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PREPARATORY ASSISTANCE FOR THE ESTABLISHMENT OF A PILOT PLANT FOR PHARMACEUTICALS

DP/MOZ/83/004

MOZAMBIQUE

Terminal Report*

Prepared for the Government People's Republic of Mozambique
by the United Nations Industrial Development Organization
acting as executing agency for the United Nations Development Programme

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Vienna

* This document has not been edited.

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INTRODUCTION

Almost all pharmaceuticals in Mozambic are imported. The high dependency on external supply influences and the trade deficit of the country has adverse effect on the National Health Care System.

The earlier feasibility studies for the establishment of a pharmaceutical industry has not been implemented due large investment needs, automated technology required and the need for extensive man power training and development.

The development objective of this project is the establishment / development of pharmaceutical industry in Mozambic. Before undertaking large investment in an industrial production unit it is appropriate to make an assesment of the requirements for a pilot scale production unit which leads to the development of local skills, technological capability and creation of infrastructure necessary for the establishment and operation of an industry. Hence is this project.

The project was implemented in October 1985 and has so far passed through three six monthly tripartite, the fourth one is due in September 1987. The project is yet on-going with the local training to be accomplished with the arrival of the international inputs at EMOFAR Beira, the site for the training work-shop.

Besides this terminal report, separate reports on the project outputs namely the feasibility parameter studies for a pilot pharmaceutical production unit and the potentials, conditions and parameters for developing pharmaceutical industry will be submitted separately in two parts.

ACKNOWLEDGEMENT

COUNTERPARTS :

Mr. J. R. Durao ..... Director, Department of pharmaceutics, Ministry of Health

Dr. R. A. Pereira ..... Chief of GIF, Ministry of Health

Mr. Almeida Caetanu ..... GIF, Ministry of Health

Mr. R. Mabeia ..... GIF, Ministry of Health

Ms. Eliza Pinto ..... Director, EMOFAR, Beira

The writer is indeed thankful to these gentlemen for their unfailing interest in the project works and constant assistance at bot' project and personal level during the last 2 years of the project continution.

The external personalities who extended assistance at various times during the progress of the project works and deserves mention are:

Mr. Carlos Ivo ..... Architect, Beira

Mr. M.J.E.R. Almeida .... Director, Maintenance Centre, Ministry of Health

Mr. C. Mutemba ..... Director, Mobeira, Beira

Mr. A. Ribeiro ..... Director, Constructions, Beira

Mr. M. Vellious ..... Director, Loumar Candy Factory, Maputo

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ACTIVITIES

The major activities performed during the last two years (October 1985 - September 1987) of project duration are briefly discussed under the following two heads:

- **assesment of infrastructure / present level of capabilities, data collection and analysis**
- **training of local personnel.**

- Infrastructure / Capabilities / Data Collection

These constitute the level and spectrum of imports, donation, local productions of pharmaceuticals for consumption, pharmaceutical education in the country, laboratory facilities, potential domestic production input's, complementary industries, the National Health Care System, hospital pharmacy, maintenance work--shops and technical manpower availability in the country.
Please refer to Annex - 01 for the summary of the strucured sample survey carried out on the ancilliary industries in Maputo, the capital city, and Beira, the second largest port city in Mozambic.

The collection of data from international sources were confined to suppliers / manufacturers of pharmaceutical formulation materials, equipment and machineries, apparatus and reagents for laboratories for specifications and cost estimates for local training at Beira and the pilot plant feasibility parameter studies.

The data collection especially on current local consumption of pharmaceuticals and certain cost data were indeed a long drawn out affair with repeatitions of a number of sub-activities primarily due to communication problems and two major devaluations of the local currency in first half of 1987.

- Training of Local Personnel

In order to make the work-shop training on tabletting effective this activity has been subdivided into phase-I and phase-II, the former phase is designed and formulated as preparatory to the latter phase.

The organisation for phase-I training in regard to the training materials, refer Annex-02 for the topics, and identification of the trainee at various levels (refer Annex-03) for Phase-II has been performed.

The phase-I have been completed at the supervisory level (4 personnels) including one as laboratory supervisor (refer Annex-04 for the preliminary laboratory training topics at the Central National Hygiene Laboratory, Ministry of Health, which is forming a nucleus for pharmaceutical analysis in mozambic with external assistance.

The trainee is now capable to analyse most of the compendia specifications of the training products, namely Aspirin, Paracetamol and Co-trimoxazol tablets.

These activities were completed as per shcedule.

The development of the layout plan adopting to the existing building, procurement of all the construction materials except two importable items epoxy paint and mosquito net were accomplished on time. The civil modifications are completed in August 1987 except painting and the electricals are continuing, foreseen to be completed in September 1987 as per schedule.

Regarding the equipment, re-establishment of sources for some pieces of the equipment has been necessary and placement of orders are made in August 1987 behind the schedule by about 6 months.

During the planning and execution of the activities certain impediments were experienced, namely air travel to Beira, inadequate language proficiency and uncoupling of Government UNICEF project with the current UNIDO project at the same site.

However, it is envisaged that there would be a time lag between the completion of remodelling, installation of equipment and start-up of training phase-II.

OUTPUTS

The outputs are sated below and the comments on the extent of achievement are made separately, for each of them.

I - A number of national technical personnel (15 to 20) at the levels of production and quality control management, production and quality control supervision, inventory control, equipment maintenance mechanic/engineer, skilled and semiskilled operators will be trained in the technology of tablet manufacture and quality control in the remodelled oral rehydration salt plant at Beira. A key national personnel will be trained (in-service) abroad in the area of pharmaceutical technology.

- As mentioned earlier the major part of this output could not be achieved yet due to the deliveries of the international inputs for the local training namely equipment, raw materials, laboratory glass apparatus and the reagents are still in the import pipe line. However as stated earlier prepararatory phase-I has been completed at the supervisory level and incomplete at the operators level.

