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DP/ID/SER.A/1094
8 December 1988
ORIGINAL: ENGLISH

17131

# PREPARATORY ASSISTANCE FOR THE ESTABLISHMENT OF A PILOT PLANT FOR PHARMACEUTICALS

DP/MOZ/83/004

MOZAMBIQUE

Technical report: Pre-Feasibility Studies in Mozambique*

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

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* This document has not been edited.

C O N T E N T S

## BACK GROUND

Mozambique, an independent state since 1975, has the geographical location in the eastern part of Southern Africa covering an area of about 806,000 square Km. The country is primarily agricultural endowed with potential natural products including minerals and nearly 90% of the population live in country side.

The post-independence nationalised health policy is based on a multi-sectoral approach. The Ministry of Health coordinates the functions of relevant Ministries and agencies in the over all National Health Care System.

Mozambique imports almost all her pharmaceutical requirements. There is no manufacturing facility for pharaceuticals in the country except the oral rehydration salt production unit at Beira the largest port city in the country. The three central and the seven provincial hospitals in the country produce only a single expectorant syrup and few antiseptic and ointment formulations for external use.

Due to her complete dependence on import, Mozambique is engulfed with the inherent demands and short falls of the system. These include the absence of reliable statistical data on drug needs, abrupt stock-outs, danger of short dated and expired products remaining in circulation, need for efficient drug monitoring system etc. In order to improve the drug supply in the country the Ministry of Health has been endeavouring to establish a self reliant technology base for a domestic pharmaceutical industry. At the request of the Ministry of Health, Astra Development, AB of Sweden drew up a development plan in 1979 for the development and establishment of a pharmaceutical industry in Mozambique which indicated that parallel to the establishment of a pharmaceutical manufacturing

plant, registration control and distribution of pharmaceuticals should be studied since both these broad activities are closely related. A detail feasibility study was submitted by Astra Development AB in 1980 for an industrial unit for production of tablets and oral liquids with an investment cost of over $31 million. The consulting firm proposed annual production of 1000 millions of tablets in 33 formulations in single shift operation of the industry.

The proposal was not implemented primarily as the Government had reservations on such a large investment with long return of investment, the adaptibility of the technology suggested and the need for a large scale manpower training in a developing country like Mozambique.

Before undertaking such large investment, it is necessary to undertake preparatory work which will lead to the development of local skills, technological capability and creation of the necessary infra-structure in the country.

The prsent study period was October 1985 - September 1987 and covers primarily the following three areas:

- potencials, conditions and parameters for the establishment of pharmaceutical industry in Mozambique, (PART-I of submission)
- local training in tabletting technology
- feasibility parameters for the establishment of a pilot plant for pharmaceuticals (PART-II of submission).

This submission deals with studies on the feasibility parammeters for the estblishment of a pilot plant for pharmaceuticals in the People's Republic of MOzambique. Certain parameters, namely the site selection, financial evaluation of alternatives of different types plant constructions (steel, combination of steel and in-situ concrete etc.) including technical details of structural designs (civil/electrical) has not been within the scope of this study, hence it is entitled as Pre-Feasibility Studies.

# ABSTRACT, CONCLUSION AND RECOMMENDATIONS

## 1.0 Most regularly necessary pharmaceuticals

Out of a spectrum of 118 products within the selected top 8 dosage forms that have been consumed in the country, 45 products consisting of 24 tablets, 6 capsules, 7 oral liquids, 3 topical ointments, 2 liquid injectable and 1 each of sterile penicillin powder, ophthalmic ointment and granular syrup are identified as most regularly necessary in Mozambique based on import expenditure, consumption volume and therapeutic group coverage.

## 2.0 Production program and process technology

2.1 The rationale in selection of the production program is that the products are essential and indispensible and embrace a variety of manufacturing technological variants that can be applied to a greater number of products in future.

The production program includes 12 formulations comprising 7 tablet, 4 oral liquid and 1 capsule as illustrated below:

- Tablet, 66 millions:
  Aspirin, Paracetamol, Chloroquin, Co-trimoxazol, Mebendazol, Isoniazid and Phenylbutazone tablets.
- Oral liquid, 1 million bottles:
  Expectorant, Multivitamin, Mebendazol and Co-trimoxazol suspensions.
- Tetracycline capsule, 10 million.

## 2.2 Production process technology

- The technological variants for the manufacture of tablets include dry granulation, wet granulation and film coating, powder filling for capsules and compounding of syrup suspension and emulsion in oral liquids.

