars were held in Zimbabwe and Venezuela, one of which was organized by the IUATLD with WHO assistance, and financed by Merrell Dow. Programme managers from more than 30 countries learned about the new TB control strategy.

International training courses, with support from WHO, were continued in Algeria, India and Japan and WHO provided support to a new training course organized by the IUATLD which offers participants the opportunity to directly observe the well-organized NTP in Tanzania.

- iii) Ad hoc review of global anti-TB drug supply.

In more than 10 countries a new TB control strategy was implemented with intensified support offered by the Programme, or preparation for its implementation was made. Generally speaking, intensified support includes the following steps:

- i) receipt of a request for assistance from a country;
- ii) initial exploratory visit to assess the overall situation and the feasibility of providing assistance;
- iii) technical mission(s) to prepare a project plan (including selection of technical strategies, preparation of NTP training materials, information systems and forms, etc.);
- iv) provision of limited financial support until other external resources are received;
- v) mobilization of external resources;
- vi) follow-up visit every 6 months to assess the progress.

9.2 Operational Research

A WHO-supported cost-effectiveness analysis of alternative supervision methods for application of short-course chemotherapy was completed. A revised version of the study report was published in The Lancet in November.

A study was initiated on the costs, effectiveness and cost-effectiveness of short-course chemotherapy in Botswana, a middle-income developing country. Data collection has been completed, and analysis has been initiated.

A "directed" intervention study was initiated in cooperation with the Government of Thailand and experts from the Netherlands. In four provinces, the study will investigate the feasibility of different case-finding and treatment approaches which can be undertaken by fully utilizing the relatively well-developed health infrastructure in Thailand.

An intervention study was initiated in Malawi to assess the effectiveness of the newly implemented treatment guidelines for smear-negative and extra-pulmonary cases. The study will also seek to develop strategies to overcome service delivery problems in the face of the HIV pandemic.

9.3 Research and Development

In collaboration with GPA, 14 research projects are currently under-way in Africa, Latin America and the Caribbean. These include 4 epidemiological studies, 5 clinical studies, 1 BCG study, and 4 preventive therapy studies.

Two ongoing surveillance studies to monitor the seroprevalence of HIV infection in tuberculosis patients, in Uganda and Tanzania, are being supported. Preliminary results indicate overall HIV infection prevalences of 50 percent and higher in both countries. A companion study in Tanzania to determine the impact of HIV on transmission of tuberculosis suggests that, despite the doubling of cases in 7 years, the transmission of TB infection measured in the form of the annual risk of infection, has not increased. This finding gives hope that effective NTPs such as that in Tanzania, which have achieved an 80% cure rate and 65% case-detection rate, can help prevent increased TB transmission in the face of the HIV pandemic.

A study of the risk of tuberculosis among postpartum women in Rwanda with TB/HIV co-infection has shown that this risk is approximately 5% per year.

Studies are under-way to provide more accurate information on the clinical presentation of both tuberculosis and other pulmonary diseases in HIV infection, to evaluate the role of serological diagnosis of tuberculosis in HIV infection, to study the efficacy of short-course therapy and long-term, post-treatment suppressive isoniazid, and to obtain information on diagnosis and treatment of tuberculosis in children with HIV infection.

A study of BCG in the newborn suggests that vaccination does not pose undue risks in children with HIV infection, providing support for the WHO policy on the use of BCG in areas where HIV infection is prevalent.

Finally, the Programme is supporting, with the financial assistance of the Global Programme on AIDS, both efficacy studies of isoniazid and short-course preventive chemotherapy and feasibility studies of isoniazid preventive therapy to determine if this intervention may help to stem the tide of HIV-associated tuberculosis.

In the area of new drug development, the Programme has supported a study demonstrating the remarkable antituberculosis activity of a new quinolone derivative, sparfloxacin, in a mouse model of tuberculosis, and the Programme is continuing to support additional studies of this compound.

In collaboration with IMMTUB, the Programme is supporting an evaluation of the usefulness of PCR in the diagnosis of paucibacillary tuberculosis, as well as studies of the application of RFLP to epidemiological studies.

9.4 Management and Coordination

Two major activities have been undertaken over the last 6 months as requested by the first CARG meeting. One is the development of a proposed management structure of the Programme, with the help of the CARG Task Force on Management Structure and the help of other WHO programmes, and four documents were prepared which will be discussed in the next session.