  In addition Mr. Almeida Caetano, one of the key national personnels in GIF, Ministry of Health has been awarded travel grant for the university studies in Brasil in pharmaceutical technology.

II - A comprehensive report defining the potencials, conditions and parameters for developing pharmaceutical industries and indicating the feasibility parameters of pilot production unit including plant layout design, cost estimates and implementation schedules.

  Quantification of the inputs in terms of technical expertise, equipment, training, etc., required from external sources for the establishment of the pilot plant.

These two outputs are complementary and the reports are planned for submission in two parts, part I and part II. There are certain facts and figures that are repeatative in the two parts of the reports.

A comprehensive draft final report defining the potentials conditions and parameters for developing pharmaceutical industries in the country is prepared as one part (Part-I).

In another part (Part-II) the feasibility parameters for the establishment of a pilot plant for pharmaceuticals will be submitted. While the parameters are analysed in the report the detail financial analysis is not within the scope of the current fiasibility studies.

IMMEDIATE OBJECTIVES

Each of the immediate objectives are stated below and the extent of the progress made is analysed separately.

I - TO UPDATE ALL RELEVANT DATA RELATING TO CURRENT CONSUMPTION AND PROJECTED REQUIRFMENTS OF PHARMACEUTICALS

- The consumption and expenditures data have been up-dated to 1985. The consumption is based on imports, donations and limited quantity of local production in hospitals and 50 pharmacies in the country. The analysis of the consumptions reveal that there is almost a progressive decline in expenditures and availability of drugs for consumption in the period of 1980 - 1985. The following table-01 illustrates the growth of consumption of pharmaceuticals by dosage form in 1985 over the base year 1982. Despite the annual population growth of 2.6%, there is the lower level of availability of drugs that led to a drop in population coverage to 35% as compared to 40% in early 1980's. The per capita consumption also dropped to US$0.40 from $1.0 in 1980 based on whole population.

  In view of the constrains, the selection of the imported essential drugs in recent years have been judicious and resulted to narrow range of product spectrum and concommittantly donations have become an integral part of the national health care systems. The trend of donations is 2.9% of global pharmaceutical expenditure in 1982, 10.3% in 1983, 30.3% in 1984 and 29.3% in 1985.

- Local Production:

The only oral formulation produced in hospitals and pharmacies is sodium benzoate expectorant. The estimated local production in 1984 and 1985 is 13,124 and 67,230 kg of the expectorant respectively. The other two dosage forms are topical ointment and lotions for external use. The volume of production is estimated to 113,962 Kg of ointment and 593,887 litres of lotions in 1984 and 1985 respectively. In addition, the oralite plant at Beira produced 585,480 and 2,354,200 sachets in 1985 and 1986 respectively.
The magnitude of local production is dependent on the availability of raw materials.

Table-01

Drug Consumption, 1982 and 1985

	Number of Products			Consumption volume (in million units)		
Dosage Form	1982	1985	%Growth	1982	1985	% Growth
- Tablets	125	70	<44>	383.60	169.60	<55>
- Capsule	14	9	<36>	19.20	13.50	<31>
- Oral liquids	26	6	<77>	1.69	0.17	<90>
- Topical ointments	25	5	<80>	2.44	0.10	<96>
- Sterile liquid	99	25	<75>	2.39	0.61	<75>
- Penicillin Injectables	5	4	<20>	2.43	2.62	8

< > means negative growth

Aspirin, chloroquin, ferrous sulfate and co-trimoxazole tablets constitute 77% of total tablets consumed in 1984 and 55% of that in 1985.

II - TO IDENTIFY SPECIFIC KINDS OF PHARMACEUTICALS PRODUCTS MOST REGULARLY NECESSARY IN THE NATIONAL MILIEW AND TO DETERMINE PRODUCTION LEVELS IMPERATIVE FOR SATISFYING DOMESTIC DEMAND IN THE IDENTIFIED PHARMACEUTICALS

- Based on the analysis of drug consumption, foreign currency expenditures, and population coverage a total of 45 products embracing 8 dosage forms are identified as most regularly necessary in the national miliew. The illustration of the identified pharmaceuticals and their consumption level in 1982 and 1985 are presented in Annex-05.

In regard to both identification of products and long range projection of these pharmaceuticals difficulty has been experienced since current consumption has declined in terms of product spectrum and volume of consumption. Historical consumptions were also useful. The projection is made on average percentage growth basis which is not identical for all products. The quantities thus obtained should be considered as minimum requirement. The long range projection (1988 to 1994) for countrys' requirement of the selected pharmaceuticals is elaborated in the reports on project outputs, Part-1.

The selected most regularly necessary products that are included within the tablet, capsule and oral liquid dosage forms represent the following levels of actual consumption within the respective dosage form in 1984 and 1985, refer table-02.

Table-02:

Products / Dosage Form	**% Consumption 1984**	**1985**
Tablet	86.4	90.0
Capsule	84.5	98.0
Oral Liquid	78.7	83.9

III - TO ASSESS THE TECHNICAL CAPACITY CURRENTLY AVAILABLE OR WOULD BE NECESSARY IN MOZAMBIQUE FOR SUSTAINING PHARMACEUTICAL INDUSTTRY OF DESIRED MAGNITUDE:

- In order to make the magnitude of the technological requirements discernible for the domestic production of the projected requirements of the three non-sterile dosage forms, namely tablet, capsule and oral liquid, the quantities are exploded interms of plant loading at [illegible] key manufacturing steps, the magnitude indicators, refer Annex-06. Due to complexity in the manufacturing technology of sterile products including penicillins, these are not suggested for local production in near future.