- The manufacturing technology suggested is based on semi-automatic equipment to be operated in man-machine combination. The packaging operation is simple and essentially manual consisting of sub-division of tablets and capsules by weighing and filling the plastic container, labelling and boxing 5x8 containers in a locally available card board box.

- The oral liquid includes syrup, suspension and emulsion. These are filled by semi-automatic machine, manually screw capped and labelled. No outer unit carton is proposed for the glass bottles. Thelabelled bottles are packed in card board boxes.

- The selection and acquisition of the suggested technology is consistent with the particular condition and capability currently prevailing in the country.

## 3.0 Materials Movement and Production Process Flow

3.1 The events in the conversion process of pharmaceutical raw materials to finished goods follow the following sequence of operation :

- Receipt and quarantine of raw and packaging materials until quality checks are performed against specifications.
- Storage of the approved materials in the designated active storage area and disposal of the rejected material.
- Dispsense standard quantities of approved materials as per batch formulation and packaging order.
- Manufacturing (compounding/mixing/tabletting/ encapsulation).
- Packaging (subdivision, sealing, labelling and boxing).
- Quarantine and control of finished products.
- Storage and accountibility of the finished products.
- Analysis of batch production records.

## 4.0 Importable Raw and Indigenous Packaging Materials

### 4.1 Raw Materials

All raw materials except water are to be imported. Although sugar is produced locally it does not conform to compedia specifications.

The raw material sources and cost estimates used in this study are based on competitive price quotes. The quality speicifications are USP/BP/EP/IP. Most of the suppliers and manufacturers considered are in pharmaceutical raw material business for many years and the quality is acceptable. In agreement with Medimoc a 10% Medimoc mark-up for handling importable pharmaceutical raw materials has been included in material cost. No customs duty however has been considered. No Medimoc mark-up is included for the packaging materials.

4.2 Indigenous packaging materials based on the structured survey studies performed on the complementary industries in Maputo and Beira for the potential sources of indigenous packaging materials, it is concluded that the packaging materials for the pilot plant productions can be sourced locally. However, these industries deserve limited revitalising support. The local manufacturers should pass through fine tuning development phase integrated with the pharmaceutical quality control.

## 5.0 Manpower and Training

### 5.1 Manpower

Currently local availability of management and technically skilled personnel is the most critical factor for the establishment, operation and maintenance of a domestic pharmaceutical plant in Mozambique. Most of the required skilled hands are to be trained and developed.

The estimated number of total plant personnel with the suggested production program and tecnlology is 85 for full capacity operation. Besides the five key level personnels, the skilled hands constitute 30 operators, 2 production supervisors, 2 maintenance foremen, 3 laboratory analysts and 3 in-process inspectors.

Among the key personnels, the University graduates for the functions of plant engineer and quality control manager are critical. National planning has been suggested for education, training development of maintenance engineer, quality control manager, plant accountant and two utility and electrical foreman. The skilled operators for production are to be selected from 56 pharmacy technicians and/or 87 pharmacy agents available in the country as engaged in NHS. It is foreseen that a few nationals at supervisory, in-process inspection and laboratory technician level in tablet manufcturing and control operations expected to be available locally by 1990with preliminary training received at the "tabletting workshop" at Beira.

5.2 Training

To overcome the critical constraint of manpower, training and development is of foremost important.

In order to develop the two key national personnels, namely, plant engineer and quality control manager a 3-stage action plan is suggested - National planning, institutional education followed by industrial training. External experts shall be needed for these two technical positions until nationals are developed. The training suggested is in two phases, - in-service training for a minimum period of 24 man-months at the start-up of the plant and external industrial training of approximately 20 man-months for the selective key and supervisory personnel. The estimated capital expenditure is US$205,000.

This plan pre-supposes preliminary work-shop training of the tabletting operators, supervisors and laboratory technical personnel at Beira.

It is envisaged, the following international agencies can contribute partly or fully in achieving the suggested training objective, -

- Collaborating foreign pharmaceutical industry
- UNIDO/UN agency(ies)
- Bilateral agreements
- Regional/Sub-regional technical co-operation (SADCC/existing 1981 accord with Mauritius Madagascar in the field of pharmaceuticals).

## 6.0 Site plan, plant design and civil works

6.1 The site slection has not been within the scope of this study, however, the criteria for site selection has been set forth. It is suggested that the pilot plant be phasewise expanded in capacity to attain the level of an industry in future. Therefore the site plan for pilot plant should permit apporximate site utilization of 40-60%.