The document "Proposed TB Control Programme Work Plan and Budget: 1992-1993" was prepared. To develop the work plans for operational research and research and development activities, two task force groups were organized and consisted of a number of outside experts and the Programme staff. The group for Operational Research was chaired by Dr Christopher Murray, and Dr John Grange chaired the group for Research and Development.

In addition to the help of outside experts and short term consultants, the Programme has 12 professionals and 6 general service staff at the Regional Offices and at Headquarters, which include short term professionals and temporary secretaries. The Secretariat is confident that this staff can successfully implement the proposed activities for the next biennium, supported by a modest number of additional staff to be recruited in the next two years.

9.5 CARG's Response

The CARG was pleased with the progress report of the Secretariat and commended the staff on the quality of their presentations and reports.

10. MANAGEMENT STRUCTURE

At its meeting on 2-3 May 1991, the CARG established a Task Force to advise on the management structure of the Programme. The Task Force (CARG-TF) met on 15-16 August 1991. It reconfirmed the principle endorsed at the CARG meeting of 2-3 May 1991, that the major thrust of the Programme encompassing all levels of WHO should be to foster and facilitate effective NTPs. It endorsed the scope, balance and management principles of the Programme proposed by the Secretariat, namely:

- i) The Programme should undertake activities in three major areas: support to NTPs, operational research and research and development;
- ii) an appropriate balance of the Programme budget would be approximately two-thirds to support for disease control and one-third to research, including research/development and operational research;
- iii) to ensure that research activities are maximally supportive of disease control, the three activity areas mentioned above should fall under the same overall management; and
- iv) the Programme should seek active collaboration with all relevant programmes in WHO.

The CARG-TF requested the Secretariat to develop more detailed proposals in response to its conclusions and recommendations. These proposals are briefly summarized here. All these proposals incorporate CARG-TF suggestions.

The proposed revised terms of reference for a reconstituted CARG, including a Standing Committee, were presented. In the interests of simplifying operational procedures, the Secretariat proposed that the CARG adopt a process for drawing lots for selecting CARG Members from TB "endemic" countries, taking geographic balance into consideration. For those donors contributing extrabudgetary resources, it is proposed that members of the CARG be chosen based on size of contribution.

The Task Force identified two options in regard to overview of the Programme's scientific and technical activities.

- i) creation of a body as a "sub-committee" of CARG specifically for the Programme; or
- ii) utilization of existing overview bodies of other programmes with appropriate modifications (such as TDR-STAC, EPI-RDG, CDD-TAG, ARI-TAG, PVD-SAGE, etc.) for this purpose.

The Secretariat assessed these options and recommends that a Technical and Research Advisory sub-Committee of the CARG (TRAC) be created to advise and report to the CARG on both scientific and technical aspects of tuberculosis control.

10.1 Management of Operational Research

In regard to operational research, most CARG-TF Members shared the view that the primary responsibility should lie with the Programme but that collaboration with other programmes would be beneficial if acceptable working arrangements could be devised. The following three options were proposed by the Task Force for the CARG's consideration:

- i) vesting responsibility for its management solely with the Programme, on the understanding that this includes the obligation to consult and collaborate with all other relevant WHO programmes with experience in operational research (e.g. CDD, EPI, ARI, TDR, HSR, DAP, etc.); or
- ii) joint responsibility with one other WHO programme, chosen from among those with experience in operational research, including but not limited to CDD, ARI, TDR, EPI, HSR, GPA, etc.;
- iii) joint responsibility with a number of other WHO programmes chosen from those listed under (ii).

The Secretariat evaluated these options and proposes adoption of option (i) for management of operational research.

10.2 Management of Research and Development

In regard to the research and development component of the Programme, the CARG Task Force endorsed the concept of two steering committees: one for basic mycobacterial research (immunology, molecular biology, etc.), and another on drug development. These would be organized jointly with the relevant steering committees of other programmes, including TDR, GPA and PVD. It requested the

Secretariat to make specific proposals to the CARG for the execution of this joint responsibility after full consultation with other relevant programmes.