- In view of the large magnitude of the production requirements and the studies of the current level of capabilities available in the country in respect of pharmacy technical manpower (refer Annex-07), drug testing facilities, industrial equipment and machineries maintenance work-shops and the technical capacity of the supporting ancilliary packaging material industries do not suggest establishment of the required level of the advanced automated technology for the pharmaceutical industry of the desired magnitude. Instead production requirements for a lower level of activities in an industrial unit has been envisaged and it is concluded that even this level of activity should be attained in a progressive manner. These are mapped out in detail in the draft final report, Part-I on the potentials, conditions and parameters for the development of pharmaceutical industry.

IV - TO PREPARE THE DESIGN OF THE INFRASTRUCTURE, SPECIFICATION OF EQUIPMENT, MANPOWER REQUIREMENTS AND COST ESTIMATES FOR THE PILOT PLANT.

- The design of pilot plant layout for a floor space of 25.5 M x 53.0 Or 1352 M2 has been prepared at an estimated cost of about $700,000. All activities of the plant operations are suggested to be in same building. However flexibility for future expansions by shifting the auxilliary functions to separate buildings as well as by phisical expansion of the proposed building it self has been maintained. The floor plan and room arrangements are planned based on the principle of ease of materials flow. Please refer to Annex-08 for the allocation of the floor space in the covered site plan.

- The estimated cost of the pilot plant equipment is over a million dollar, raw materials for the specified production program is in the tune of $690,000 and the local packaging materials is about $105,000. These component costs, plant layout and details of man power and investment cost will be submitted separately with the draft final report on the feasibility parameter studies for the establishment of the pilot plant.

- The local packaging materials (Pilot plant production) and specifications are illustrated in Annex-09.

V - TO QUANTIFY THE INPUTS IN TERMS OF TECHNICAL EXPERTISE EQUIPMENT, TRAINING, ETC., REQUIRED FROM EXTERNAL SOURCES TOWARDS ESTABLISHING THE PILOT PLANT.

- This has been estimated in terms of technical expertise for in-service training (24 man months) at the start-up of the pilot plant and external training (20 man months) of selected key and supervisory personnels prior to start-up. The estimated pre-production capital expenditure for this training is approx. US$200,000. This input cost data is a part of the feasibility parameter studies for pilot plant to be submitted separately.

VI - TO STRENGTHEN THE FACILITIES AVAILABLE IN THE EXISTING ORAL REHYDRATATION SALTS PRODUCTION UNIT AT BEIRA BY PROVIDING ADDITIONAL EQUIPMENT, ETC., FOR TRAINING IN TABLET MANUFACTURING

- This immediate objective has so far been achieved by about 20% - 25%. The remodelling layout of the ORS plant, the training premises has been developed adapting to existing building in consultation with the local architect; one item of construction material (200 L white epoxy point) from Swaziland has been yet in pipe line and civil construction has been almost completed except painting.
- The electrical board and cables are installed and the laboratory will soon be shifted to the pre-planned down town regional hygiene laboratory for food and water at Beira.

- The remaining civil and electrical works are to be completed (including painting) by September 1987.

- The orders for equipment, laboratory glass apparatus, raw materials are being placed in July/August 1987. The price quotes of the laboratory reagents, to be delivered by the Government, are at present consolidated at the Ministry of Health and orders are being placed by Medimoc in September 1987. All these deliveries are expected at site towards December 1987.

VII - TO ORGANISE, FORMULATE AND IMPLEMENT A PROGRAM FOR THE TRAINING OF LOCAL PERSONNEL AT VARIOUS LEVELS AT BEIRA

- This objective although has not been achieved yet some organisational/formulation work has been performed.

- Phase-I specific lessons on tabletting technology as preparatory to the practical training (phase-II) at Beira has been completed at supervisory level and continued at operators level.

- Aspirin and Paracetamol tabletting know-how and quality control methods are planned to be started first as stage-I of phase-II followed by co-trimoxazol as stage 2 for ease of adaptability.

- Trainee list has been prepared, refer Annex-3, and for the phase-I trainning topics, refer Annex-2.

UTILISATION OF RESULTS

The project is yet on going and the results so far obtained is limited in view of the inputs for the work-shop training yet in pipeline and the feasibility parameter studies is in the preliminary draft form.

However certain data on the country's projected requirements for pharmaceuticals in the long range plan (1988=1994) and the production plan for the studies on the envisaged pilot plant have been transmitted to certain foreign countrys in response to their quaries on the subject.

- In addition in the mean time one of the supervisory level trainee (phase-1) for the laboratory (Ms.Benedita) has gained the capability of physical and chemical analysis of imported tablets that are planned for the work-shop training at Beira, namely aspirin, paracetamol and co-trimoxazol tablets and performs routine analysis at the National Hygiene Laboratory for Food & Water, Ministry of Health where the nucleus for pharmaceutical analytical facilities are currently at the forming stage.

- On installation of the tabletting & laboratory equipment currently under import, the training work-shop facilities first in its kind in the country, should enable the Government to consistently produce trained manpower in tabletting technology.

- The embryonic facility is suggested to be integrated with technical institutes - the course curriculum of the pharmacy and chemical institutes in the country to transfer the capability horizantally to the community. The trainee outputs of the work-shop should be able to apply the manufacturing technics to greater number of talets and produce them at larger scale in future.

- The reports on the feasibility parameter studies for the pilot plant for pharmaceuticals and the potentials conditions and parameters for the pharmaceutical industry should provide the Government a guideline for plan of action for the overall growth of pharmaceutical sector in the country. It should also provide the investors a knowledge of the market requirements and its potentials.

- On the whole the training work-shop is a nucleus, that should enable the Government develop a technical manpower base in tablet manufacture and attract foreign investors to promote pharmaceutical industry in the country

- However it should be borne in mind that there are opposing factors that might adversely affect the optimal utilisation of the work-shop and/or the project outputs indicated earlier. These factors are illustrated below in the estimated order of incidence as foreseen:

  - Unavailability of importable materials for training such as raw materials & laboratory reagents,

  - Stock outs of spare parts for equipment and machineries,

  - Unplanned/inadequate trainee inputs at various levels,

  - Interruptions of power supply,

  - Absence of a full time mechanic,

- Absence of external consultant at Beira especially in early periods and during new training-product introductions,
- Unavailability of reports in local language,
- Lack of external/agency follow-ups,
- Ineffective contact with foreign collaborating industries.