6.2 The single storied building design consists of 3 bays:

- service bay, within facilities for cafeteria, office, laboratory, lockers and change-rooms, utility and maintenance workshop, 345 $m^2$.
- manufacturing cor area for tablet-capsule dry processing area (excluding corridors) ending to the packaging hall through the sub-division rooms, 225 $m^2$.
- pharmacy, dispensing, material drying and oral liquid wet area leading to the common packaing hall through the sub-division rooms, 180 $m^2$.

The two warehouses, for raw-packaging materials, 110 m2 and finished goods quarantine and store, 184 $m^2$ are located at opposite ends of the building, allowing materials flow in one direction.

The estimated floor space is 1352 m² consisting of the following occupancy :

- Raw and packaging materials, 190 m²
- Pharmacy and Cold storage, 60 m²
- Manufacturing and packaging, 488 m²
- Laboratory and utility, 161 m²
- Finished goods, 184 m²
- Auxiliary facilities, 269 m²

In discussion with the local architects, civil cost estimates have been made for a total of US$700,000 at 1986 construction rates.

6.3 Detail specifications of structural features including comparative studies on different building construction alterr tives, namely, pre-fabricated steel structure, combination of steel (manufacturing area) and concrete construction (warehouse, packing hall, etc.) has not been made.

Despite pre-fabricated steel construction has certain advantages, primarily the reduced construction time and early start-up of the plant, the more conventional form of in-situ concrete construction is suggested since the technology is indigenous in Mozambique. In any event, the civil construction, electrical plant and installation of plant equipment and machineries should be closely supervised with external engineers and technicians. Since this will be the first pharmaceutical dosage form formulation plant in Mozambique it is recommended that the contractors should preferably be of foreign base having experienced in the field.

## 7.0 Collaboration with a suitable foreign industry

Establishment of a joint venture in collaboration with a foreign pharmaceutical industry at public-private or public-public level preferably having experience in developing country is foreseen to facilitate the establishment and operation of a domestic pharmaceutical production unit as well as the sectoral gr[illegible] in Mozambique.

The following specific advantages are cited:

- construction, supervision, installation of machineries and start-up of the plant
- plant utility and maintenance functions
- manpower trianing : extenal and in-service
- adaptation and integration of plant technical and management systems and procedures
- future plant capacity expansion, phasewise introduction of new products/dosage forms and progressively developing the pilot plant to industrial level.
- fine tuning development of domestic complementary packaging material manufacturers
- introduction of registration and drug regulatory administrative systems and procedures
- trading advantages, namely raw material imports.

## 8.0 Time Schedule for implementation

It has been assumed that the in-situ concrete type of construction will take about 2 years since the site plan is finalisedsubject to employment of foreign based contractors and supervision of the civil and electrical and machineries installation by foreign engineers and technicians.

Full production capacity will be reached in phase of 2 years, the start-up year should utilize about half the plant capacity.

9.1 The economic analysis is aimed at the evaluatin of the local production cost. The investment necessary for the establishment of the proposed pilot plant at 1986 cost is estimated to be US$3.55 million.

The split is as under :

| | | US$ |
|---|---|---|
| - Land | ... | Nil |
| - Civil works building | ... | 700 |
| - Furniture, Machinery and equipment | ... | 1241 |
| - Pre-production capital expenditure | ... | 730 |
| - Working capital | ... | 856 |

9.2 Further due to fluctuations of cost in international markets and successive devaluations of local currency it is suggested that at the implementation phase, the total investment and production cost analysis is re-examined including the most cost-effective type of construction keeping in view the local conditions and capabilities.

9.3 At 21% of sales revenue the production margin is $400,000 when operating at full plant capacity. The sales revenue equates to an overall price increase of about 13% of the 1986 import price of the planned 12 finished products. Having the planned volume locally produced the annual saving in foreign currency is estimated to the tune of US$565,000.

9.4 The gross profit of 21% of net sales is generally acceptable. However, the long term financial impacts should be evaluated as indicated earlier. However it should be borne in mind that besides the financial implications, there are a number of significant advantages in the establishment of a pilot plant for pharmaceuticals in Mozambique. Some of these long-term effects foreseen are indicated below :

- establishment of a self-reliant pharmaceutical technology base in the country that would be progressively developed to the industrial level
- avenue for local education, training and development of technical and management man power for industrial level operation as integrated with the academic technical institutes in the country.
- local packaging material suppliers will be revitalised and fine tuned to meet the needs of the pilot plant
- development of overall infra-structure in the country enabling the Government promote foreign investment in pharmaceutical industries through collaboration

# LIST OF ANNEXURE

# 1.0 MARKET INFORMATIONS

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1.2 Health Care System (NHS)

1.3 Importation and Marketing System

1.4 Import Expenditure on Drugs

1.5 Donations

1.6 Drug Consumption

1.7 Product Registration, Generic Names and Patent Laws

1.8 Institutional Mechanism of Drugs Administration.

## 1.1 Population

The population in Mozambique is 14.2 million (1987) and is expected to climb to 20 million by the year 2000. The population growth rate is 2.6%. Among the ten provinces in the country, the three namely, Maputo, Nampula and Zambezia cover 26% of the area and contain about 52% of population.