The range of options considered with regard to management of research and development for tuberculosis control included the following:

- i) scientific, administrative and financial management provided solely by the Programme;
- ii) management provided solely by TDR, which would require a change in the TDR mandate;
- iii) joint management by GPA, PVD, TDR and the Programme, made possible through consolidated steering committees;
 - (a) without changing TDR's mandate, or
 - (b) changing the mandate of TDR so that funds could flow to tuberculosis research projects also through TDR.
- iv) management of tuberculosis and leprosy research in a consolidated fashion by CDS. This option requires a change in the TDR mandate.

However, Option (ii) is not considered appropriate on the grounds that: (a) WHO's position is that the Programme should have a dual focus on control and research, as endorsed by the Forty-fourth World Health Assembly¹; (b) the CARG and CARG-TF endorsed the principle that both control and research activities should fall under the same management.

Option (iii)(b) would be attractive if the change in TDR's mandate led to an expansion of total available resources for the Programme's activities in research. TDR's Standing Committee recently decided that Option (iii)(b) would not be recommended. Thus, WHO suggested Option III(a).

A possible modus operandi for this option had already been worked out by the programmes concerned in WHO.

This option is administratively rather complicated due to the involvement of four programmes (GPA, PVD, TDR and the Programme), but it is an economical way for the Programme to expand TB research and development activities.

10.3 CARG's response to management structure proposals

The proposals regarding the management structure were vigorously debated. The Secretariat received a number of suggestions and comments on the management structure proposals which will be taken under consideration in developing the final details of the structure. The Secretariat reassured participants that the change in the constitution of the CARG and the terms of reference for the new CARG would be consistent with resolution WHA 44.8 and that the Director-General would appropriately reconstitute the CARG with input from the Programme.

¹ "The Forty-fourth World Health Assembly...ENDORSES the dual approach of action and research adopted by the programme as the best means of achieving a reduction in tuberculosis mortality and morbidity," in WEA44.8.

The composition and the method of selecting members of the new CARG was extensively discussed. There was complete agreement with the general approach of having broad geographic representation, a large representation of members from high prevalence countries, significant representation from donor agencies, and representation from NGOs. Heavy involvement of NTP managers from developing countries will help ensure that the Programme remains focused on the needs of developing countries and will potentially ensure more rapid implementation of the global programme. Donor agency involvement is necessary to ensure continuing financial support.

There was a general concern that the proposal for reconstituting the CARG would not give the Secretariat enough flexibility in selecting the most appropriate number of CARG members. There was also a concern that tuberculosis experts from developed countries would be excluded since donor agencies might send representatives with other kinds of expertise. Several participants felt strongly about including tuberculosis experts from developed countries on the CARG. Increasing the size of the CARG to accommodate this was suggested. Regarding the role of the WHO regional offices in selecting members, regional offices will be consulted in an informal way but will not make formal nominations. Permanent representation of the IUATLD on the CARG was supported by many participants. It was decided that IUATLD would certainly be invited to serve on the CARG, but that permanent membership status would not be granted automatically for any organization since circumstances in the future are impossible to predict.

Another significant aspect of the proposal which received several comments was the need to clarify more fully the responsibility of the Technical Research Advisory sub-Committee to review regularly the operational aspects of the Programme in addition to the research activities. In addition, it was suggested that NGOs should be included within each of the bodies of the Programme, especially the scientific bodies. NGOs can also encourage and prepare the groundwork for WHO involvement in a country.

The importance of collaboration and coordination between the three research steering committees was emphasized.

The Secretariat's proposal on management of the Research and Development component of the Programme was the most vigorously debated. Some participants stated that the Secretariat's proposal will make it impossible for the TDR Programme to solicit and use funds from donors to conduct tuberculosis research and development activities. They also stated that TDR has an excellent reputation among many donor agencies in carrying out high quality scientific activities and also has a Product Development Unit and an organized operational research network. Therefore, some donors would prefer to channel funds for tuberculosis research into the TDR Programme, and some of these may choose not to contribute, at least at the present time, because the Programme does not have a proven track record with regard to research. However, many participants and donors recognized the importance to ensure research activities being maximally supportive of disease control, thus they felt that it is in the best long-term interests of the global tuberculosis control effort that the Programme retain responsibility for Research and Development. Also, the Secretariat indicated a willingness to modify the management structure should future conditions indicate it is necessary to do so.