ABSTRACT, CONCLUSIONS & RECOMMENDATIONS

The reports on the outputs, namely the feasibility parameter studies for the pilot plant for pharmaceuticals and the potentials conditions and parameter for the pharmaceutical industry will be submitted separately. The comments therefore are discussed below in two parts:

Part - I: Brief comment on overall observation in regard to the establishment of a domestic pharmaceutical production unit;

Part - II: Comments on consolidation of remaining part of the project, namely the local training.

Part - I:

On studying the consumption data of pharmaceuticals 45 formulations comprising 8 dosage forms are identified as most regularly necessary in the national milieu. A long range projection of country's requirement for the identified pharmaceuticals are made (1988-1994). In view of the inadequate availability of manpower & infrastruture the establishment of local industrial scale production unit is not suggested immediately. Instead training work-shops should be initiated which will lead to pilot scale domestic units which in turn can be expanded progressively to industrial level. The collaboration with a foreign industry is foreseen to facilitate achieving the development objective.

The local production is suggested to start with the three non sterile dosage forms, namely tablet, capsule & oral liquid. There are potential indigenous packaging material suppliers in Mozambic (refer Annex-01) and it is suggested that these are sourced locally. The local manufacturers however has to pass through a fine tuning development phase integrated with pharmaceutical quality control.

Part -II:

In order to consolidate the rest of the project objective the need for the accomplishment of the following activities and inputs are foreseen.

1. **Importation:**

Most of the equipment have been ordered by July/August and the laboratory reagents are to be ordered by August 1987.

Three room airconditioners, one room dehumidifiers are yet to be ordered.

In regard to construction materials only the paints are yet in pipeline from Swaziland and eagerly awaited.

2. **Re-location auxilliary facilities of training premises:**

The civil works are at the last leg awaiting painting to finish off. The electrical works are on going and expected to complete by August 1987.

The remodelling plan includes a temporary dislocation of the auxilliary facilities, a planned transition phase (phase-1), of the training premises as indicated below until the Government/UNICEF expansion project of ORS facilities are completed at site an estimated period of one year and the facilities are permanently shifted (phase-II).

DISLOCATED AUXILLIARY FACILITIES	PROPOSED TEMPORARY LOCATION
-Laboratory	- Regional hygiene laboratory for food and water
-Stores	- Medimoc warehouse
-Office	- Provincial hospital
-Cafeteria	- Nautical club / Hospital dinning facilities

3. Trainee inputs:

- Key personnel/supervisory personnel:

  The trainees are identified (Annex-02) except the new employees.

  It is suggested, Mr. Mabeia, the key personnel in GIF and Ms. Eliza Pinto, Director of EMOFAR, Beira receive both the technical and the management of work-shop training facilities including principles of materials management during the training phase-II.

  In order to complete the training program the supervisory personnel who received phase-I training in Maputo (indicated below) should attend the pratical training at Beira.

- Supervisory personnel:

  -Ms.Benedita (quality control laboratory supervisor)
  -Ms.Arminda (production supervisor)
  -Ms.Isaura (production supervisor)
  -Mr.Zefanias (future plant-Medimoc co-ordinator)

- Maintenance technician

  At present a part-time technician is stationed at the ORS plant, Beira. A full time mechanic is needed at the training premises for the maintenance of the machineries & equipment of the combined pharmaceutical operations of ORS and the tabletting work-shop. It is suggested that a person be identified, educated at the industrial institute and exposed to industrial training in future. Until such time the present part-time technician assigned at EMOFAR should receive the formal maintenance training at Beira when the new tabletting machineries installed.

4. Installation of the equipment & machineries:

- The installation is planned to be accomplished by the limited technicians that are available locally at maintenance centre, Ministry of Health in presence of the consultant and on receipt of the installation manuals as requested.

- The production and the utility equipment will be installed at one run while the laboratory equipment in 2 phases. At the first phase temporary installation of certain selective laboratory equipment will be done the down town regional laboratory as stated earlier followed by permanent placement at the new laboratory at site at the conclusion of the construction works by the Government/UNICEF. The laboratory equipment which are common with those of the regional laboratories shall not have to be installed during the transition phase.

- The in-process control equipment, namely tablet disintegration testing unit, friabulator, hardness tester, weighing balance are planned to be installed at the designated room at the training work-shop.

- The utility equipment includes window air conditioners, one room dehumidifier to be installed in the tabletting room and one unit of pall filter to be installed (preferably wall mounted) in the room of the helicoidal mixer over the kettle.

5. Packaging technology of the training products:

It is suggested that along with the training on the manufacturing technology of tablet at the training work-shop packaging technology is also included especially on batches conforming to specifications. The GMP requirements for labels and labelling should be of interest and be included in the program.

It is planned that sub-division of tablets will be carried out by weighing on a table-top scale in 1000 units of tablets, putting in a polythene bag, heat sealing the bag and finally labelling the bag if no outer such as HDPE plastic or tin containers are used.

6. Institutional co-ordination activity:

The necessity for the following co-ordination activity is foreseen prior to completion of the training as well as for the post-training transition period until the dislocated auxilliary facilities are re-established at site.

- UNIDO VS Equipment suppliers

  It is important that UNIDO ensures, the equipment suppliers send the installation, maintenance and operating manuals as soon as possible to enable the Government organise equipment installations by translating into local language and familiarising the available limited local mechanic/technicians before undertaking the job.

- Department of Pharmaceutics and Maintenance centre, Ministry of Health

  The timely availability at Beira of the required number of mechanics/technicians of the maintenance centre, (Maputo) to install all necessary equipment and machineries as planned is important for the start-up of the training.