The age group, 0 - 14 years, represent 46% of population. The mortality rate in this group is estimated to be as high as 100 to 200 per 1000.

The projected population, its distribution by urban and rural areas, and by age and sex (1978-1990) for the years 1978-1995 is indicated in Annex-01 and 02.

The country employs 5.2% of her productive population in 613 known manufacturing enterprises (employment 10 or more) of different size and ownership.

## 1.2 Health Care System

### 1.2.1 General

The National Health Policy is directed towards the mass of the population with priorities laid on preventive care. The health care provided is integrated through a multi-tier system - a package of preventive, curative and rehabilitative actions. It starts from the basic & most peripheral level - the primary health care for preventive and curative treatement and progressively reaches to more complex and specialised level of treatment through health care institutions - the secondary, tertiary and the quarternery levels, refer table 1-1.

The current constrains in resources restricts optimal coverage of the population through the NHS.

### 1.2.2 Primary Level of Health Care

The rural population is concentrated in Communal villages, 1500 to 6000 people per village.

A community health worker at the remotest delivery point, called APE, selected by the community (villagers) trained by the Ministry of Health in the elements of first aid, symptomatic diagonisis of simple illness.

The APE has 4 years primary school education and 6 months of medical education.There are 640 APE's, who are supplied with 330 pages of "Therapeutic Guide" - 1981 in two parts containing schedules of common disease and supervised by the health post/health centre. The health post/health centre is headed by Health Agent.

### 1.2.3 Secondary Level of Health Care

Primary Health Care is supported by the secondary level. This level permeates from the capital of 25 districts out of the total of 110 in the country. Within predominantly curative medical actions more frequent problems of some specialities are also covered.

### 1.2.4 Tertiary Level of Health Care

The level of responsibility extends to the whole province currently to a total of 7 provinces out of 10 in the country. At this level, medical actions include more complex specialities including opthalmology, intensive care, physical and rehabilitative medicine and more complex diagnostic agent.

### 1.2.5 Quarternary Level of Health Care

This level represents the most specialised of all health care levels. The level is of regional nature and consists of the 3 central hospitals in Maputo, Beira and Nampula responsible for south, central and north regions of the country.

Curative care of even more complex specialities including auxilliary diagnostic means namely immunology and endocrinology laboratories are included in this level of health care.

### 1.2.6 Health Heirarchy

**Table 1-1: Health Care Institutions (1985)**

| Level of Health Care | Institutions | Number of Institutions |
|---|---|---|
| 1 -Primary | - Health Post(in communal villages) | 475 |
| | - Health Post(urban) | 919 |
| | - Health Centre | 227 |
| 2 -Secondary | - Rural Hospital & General Hospital | 27 |
| 3 -Tertiary | - Provincial Hospital | 7 |
| 4 -Quarternary | - Central Hospital | 3 |

## 1.3 Importation and Marketing System: Storage & Distribution Net Work

1.3.1 The import is confined within the 323 essential drugs under generic names embodied in the 1984 revised edition of the National Formulary. Under the National Health Care System (NHS) Mozambique imports almost all her requirements of Pharmaceuticals by open international tender through the cost effective and centralised procurement system by the single state company MEDIMOC. The local productions include oral rehydration salt and sodium benzoate expectorant, lotions and ointment produced and consumed through the hospitals and pharmacies (refer table 1-8).

### 1.3.2 Storage and distribution

There are two regional warehouses in Maputo, the capital city and Beira the largest port city in the country. Currently Maputo warehouse takes care of southern region of the country and Beira warehouse shares the greater storage and distribution load for the rest of central and northern regions of the country.

With continued assistance of the government of Italy (1985-1990), $23.3 million are being utilised in 2 phases in up-grading the storage, transportation and distribution of essential drugs primarily at the regional and provincial level. Under the scheme, the storage facilities for the 3 regions of the country (southern, central and northern regions) are rationalised

by up-grading Nacala provincial warehouse to the regional level assuming a better service to the northern part of the country. There are ten (sub-regional) warehouses at the provincial level which are served by the 3 regional warehouses at Maputo, Beira and Nicala. Although there is no formal warehousing system in each district of the peripheral 110 districts, there are informal drug storage facilities.