11. WORKPLAN AND BUDGET

The Secretariat presented its proposed workplan and budget for 1992-1993.

11.1 Workplan

The proposed priority areas of the Programme for 1992-1993 are:

- i) To establish and strengthen the Programme with an effective and flexible management structure that is open to outside input. The Programme should provide effective leadership in global coalition building. This is the key for mobilizing the necessary resources and using the resources effectively and efficiently.
- ii) To undertake aggressive advocacy activities to create awareness and a sense of urgency among all Member States, other UN agencies, bilateral agencies, NGOs, scientists and the general public.
- iii) To provide technical, managerial and information assistance to all Member States in order to narrow the gap among countries in technical understanding and expertise.
- iv) To provide intensified support to a limited number of Member States to assist them in establishing effective NTPs.
- v) To assess the current global situation of anti-TB drug supply, including production, quality assurance, procurement, delivery and consumption.
- (f) To undertake targeted research and development activities that will yield results in 3-5 years.

The Programme will collaborate with other parts of WHO (including Regional Offices and related programmes), Member States, donors, NGOs, and others in carrying out this workplan. Collaboration with other WHO programmes will extend the range of available technical inputs beyond those which could be obtained solely with the Programme's resources, and is thus an efficient use of overall resources provided to WHO.

11.2 Budget

This is the first time that the Programme has presented, independently of the WHO budget, a consolidated biennial work plan and associated budget. The general format for the budget was developed after consultation with the CARG Task Force in August 1991. In developing the proposed work plan and the associated budget, activities were considered at the levels used for the formulation of the WHO Programme Budget: Country level; Regional and Inter-country level; and Global and Interregional level.

At its meeting in May 1991, the CARG requested the Secretariat to prepare budgets relating to different levels of programme activity. Following a detailed review of the likely financial situation of the Programme in 1992-1993, it was decided to offer budgets at two levels of activity: these are termed the "Proposed Programme Budget" (PPB) and the "Contingency Budget" (CB), the latter being set to anticipate an approximate 20% shortfall in resources. The proposed Contingency Budget for 1992-1993 is US\$ 14 927 700.

For 1992-1993, the total PPB is US\$ 18 545 400 of which \$ 4 179 300 is assured from the WHO Regular Budget. The more direct forms of support to national initiatives in tuberculosis control amount to approximately two-thirds of the total budget (Country level activities, including country-specific operational research, 34%; Regional and Intercountry level activities, 14%; and the National Programme Support component of "Headquarters" activities, 16%). Approximately one-quarter of the PPB is allocated to globally-managed research activities ('global' Operational Research, 8%; and Research and Development, 14%). The balance covers Programme Management and Coordination (9%) and costs for Administrative Support Services (5%). Country-specific and 'global' Operational Research together account for approximately 16% of the total budget.

The distribution of the overall budget among WHO budget elements shows the predominance of funding for operational support (58%), followed by Programme management--mostly staff--(36%), and meetings (6%).

Because the Programme was operating from a small base (less than US\$ 2 million per year) prior to 1990, the budget of the Programme has almost doubled over the last two years. The proposed budget for 1992 will be 91% larger than that of 1991, and that of 1993 will be 31% larger than that of 1992.

The main consequence of the Contingency Budget is a slow-down of the effective support to NTPs. Its other consequence is the significant reduction of funds for research and development and 'global' operational research activities in order to preserve the proportion of the total budget devoted to direct support to NTPs.

11.3 Financial situation of the Programme

Financial resources for supporting the proposed Programme for 1992-1993 derive from various sources:

- i) WHO Regular Budget allocations for 1992-1993;
- ii) extrabudgetary funds carried over from the 1990-1991 biennium;
- iii) extrabudgetary income anticipated in 1992-1993, which also includes contributions earmarked to the Programme through other WHO programmes;
- iv) other income (such as interest).

Under category (i), the WHO Regular Budget allocations for tuberculosis totals US\$ 4 179 300, of which US\$ 2,477,500 is at Country level, US\$ 302,600 at Regional and Intercountry level, and US\$ 1,399,200 at Global and Interregional level. This distribution and the procedures used to manage Regular Budget funds will remain unchanged. Activities to be supported by Regular Budget funds are fully "preserved" in the Contingency Budget.