- EMOFAR and Regional Laboratory, Beira

  Despite agreement has been reached in principle at the Ministry of Health, Maputo, finer details on the sharing of common equipment and daily routines should be worked out at Beira. Water is the only and most important local formulation ingredient. The incoming city water and the filtered water at the EMOFAR tabletting work-shop should be routinely tested. Incoming water should be potable.(1)

(1) Reference: International Standards for Drinking Water, 3rd Edition, WHO.

- EMOFAR and Nautical Club / Hospital, Beira.

  In order to use the available under utilised room at the off-street sea-side nautical club or the dining facilities of the nearby provincial hospital for lunch of the EMOFAR work force, the need for a formal understanding is foreseen.

- Besides the above the institutional co-ordination agreement has been reached with Medimoc, Beira for use of the material storage facility and with the near by provincial hospital for the use of the office space until the new construction by the Government / UNICEF is completed at site.

  - Ministry of Health and Ministry of Education:

    In order to integrate the training work-shop facilities with the community namely technical institutes this co-ordination activity is a pre-requisite.

7. Employment activity

Three categories of new personnel are planned to be employed by the director of EMOFAR, namely 1 consultant, 2 trainee analyst for the laboratory preferably from chemical institute and 6 semiskilled operators for production. Six skilled operators are already selected from the ORS section, refer Annex-03.

- Consultant

The Ministry of Health is in the process of selecting a suitable person as consultant from a company named Coditec in Brazil. The arrival time of this consultant at site is dependant on the approximate time of the equipment reaching Mozambic. It is suggested that the consultant should be present at site to receive and clear the consignments of equipment and the spare parts.

- Laboratory trainee analyst

For the tabletting work-shop, 2 persons preferably of the chemical institute with 9 years of school educational background have been suggested to be recruited for quality control Laboratory.

- Semiskilled operators

Six are in the process of recruitment at Beira with 4-6 years of school education.

8. **Skill/training activity**

- In order to perform this important activity conveniently and in an effective manner it is suggested that the teaching function be split in 2 stages by the technological variants of the manufacturing process of the training products and the laboratory testing methods.

- Product Phasing

Of the three tablets selected for training, namely aspirin, paracetamol and co-trimoxazol the former two follow the dry granulation and the latter follow wet granulation. Therefore dry granulation technic be taken up at the first stage followed by the wet granulation. In the mean time local capability should be developed for plant water analysis. The purified water should conform to purified water USP when purified through a suitable system.

- Laboratory testing

It would be necessary to overview the overall quality control functions as institution building process and implement it in terms of incoming materials, in process control and finished product testing. In order to ensure ease of adaptibility some sort of phasing of the laboratory tests should be planned phisical / chemical / microbiological following WHO guide lines (Establishment of drug quality control laboratories, vol.I, chemistry and Microbiology, Alexandria, copy deposited, refers to Annex-10 on deposits.

- Co-trimoxazol tablet analysis

In order to adapt the new modified (BP-1980) analytical test prodedures it is planned and agreed that at least one of the two available EMOFAR laboratory analysts should receive a 4-week preliminary laboratory training at the National Hygiene laboratory for Food and Water, Ministry of Health where it has been implemented. This horizontal transfer of capability should be instituted as soon as possible prior to installation of machineries. Please refer Annex-10 on deposits for the test procedure.

- In order to develop the skill of the laboratory analysts in microbiological analysis of plant water and pharmaceutical raw materials for both ORS and tablets it is suggested that the facilities of the well equipped regional laboratory for food and water at Beira be utilised until the tabletting work-shop laboratory is relocated permanantly at site and the microbiological analyst is developed.

- It is suggested that a close supervision be maintained on the laboratory practices, documentation etc., during training and post-training follow-ups to ensure adherence to good laboratory practices.

9. **Utility supplies at the training work-shop:**

- The city water and power supplies at Beira has been consistently erratic.

- Currently the facility and the technical capability of the laboratory at EMOFAR is inadequate to monitor and mantain water quality at the training workshop. Institutional co-ordination with the regional laboratory at Beira yet at forming stage is suggested for routine chemical and microbiological analysis of plant water following the standard procedure and reporting formats developed. Incoming water shoud be potable. In order to purify the potable water to the 'purified - USP' grade for use as a raw material for preparation of granulation fluid for wet granulation in tablet manufacture by portable ion exchange and/or reverse osmossis technic is suggested to be adapted. The disposable DSLK 2 NLZP absolute filter cartridge capacity is of low capacity. A permanent system shall have to be installed based on incoming water analytical data to optimise the economic life of the filter and to ensure 'purified' grade of water based on local conditions.

- Long power outages has been common at Beira raising the temperature and humidity in production rooms that are liable to cause equipment performance and tablet quality problems. It is suggested that adequate inventory of the compressors for the room air conditioners be maintained and the existing 37.5 KVA emergency diesel driven power generator is combined with the one of 100 KVA planned in the on-going Government /UNICEF project. The current total need (maximun demand) is estimated to be 180 KVA.

- Steam facility:

  It has been an assesment that the present level of technical capability for continued operation and maintenance of a steam generator at the ORS plant at Beira is uncertain.

  Although steam heating arrangement is normally provided to a kettle for the preparation of granulation fluid (in this case aquous starch paste), due to reasons of adaptibility electrical heating system to the kettle has been suggested. As soon as local capability is gained or continued operation and maintenance of the steam generator is assured the unit provided may be substituted with suitable steam jacketted kettle for the preparation of the granulation fluid.

Annex 01

Sample Survey - 1985

POTENCIAL DOMESTIC ANCILLRY INDUSTRIES.