Land routes are the primary communication links in the distribution network which however has been consistently impeded in about 3 provinces in Mozambique, namely Inhambane, Tete and Cabo Delgado primarily due to the resistance imposed by armed bandits.

Besides, of the total of 50 urbanised pharmacies in the country 37 are state controlled, administered by FARMAC and served by Medimoc and the rest 13 are private owned.

1.3.3 The following table illustrates the trend of import expenditure per utilising sector justifying the large percentage of expenditure are aimed at judicious coverage of the vast 90% of the population non-urbanised in the country who are served through the NHS.

**Table 1-2: Trend of Import Expenditure per Utilising Sector**

| Year | Total OOO MT | N H S OOO MT | % | Pharmacies OOO MT | % |
|---|---|---|---|---|---|
| 1983 | 307,580.2 | 153,811.8 | 50 | 153,786 4 | 50 |
| 1984 | 232,491.0 | 183,215.8 | 78.8 | 49,275.2 | 21.2 |
| 1985 | 275,152.3 | 223,660.9 | 81.3 | 51,491.4 | 18.7 |

## 1.4 Import Expenditure on Drugs

### 1.4.1 General

Natural disasters and destablishing acts of banditism at strategic economic sites and routes led the country to progressive decline on the over all national export/import coverage ratio (0.35 in 1981 and 0.18 in 1984), consequently foreign currency expenditure on import of drugs suffers deterioration, refer table 1-3.

**Table 1-3: Evaluation of dollar expenditure on Drug(1)**

| Index | Expenditure of Drug Imports (Millions of US Dollars) 1981 | 1982 | 1983 | 1984 | 1985 |
|---|---|---|---|---|---|
| Pharmaceutical imports | 11.85 | 8.72 | 6.16 | 4.37 | 5.32 |
| % Health Budget | 21.92 | 16.30 | 12.00 | 16.00 | 23.10 |

(1) Includes donations; values at the then prevailing varying dollar exchange rates.

### 1.4.2 Per capita consumption

The medication coverage of the population was 40% in 1980 which has declined to 35% in 1984.

The per capita consumption including donations is indicated in table 1-4.

**Table 1-4: Trend of Per capita Income & per capita Consumption**

| Index | Value in US Dollar | |
|---|---|---|
| | 1980 | 1984 |
| Per capita income | 182 | 133 |
| Per capita consumption (based on whole population) | 1.0 | 0.40 |

- The per capita consumption includes donations and the decline is significant.
- Mozambique imports drugs at very low cost compared to the consumption cost in many other countries. The per capita consumption may be compared to certain other countries.

| | |
|---|---|
| Bangladesh | $ 0.60 |
| India | $ 1.60 |
| China | $ 3.00 |

## 1 5 Donations

1.5.1 Donation increasingly plays an important role in the national health care system. In 1984, a total of 34 countries/organisations and in 1985, 39 countries/agencies have participated in donations. In order to utilize donations effectively as complementary regular imports, the donation is formally planned at the Ministry of Health in presence of the donating countries/agencies. The value of donations of the pharmaceuticals received between 1983 to 1985 is indicated in table 1-5. Similar trend is foreseen to continue in 1986 and 1987.

**Table 1-5: Trend of Donations**

| Year | Value x 1000 | | % of Global Consumption |
|---|---|---|---|
| | Meticais | Dollar | |
| 1983 | 25,353.5 | 634.95 | 10.3 |
| 1984 | 52,812.2 | 1,323.95 | 30.3 |
| 1985 | 41,905.0 | 1,022.32 | 29.3 |

1.5.2 The Principal dosage form among the donated pharmaceuticals is tablet. In 1982 the regular Medimoc import of tablets was supplemented by donation of 7.82 million tablets (2.03% of import) and in 1984 significant quantity of 39.4 million of tablets (11.5% of import) in the corresponding year. The donation in 1985 was 39.30 million tablets, and this is 23.3% of tablets imported.

## 1.6 Drug Consumption:

### 1.61 Consumption trend of the top five dosage forms

The consumption level is calculated as the total of the pharmaceuticals received through import and donation. Besides the imports, small quantities of expectorant and topicals are produced locally (refer table 1-8). The conusmption of the top 5 dosage forms of pharmaceuticals during 1982 to 1985 is presented in order of incidence in table 1-6. There is almost a progressive decline in consumption of drugs during 1982 to 1985.