Under category (ii), it is estimated (as of 23 November 1991) that a balance of US\$ 532 700 will be available from prior extrabudgetary contributions to WHO/HQ at 31 December 1991.

Under category (iii), anticipated extrabudgetary income for 1992-1993 from firm pledges (as of 23 October 1991) for undesignated contributions and from designated contributions for activities in the Proposed Programme Budget, is estimated at approximately US\$ 3 750 000, taking into consideration the fluctuation of the exchange rates.

Under category (iv), income accrued on extrabudgetary contributions amounting to US\$ 59 600 will be credited to the Programme in 1992.

The Programme's anticipated financial status for 1992-1993, estimated on 23 November 1991, is shown in Annex C.

As of 23 October 1991, the apparent shortfall in resources for financing the PPB is US\$ 10 023 800 for the full plan of activities, or US\$ 6 406 100 at the contingency level.

It is expected that the apparent shortfall in resources will be reduced by:

- i) Pledges for 1992 and/or 1993 from previous donors to the Programme who have not yet indicated the size of their contributions for these years;
- ii) pledges from previous donors who have not yet pledged for the second year of the 1992-1993 biennium;
- iii) increased pledges from existing donors; and
- iv) pledges from interested parties who have not yet contributed to the Programme.

11.4 CARG's response to the budget, workplan, and financial situation

Overall, participants were very pleased with the proposed workplan and budget which they felt was clear and professionally and fairly presented. The Secretariat has the endorsement of the CARG to proceed with the implementation of these plans.

The Secretariat responded to numerous questions about the proposed workplan and budget, clarified areas of interest and concern, and described the proposed work and budget in greater detail. The importance of operational research, especially at the NTP level, for evaluating and improving control programme activities was clarified and re-emphasized.

The absence of secretarial support at the regional level was of some concern. The demands of the proposed workplan on headquarters, regional, and intracountry personnel was of concern. The Programme was urged to allow staff sufficient time to learn how best to articulate the Programme and provide the best assistance.

The lack of information on multilateral contributions to NTPs was a concern. The Secretariat will try to obtain this information.

There was some concern expressed that some research projects may not yield useful results in the short term. Several members urged that increased emphasis be placed on preventing the emergence of drug-resistant organisms. A number of suggestions were made for addressing this problem, such as including academic centres in WHO training programmes. The Secretariat was asked to convene an expert group to address the problem.

Several donors, such as Japan and the Netherlands, expressed their intention to increase financial support. Others expressed their intention at least to maintain their current level of support. All donors indicated a strong desire to remain involved with the Programme with the hope that financial support could be forthcoming in the future.

12. DR VELAYATI'S COMMENTS

During the course of the meeting, His Excellency, Dr Ali Akbar Velayati, Minister of Foreign Affairs of the Islamic Republic of Iran, addressed the CARG. Dr Velayati urged WHO to strengthen microscopy at the peripheral level, establish regional reference laboratories, improve access to drug supplies, establish TB/HIV committees in each WHO region, and supply the latest and best diagnostic techniques and facilities. The Islamic Republic of Iran offers to cooperate with WHO to expand production of BCG and tuberculin, provide antituberculosis drugs to low income countries at a low price, and establish a regional reference centre to provide technical assistance and training.

13. RECOGNITION OF DR ANNIK ROUILLON

After serving for 12 years as Executive Director of the IUATLD, Dr Annik Rouillon is retiring. The WHO Secretariat, CARG members, and all meeting participants, in recognition of her long and distinguished career in the fight against tuberculosis, and especially her contributions to the establishment of the new global TB programme, gave her a standing ovation and wished her a pleasant and happy retirement.

14. NEXT CARG MEETING

Dr Henderson suggested that the next meeting should last 3 days since there will be much work to be done. Several members indicated a preference for next November in close proximity to the time of the IUATLD meeting. However, conflict with the World Congress on Tuberculosis, to be held in the Washington, D.C. area in the U.S.A. from 16-19 November 1992 should be avoided.