A. Containers/Closures

Type of Material	Supplier/Location (ownership)	Size/operational Difficulties stated	Conditions for supply
- Aluminium Closures	Metal Box/Maputo (Private, UK subsidiary)	-250 Employees/ RM, Machine, Spare parts.	Contract. Assistance for RM, Minimum 30 days lead time.
- Plastic Bottles and Closures	Unidade de Direccao de Plasticos, E.E/Maputo (State owened)	-Consists of 5 industrial units Plastic granules, Engineering services, Spare parts.	Prior contract, Financial support.90 days notice,would to be supplied.
	Plastic: SOPLAS/Beira (State owned)	-3 industrial units in Beira each about 80 employees/spare parts, RM, maintenance	Contract, Finance, RM
- Aluminium, Tin Containers	Aluminium de Mozambique/Beira, Subsidiary factory of Maputo (State owned)	-65 employees annual capacity 15,000 pcs./ RM, only for containers of domestic uses.	(1)
- Cardboard Box	Carbeira/Beira - subsidiary of Carmoc, (State owned)	-120 employees Spare parts,adhesive/ glue.	Contract, 60 days
- Amber Glass Bottle	Vidreira/Maputo (State owned)	-1986 cap.- 99MT/day. 1989 cap.-174MT/day, /power supply, Technical staff	9 months notice for new mould of 25 mm neck size, contractual agreement.

Annex 01(cont

POTENCIAL DOMESTIC ANCILLARY INDUSTRIES

Type of Material	Supplier/Location (ownership)	Size/operational Difficulties stated	Conditions for supply
B. Printing Materials			
- Labels and Cartons	Spanos Graphica, LDA./ Maputo (Private, some State support)	-Employee - 103 Ann. Production Capacity: label per Mo.-90 m 3 size carton per Mo.- 25,000/ paper, board and Ink.	Art paperand boards to be supplied, 3 months delivery time, Min. order 3 mil. labels, contractual agreement.
	Cetibel/Beira (Private enterprise)	-Employee - 50 Ann. capacity: 19,300 cm2 paper surface processing	
C. Formulation Material			
- Sugar	Institute Nacional de Sugar/Maputo (State owned)	-6 factories operation / technical manpower, Finance, clarifying materials for sugar	Only brown sugar (1)

Abbreviations: (1) Unsuitable for Pharmaceutical use / Does not conform to specifications.

RM = Raw Material
MT = Metric Ton,
MO = Month
Ann = Annual
Cap. = Production Capacity
mil. = Millions

ANNEX 02

TRAINING TOPICS (PHASE - I) : TABLETTING

Lesson No.		T o p i c
01	-	Cleanliness and Production Hygeine in a Pharmaceutical Plant.
02	-	Pharmaceutical Dosage Forms and Packaging of Pharmaceutical Products
03	-	Important Units of Measurements
04	-	Pharmaceutical Formulations: Tablets
05	-	Process Technology : Tabletting - Flow Sheets tablet manufacture - Dry granulation - Wet granulation - Direct compression
06	-	Process Technology : Tablet coating
07	-	Pharmaceutical Product: Storage, Shelf life an Stability Studies.
08	-	Visuals : -Cleanliness -Safety at work -Laboratory accidents
09	-	Monitoring and Maintenance plant Water Quality

ANNEX 03

TRAINEE FOR TABLETTING WORK-SHOP TRAINING AT BEIRA

Functional Level/Category (1)	Numbers (2)	Name (3)	Status: Phase I/Phase II (4)	Education and Experience (5)
- Plant Manager/ Production manager	2	- Mr. R. Nabeia - Ms. Eliza Pinto (a)	Phase - II	- Ph.D and Key personnel in GIF - Director, ERDFAR onnel in GIF
- Production Supervisor	2	- Ms. Aminda - Ms. Isaura	Phase - I completed	- 9 years school, 3 years pharmacy institute, few years hospital pharmacy and essencial drugs distribution (NHS).
	1	- Mr. Elario	Phase - I , yet incomplete	- 6 years school, 2 years in Pharmacy institute and 3 years ORS plant (Beira) Prodution supervisor.
- Skilled Operators	6	- Chapepa, Falange, Lindinho, Rodolfo, Nupera, Vilacanjo	Phase - I Incomplete	- 4 to 6 years school, 3 to 4 years experience as ORS production operators.
- Semiskilled Operators	6	- (New employment, Beira to be made)	-	- 4 to 6 years school
- Quality Control Manager (Potencial)	1	- Mr. Melchior (1)	Phase - I; (yet to be completed at the National Hygeine laboratory, Maputo)	- 11 years (pre-University) schooling; 3 years pharmacy institute, 3 to 4 years laboratory experience ORS plant, Beira.
- Quality control Supervisor (potencial, future industry)	1	- Ms. Benedita	Phase - I , Completed	- 9 years school, 3 years chemical institute, 3 years pharmacy institute , 3 months UNIDO Fellowship trainee in France, 1 month in GDR (1986), Laboratory training in National Hygeine Lab, Maputo on Aspirin, paracetamol and co-trimoxazol tablets analysis potenti.

(a) Ms. Eliza Pinto, the Director of the ORS plant and the training Work-shop is suggested to be exposed to the laboratory technical and administrative supervisory technics.

ANNEX 03

TRAINEE FOR TABLETTING WORK-SHOP TRAINING AT BEIRA

Functional Leve/Caegory (1)	Numbers (2)	Name (3)	Status:PhaseI/Phase II (4)	Education and Experince (5)
-Laboratory Analyst	1	- Mr. Albino (1)	-	-9 years school, 3 years pharmacy institute, 3 years lab. experience ORS plant, Beira
	1	- Anachuma	-	- 7 years school, 3 years ORS Production operator, currently ORS laboratory trainee.
	1	- (New employeent to be made)	-	- 9 years school, 3 years pharmacy institute, few years drugs distribution (NHS).
-Quality Control in-process inspector	1	- Ms. Joana	Phase - I , Incomplete	- 7 years school, 3 years production operator in ORS, currently lab. trainee ORS plant, Beira.
-Plant - Mechanic co-ordinator	1	- Mr. Esphania	Phase - I , Completed	- 9 years school, 3 yars pharmacy institute, few years essential drugs distribution (NHS).
-Maintenance Mechanic (2)	1 part-time	- (Unavailable)	-	- 4 years school, 5 years industrial institute, few years experience in maintenence centre currently engaged 3 half days a week at ORS plant.