**Table 1-6: Consumption trend of the five principal dosage forms during 1982 to 1985.**

| Dosage form | Unit | Consumption in Millions of Unit | | | |
|---|---|---|---|---|---|
| | | 1982 | 1983 | 1984 | 1985 |
| 1 -Tablet | Pieces | 383.58 | 272.62 | 384.82 | 169.63 |
| 2 -Capsule | Pieces | 19.12 | 7.38 | 22.49 | 13.50 |
| 3 -Liquid injectable | Ampoules | 2.89 | 2.19 | 2.95 | 0.61 |
| 4 -Topical ointment | Tubes | 2.44 | 1.37 | 1.03 | 0.10 |
| 5 -Oral liquid | Bottles | 1.69 | 1.15 | 0.79 | 0.17 |

Tablet is the predominant dosage form. Aspirin, Chloroquin & Co-trimoxazol occupies as much as 55% of total tablet consumption in 1985.

There has been substantial reduction in the spectrum of products imported during 1980 to 1985. The product spectrum suffered a negative growth of 77% in oral liquids, 44% in tablets, 36% in capsules and 80% in topical ointments in 1985 over 1982 base.

### 1.6.2 Consumption of the Most Regularly Necessary Products in the National Milieu:

Based on the studies made on drug consumption during 1980 to 1985 in different levels of National Health Care System, a total of 45 formulations in 8 dosage forms are identified as most regularly necessary in Mozambique. Please refer table 1-7(a) for identified products.

Tablet, capsule and oral liquid dosage forms comprise 37 products. Table 1-7(b) indicates the consumption level of these products within the three oral dosage forms in 1984 and 1985.

Table 1-7(a): Identified Most Regularly necessary Products

| A: Tablets | Milligram /Tablet |
|---|---|
| 1. Acetyl salicylic acid | 500 |
| 2. Aluminium hidroxide | 500 |
| 3. Ascorbic acid | 100 |
| 4. Aminophylline | 100 |
| 5. Bisacodyl | 5 |
| 6. Butylscopolamine | 10 |
| 7. Chloroquin phosphate | 250 |
| 8. Co-trimoxazole | 400 + 80 |
| 9. Chloropheniramine | 4 |
| 10. Amelirido | 5 |
| 11. Diazepam | 2 |
| 12. Diazepam | 10 |
| 13. Furesemide | 40 |
| 14. Ferrous sulfate + folic acid | 200 + 0.25 |
| 15. Isoniazid | 100 |
| 16. Methydopa-L | 250 |
| 17. Metronidazol | 250 |
| 18. Mebendazol | 100 |
| 19. Phenylbutazone | 200 |
| 20. Propanolol | 40 |
| 21. Prednisolone | 5 |
| 22. Paracetamol | 500 |
| 23. Praziquantel | 600 |
| 24. Sulfadiazine | 500 |

**Table 1-7(a): Consumption of the Most Regularly necessary Products**

| | | |
|---|---|---|
| B: | Capsules | mg/capsule |
| | 1. Ampicillin | 250 |
| | 2. Amoxicillin | 500 |
| | 3. Tetracycline | 500 |
| | 4. Rifampicin | 300 |
| | 5. Vitamin-B complex | - |
| | 6. Multivitamin | - |
| C: | Oral Liquid: Bottles 100ml | mg/5 ml |
| | 1. Chloroquin | 200+40 |
| | 2. Co-trimoxazol | 200+40 |
| | 3. Chloramphenicol Palmitate | 125 |
| | 4. Expectorant | 250 |
| | 5. Ferrous sulfate | 135 |
| | 6. Multivitamin | - |
| | 7. Vitamin-B complex | - |
| D: | Penicillin Oral Granules: Bottles | |
| | 1. Ampicillin | 250 |
| E. | Sterile Liquid (SVP) Ampoules | mg/ampoule |
| | 1. Chloroquin | 250 |
| | 2. Lidocaine with adrenalline | 400.02 |
| F: | Sterile Pen.Powder: Vials | |
| | 1. Procaine Penicillin | 3 mu |
| G: | Ophthalmics: Ointment | 3.5g/tube |
| | 1. Tetracycline | |
| H: | Topicals: 2.0g/tube | 2.0g/tube |
| | 1. Benzyl benzoate | 1% |
| | 2. Tetracycline | - |
| | 3. Methol and Methyl salicylate | 1% + 3% |