ANNEX A

LIST OF PARTICIPANTS

CARG MEMBERS

| | |
|-----------------------|--|
| Dr B. Bloom | Professor, Department of Microbiology & Immunology, Albert Einstein College of Medicine of Yeshiva University, New York, USA |
| Dr M. Borgoño | Adviser to the Ministry of Health, Ministry of Health, Santiago de Chile, Chile |
| Dr P. Chaulet | Professeur, Clinique de Pneumo-Phtisiologie, Centre Hospitalier et Universitaire de Beni-Messous, Alger, Algeria |
| Dr J. Grosset | Directeur, Département de Bactériologie et Virologie, Faculté de Médecine, Pitié-Salpêtrière, Paris, France (also representing Association française Raoul Follereau (FF)) |
| Dr N.D. Huong | Directeur, Institut National de la Tuberculose et des Maladies Respiratoires, Hanoi, Viet Nam |
| Dr A. Salomao | National Director of Health, Ministry of Health, Maputo, Mozambique |
| Dr T. Shimao | Chairman, Board of Directors, Japan Anti-Tuberculosis Association, Tokyo, Japan (Chairman) |
| Dr D. Snider | Director, Division of Tuberculosis Elimination, National Center for Prevention Services, Centers for Disease Control, Atlanta, USA (Rapporteur) |
| Dr K. Styblo | Director, Tuberculosis Surveillance Research Unit, The Hague, The Netherlands |
| Dr U Tin U | Director-General, Department of Health, Ministry of Health, Yangon, Myanmar |
| Dr S.P. Tripathy | Director-General, Indian Council of Medical Research, New Delhi, India |
| Dr Ali Akbar Velayati | Minister of Foreign Affairs of the Islamic Republic of Iran, Teheran, Islamic Republic of Iran |

GOVERNMENTS

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Mr A. Meloni, Premier Conseiller, Mission permanente de l'Italie auprès de l'Office des Nations Unies et des Organisations internationales à Genève

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Mr S. Akagawa, Deputy Director, Accounts Division, Minister's Secretariat, Ministry of Health and Welfare, Tokyo

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UNDP

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IILEP

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Dr D. Enarson, Research Director, International Union Against Tuberculosis and Lung Disease, Paris

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Miss M. Cone, International Federation of Pharmaceutical Manufacturers Associations, Geneva

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ANNEX B

COORDINATION, ADVISORY AND REVIEW GROUP
FOR THE TUBERCULOSIS CONTROL PROGRAMME
22-23 NOVEMBER 1991

PROGRAMME

Friday, 22 November 1991

- 09h00-09h30 Opening
- Statement by the Assistant Director-General,
 Dr R.H. Henderson
 - Introductions
 - Statement of Chairman
 (first CARG meeting report)
 - Adoption of agenda
- 09h30-10h00 Experience of the World Bank/WHO-
 assisted China TB Control
- 10h00-10h30 TB Control in the face of the HIV
 epidemic: the Malawi example
- 10h30-11h00 Break*
- 11h00-11h20 TB Control in Eastern Europe:
 the Romania example
- 11h20-12h30 Issues related to drug supplies and
 drug development, including the role
 of the pharmaceutical industry
- 12h30-14h00 Lunch*
- 14h00-14h30 Progress report
- 14h30-15h00 Management structure
- 15h00-15h30 Break*
- 15h30-17h30 Management structure (continued)
- 18h00-19h30 Reception - French restaurant

Saturday, 23 November 1991

08h30-10h30 Workplan and budget

10h30-11h00 Break

11h00-11h30 Financial situation

11h30-11h45 Proposed agenda and date of next meeting

11h45-13h00 Conclusions and recommendations

13h00 Closure of meeting

ANNEX C

Anticipated Financial Status for 1992-1993*

| SOURCE OF INCOME | | US \$ |
|--|--|-----------|
| (a) | Regular budget | 4 179 300 |
| (b) | Estimated balance of extrabudgetary contributions to be carried forward, at 31 December 1991 | |
| | i funds deposited prior to 1 November 1991 | 532 700 |
| | ii funds deposited with WHO after 1 November 1991 | 969 000 |
| | Subtotal | 1 501 700 |
| (c) | Firm outstanding pledges, as of 23 November 1991 | 3 210 500 |
| (d) | Interest | 59 600 |
| Anticipated resources available to finance 1992-1993 Proposed Programme Budget | | 8 951 100 |

* Estimated at 23 November 1991

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