(1) - Mr. Melchior / Mr. Albino - Should undergo preliminary 4 - week laboratory training in analysis of co-trimoxazol following new test method adopted by who consultant in National Hygeine Laboratory Ministry of Health.

(2) - Also include Mr. Elavio as trainee for production equipeent Maintenance at the training work-shop for tabletting.

Annex 04

Local Training (phase I): Topics For Laboratory TRAINING (1) National Hygeine: Laboratory For Food & Water, Ministery of Helth - Maputo

PRODUCTS	TESTS
1. ASPIRIN	- CHEMICAL IDENTIFICATION - SALICYLIC ACID CONTENT IN TABLET - CHEMICAL ASSAY: PREPARE FLOW SHEET - DISINTEGRATION - FRIABILITY - HARDNESS IN Kg(RECORD RANGE AMONG TABLETS) - DIMENSIONS: DIAMETER AND THICKNESS - DETERMINATION OF WEIGHT VARIATIONS - INDIVIDUAL WEIGHTS AND AVERAGE WEIGHT - LOSS ON DRYING (UNDER VACUUM) - HEAVY METALS: LIMIT TEST - SULFATED ASH DETERMINATION METHOD
2. PARACETAMOL	- CHEMICAL IDENTIFICATION INCL.M.P.DETERMIN. - ASSAY:SPECTROPHOTOMETRIC:PREPAREFLOW SHEET - DISINTEGRATION - FRIABILITY - HARDNESS TESTING(RECORD RANGE AMONG TABLETS) - LOSS ON DRYING (UNDER VACUUM) - DIMENSION: DIAMETER & THICKNESS:VARIATIONS - HEAVY METALS: LIMIT TEST
3. CO-TRIMOXAZOL	- IDENTIFICATION:TLC WITH REF. SAMPLE, SPRAY-SPOT - CHEMICAL ASSAY:SULFAMETHOXAZOL TRIMETHOPRIM ADOPTING METHOD USED FOR MIXTURE: BP 1980 - DIMENSIONS FLOW SHEETS: DIAMETER AND THICKNESS - DISINTEGRATION, FRIABILITY & HARDNESS - LOSS ON DRYING (UNDER VAC.)

(1)- Trainee: 1. Ms. Benedita (completed)

2. Mr. Melchior)
) (yet to complete.)
3. Mr. Albino)

Annex - 05

Consumption of the Most Regularly necessary Products

The consumption of the identified most regularly necessary products in 1982 and 1985 is indicated below:

		Milligram / Tablet	Consumption 1982 x1000	Consumption 1985 x1000
A:	Tabletes			
1.	Acetyl salicylic acid	500	98,590.02	40,257.16
2.	Aluminium hidroxide	500	5,625	2,150
3.	Ascorbic Acid	100	6,593	76.1
4.	Aminophylline	100	4,500	5,023.5
5.	Bisacodyl	5	12,254.2	3,187
6.	Butylscopolamine	10	8,410	41,264.96
7.	Chloroquin phosphate	250	140,840	30,389
8.	Co-trimoxazole	400+80	7,976.2	8,405.7
9.	Chlorpheniramine	4	2,653	3,247
10.	Amelirido	5	176	2,350
11.	Diazepam	2	4,202	1,535
12.	Diazepam	10	1,000	3.76
13.	Furesemide	40	3,204	240
14.	Ferrous sulfate + folic acid	200+0.25	39,365	1,407
15.	Isoniazid	100	5,967	12
16.	Methydopa-L	250	477	411.5
17.	Metronidazol	250	307	1,158
18.	Mebendazol	100	455	4,453
19.	Phenylbutazone	200	8,180	3,507
20.	Propanolol	40	455	500
21.	Prednisolone	5	300	7,001
22.	Paracetamol	500	2,263.6	1,437.36
23.	Praziquantel	600	3,402	-
24.	Sulfadiazine	500	2,040	-
			359,235.02	158,016,04

	mg/capsule	Consumption 1982 x1000	Consumption 1985 x1000
B: Capsules			
1. Ampicillin	250	5.150	85
2. Amoxicillin	500	116	2305.4
3. Tetracycline	500	10.792	6665.1
4. Rifampicin	300	2.18	593
5. *Vitamin-B Complex	-	6867.6	364.9
6. *Multivitamin	-	22.295	3257.6
		7024.017	13271
C: Oral Liquid : Bottles 100 ml	mg/5ml		
1. Chloroquin	200+40	160	.25
2. Co-trimoxazol	200+40	12	.163
3. Chloramphenicol Palmitate	125	46.6	30.275
4. Expectorant	250	303.2	5.592
5. Ferrous sulfate	135	70.1	62.5
6. Multivitamin	-	395	1.225
7. Vitamin-B complex	-	120	8.087
		1106.9	108.092
D: Penicillin Oral Granules: Bottles			
1. Ampicillin	250	791	-
E: Sterile Liquid (SVP) Ampoules	mg/amp.		
1. Chloroquin	250	120	42.94
2. Lidocaine with adrenalline	40,0.02	235	.005
F: Sterile Pen. Powder: Vials			
1. Procaine Penicillin	3 mu	1.01	19.85
G: Ophthalmics: Ointment	3.5g/tube		
1. Tetracycline		9.055	380.65
H: Topicals : 20 g/tube			
1. Benzyl benzoate	1%	15	-
2. Tetracycline	-	7709	-
3. Menthol and Methyl salicylate	1% + 3%	265	.7

* Actual consumption as tablet

Annex 06

MAGNITUDE OF PRODUCTION CAPACITY REQUIREMENTS FOR THE LOCAL PRODUCTION OF MOST REGULARLY NECESSARY TABLET, CAPSULE AND ORAL LIQUID PRODUCTS.