**Table 1-7(b): Consumption of the identified most regularly necessary products in tablet, capsule and oral liquid dosage forms (1984 and 1985)**

| Product dosage form | Number of formulation | Consumption 1984 Unit Million | 1984 % of total consumption | 1985 Units Million | 1985 % of total consumption |
|---|---|---|---|---|---|
| Tablet | 24 | 382.48 | 96.7 | 155.66 | 91.6 |
| Capsule | 6 | 25.57 | 88.8 | 13.27 | 93.2 |
| Oral liquid | 7 | 0.622 | 78.7 | 0.108 | 63.4 |

- The single aspirin tablet constitutes 53.7% and 25.9% of 1984 and 1985 annual consumption volume of the selected 24 tablet formulation.
- Tetracycline capsule constitutes 50.6% and 50.2% of the global capsule consumed in the country in 1984 and 1985 respectively.
- The expectorant is the principal oral liquid formulation that occupies 77.4% in 1984 - and the hoemantinic ferrous sulfate 62.0% of 1985 oral liquid consumption of the identified products.

### 1.6.3 Current consumption through local production

The local productions pharmaceuticals embrace 16 formulations in 3 dosage forms, namely 1 oral liquid, 6 topical ointments and 9 lotions. In addition, 585,480 and 2,354,200 sachets of the anti-diarrhoeal oral rehydration salt were produced in 1985 and 1986 respectively at EMOFAR, Beira. The annual country requirement of the ORS has been estimated to be 6 million sachets. Limited quantities LVP is produced in the central hospital in Maputo.

The estimated local production of the oral and topical produced in 1984 and 1985 in the 7 provincial, 3 central hospitals and 50 pharmacies (state controlled and private owns) in Mozambique are illustrated in table 1-8.

Due to economic constrains the volume of local productions of pharmaceuticals is dependent on the quantity of importable raw materials availability. The expenditures in ointment and lotions for external application, is about 12% in 1983 which is the maximum in recent year.

**Table 1-8: Estimated local production of Pharmaceuticals**

| Group | Product | Unit | Quantity x 1000 1984 | 1985 |
|---|---|---|---|---|
| - Expectorant | Sodium Benzoate Syrup | Kg | 13.1 | 67.2 |
| - Antiseptic lotion | Chlorohexidine, Eosine, Gentian violet, Iodine tincture, Hexachloro benzine, Chloramine, Sodium nitrite and Broic acid. | Litre | 50.7 | 593.8 |
| - Topical ointment | Prednisolone, Camphor, Acid salicylic, Emxofize, Oleo de-cade and Co-trimoxazol. | Kg | 30.2 | 113.9 |

- Plan for local production of topical ointment (1987/1988). OXFAM and EEC is currently financing a project for local production of topical ointments in Mozambique, annual capacity of 60,000 Kg, at an investment of US$80,000 approx.

## 1.7 Pharmaceutical Product Registration, Generic names/Trade names and Patent Laws

1.7.1 There is no formal drug registration system in Mozambique. The imports however are confined within the National Formulary.

The National Formulary is periodically up-dated and the latest revision (1984) has embodied 323 essential drugs as recommended by the 7-membered Drug Technical Advisory Board.

Since the products selected for production in the pilot plant are available in the National Formulary no difficulty is foreseen in getting them registered with the Ministry of Health. The enactment of a legal procedure however is foreseen to be necessary for any joint venture establishment in future.

1.7.2 Currently there is no legal regulation as to name a product (trade or generic) that are to be produced in the country since the National Formulary contains products as numbered divided by thereapeutic groups under generic names, the products to be produced in Mozambique shall bear only generic name.

The use of generic names is parallel to the present institutional teaching programes and the drug prescriptions that are made in the country.

1.7.3 Patents - at present there is no patent law in Mozambique for process or product.

## 1.8 Institutional Mechanism of Drugs Administration

1.8.1 The present drugs administrations system is composed of the following essential elements in a simple and sound base.

- Periodically up-dated National Formulary for consumption of essential durgs in the country.
- Seven membered drugs technical advisory board for planning.
- Directorate of drugs administration, Ministry of Health as the central body for planning and co-ordination, and
- Centralised import, decentralised storage and distribution of drugs by the national trading company, MEDIMOC.