A. TABLETS + CAPSULES:	UNITS	1988	1990	1992	1994
- Tablets (Millions)(1)	Pieces	906.4	1181.3	1445.1	1719.6
- Capsules (Millions)(1)	Pieces	90.4	110	136.8	169.6
- Total blend/Mixure	M.Tons	514.2	664.7	805	975.1
- Mixing/day	M.Tons	2.34	3.02	3.74	4.43
- Tablet compression (300,000 TABLET/DAY)	Tab.Press Pieces	14	19	22	27
- Tab.coating 50Kg/day	No.of days	290	350	420	510
- Coating Pan	Pieces	9	13	15	19
- Encapsulation Per day	000's Pieces	452	550	684	848
B. ORAL LIQUIDS:					
- Syrup,suspension,(1) emulsion	Million Bottles	3.13	4.00	5.03	6.48
- Compounding/day	Litres	1575	2000	2525	32.5
- Packaging line rate (100ml Fill, Fill-Label-Pack)	Bottles/Min	45	56	70	90

(1) Figures indicate long range projection (1988-1994) of the products identified as most regularly necessary, tablets (24-formulations), capsules (6-formulations) and oral liquid (7-formulations).

Annex 07

MANPOWER AVAILABILITY IN MOZAMBIC WITH INSTITUTIONAL PHARMACY EDUCATION AND EXPERIENCE - 1986

CATEGORY	AVAILABILITY NUMBERS 1986 (a)	INTITUTIONAL EDUCATION	PROFESSIONAL EXPERIENCE
- University Graduate (Pharmaceutical Science)	3	- Five Years University Studies in Cuba	- 1 GIF,1 National Hygeine Lab, 1 Distribution essential drugs, Department of pharmaceutics. Ministry of Health.
- Pharmacist	4	- Liberation Studies in Mozambic	- 3 Foreigners in Hospital & National Hygeine Lab, 1 National in Pharmacy Institute
- Pharmacy Technician	56	- Nine Years School+3 Years Pharmacy Institute in Mozambic	- Hospital Pharmacy: Centre & Provincial Hospital & Laboratories
- Pharmacy Agents	87	- Six Years School+2 Years Pharmacy Institute in Mozambic	- Health Centres (RHE. Dispensing drugs
- Pharmacy Auxiliaries	211	- Four Years School+1 Year Pharmacy Institute in Mozambic	- Assistants to Pharmacy Technicians & Pharmacy Agents (RHE.

(a) - Additional 3 nationals are studying in GDR & BRAZIL to return between 1988-1990 and 2 more are at planning stage.

ANNEX -08

COVERED SITE PLAN
PILOT PLANT

Plant Functional Areas	sq. m.	% of Total
Raw and Packaging Material Warehouse	190	14.0
Pharmacy and Cold Storage	60	4.5
Manufacturing :		
-Tablet/Capsule manufacturing	185	13.8
-Tablet/Capsule subdivision	40	3.0
-Oral liquid manufacturing	80	6.0
-Corridor	100	7.5
Packaging	83	6.0
Quality Control laboratory	70	5.0
Utility and maintenance workshop	91	6.9
Finished goods quarantine	60	4.5
Finished goods warehouse	124	9.0
Office area	124	9.0
Lockers, sanitary and medical services	85	6.5
Cafetaria	60	4.5
T O T A L :	1352	100.0

ANNEX- 09

Potencial Domestic Packaging Materials,

Manufacturers and Specifications

Material	Specifications	Local Manufacturer
- Glass bottles	- USD, NF, Sodalime Roundamber colour Size: 120 ml. Neck 25 mm	- Vidreira de Moçambic, Maputo
- Roll-on-metal screw cap	- Aluminium, Diameter 25mm mode: Plastic liner	- Metal box, Maputo
- Plastic jar with lid	- HDPE, size: 10x.92mm (1)	- Unidade de Direcção de Plasticos, Maputo
- Card board box	- 40cm.25cm.12.5cm (1)	- Carmoc, Maputo Carbeira, Beira
- Label for:		
- glass bottles	64 x 88 mm GSM - 80	- Spanos graphica, Maputo
- plastic jar	64 x 88 mm GSM - 80	- Spanos graphica, Maputo Cetibel, Beira
- card board box	104 x 80 mm GSM - 50	- Spanos graphica, Maputo

(1) Size specification is dependant on quantity Packed.

ANNEX- 10

Deposits

The following materials have been deposited to the custody of the persons/institutions noted against the item:

	Material	Custodion
1.	Training (phase -1) materials (lessons)	
	-one copy	-Ministry of Health Mr.Mabeia (GIF)
	-second copy	-EMOFAR, Beira Mrs.Eliza(Director)
2.	-List of equipment, glass apparatus, laboratory reagents and raw materials.	
	one copy	-Ministry of Health Mr.Mabeia (GIF)
	second copy	-SIDFA
3.	-Connecting tube for the water filter (Pall filter) to connect 1/2" water pipe with the filter holder (fabricated outside) - one unit	-Mr. Mabeia, GIF
4.	-Batch production history formats for co-trimoxazol	-Mr. Mabeia Ministry of Health
5.	-Layout plan EMOFAR remodelling	As above
6.	-Locally adapted test procedure for the analysis of co-trimoxazol tablet	-National Hygeine Lab.Ministry of Health Ms. Verina Ms.Lawrinda and Mr.Mabeia, GIF
7.	-Standard procedure: Monitoring and maintenance of plant water quality (Non-potable, potable and purified water)	Mr. Mabeia, GIF Ms. Eliza Mr. Maos (Regional laboratory, Beira)