## POPULATION GROWTH RATE 1978-1990 (Source: The National Planning Committee)

| Indices | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Numero de habitates (em Milhoes) 0-14 anos | 5181 | 5320 | 5464 | 5628 | 5797 | 6172 | 6358 | 6549 | 6765 | 6988 | 7456 | 7702 | 7955 |
| 15-44 anos | 5055 | 5191 | 5331 | 5492 | 5656 | 5727 | 5899 | 6076 | 6276 | 6483 | 6582 | 6799 | 7022 |
| 45 anos ou mais | 1514 | 1555 | 1597 | 1645 | 1694 | 1642 | 1692 | 1742 | 1800 | 1859 | 1799 | 1858 | 1919 |
| Total: | 11751 | 12067 | 12394 | 12766 | 13149 | 13543 | 13950 | 14368 | 15842 | 15332 | 15838 | 16361 | 16897 |
| Distribuicao por sexos Masculino(%) | 49.62 | | | | | | | | | | | | |
| Feminino (5) | 50.37 | | | | | | | | | | | | |
| Taxa de crescimento anual da populacao | 2.7 | 2.7 | 2.7 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 |
| Populacao rural(%) | 90 | | 85-90 | | | | | | | | | | |
| Populacao Urbana(%) | 10 | | 10-15 | | | | | | | | | | |

## POPULATION, GROWTH AND HEALTH COVERAGE 1979-1995

| Anos / Indicadores | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 | 91 | 92 | 93 | 94 | 95 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Taxa de Crescimento da Populacao prevista (%) | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 |
| Populacao total prevista (em Milhoes) | 11.58 | 11.88 | 12.19 | 12.51 | 12.84 | 13.17 | 13.51 | 13.86 | 14.22 | 14.59 | 14.97 | 15.36 | 15.76 | 16.17 | 16.59 | 17.02 | 17.46 |
| Taxa de Cobertura Sanitaria esperada (%) | 36 | 40 | 44 | 48 | 52 | 56 | 60 | 64 | 68 | 72 | 76 | 80 | 84 | 88 | 92 | 96 | 100 |
| Populacao medicada (em Milhoes) | 4.17 | 4.75 | 5.36 | 6.00 | 6.68 | 7.38 | 8.11 | 8.87 | 9.67 | 10.50 | 11.38 | 12.29 | 13.24 | 14.23 | 15.26 | 16.34 | 17.46 |
| % da Populacao com 0-14 anos | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 | 46 |
| Populacao com 0-14 anos medicada (em Milhoes) | 1.92 | 2.19 | 2.47 | 2.76 | 3.07 | 3.39 | 3.73 | 4.08 | 4.45 | 4.83 | 5.23 | 5.65 | 6.09 | 6.55 | 7.02 | 7.52 | 8.03 |

Source: ASTRA Development AB.

## 2.0 PRODUCTION, QUALITY CONTROL AND WAREHOUSING

2.1 Product Selection Rationale

2.2 Production Prorgram

2.3 Manufacturing Technological variants

2.4 Detailed Production Methods:
- Manufacturing and Packaging

2.5 Phasing of Product Introduction
- Adaptation of Technolgy
- Work Environment

2.6 Rated Production Capacity and Plant loading

2.7 Quality Control Functions

2.8 Raw/Packaging Materials and Finished Goods Warehouse
- Raw and Packaging Materials Warehouse
- Material Storage, Use and Documentation.

## 2.0 Production, Quality Control and Warehousing

### Production

#### 2.1 Product Selection Rationale

2.1.1 Complexity of dosage formmanufacture. The six pharmaceutical dosage forms are arranged below in the decreasing order of complexity of production technology.

-Injectables IM/IV
-Ophthalmics
-Tablets/Topicals ointments and lotions
-Capsules/Oral liquids.

2.1.2 -The products selected for the pilot plant manufacture comprise tablets, capsules and oral liquid dosage forms, refer table 2-1.

-The products have been identified taking into consideration the following factors :

--The products are classified as essential drugs in Mozambique National Formulary of Medicaments and WHO Model List of Essential Drugs (Fourth Revision), Technical Report Series 722, Geneva, 1985 and UNIDO illustrative list of 26 essential drugs, "The Use of Essential Drugs", Technical Report Series, No. 685.

--These are included among the 45 products that are identified as most regularly necessary in Mozambique, refer table 1-7(a).

--WHO committee reports of meetings on drug policies[1], 1979.

-From the manufacturing view point the selection rationale lends itself to diverse manufacturing technology, refer to 2.3.1 for manufacturing technological variants. The diversity in technology included in the production program would enable phasewise introduction of wide range of new products within the acquired technological variants.

(1) Formulation of dosage forms and in-process quality control of essential drugs in developing countries, Geneva, 3-6 April, 1979.

Table - 2.1 Selected Products :

| | Products | Dose/Unit |
|---|---|---|
| I. | TABLETS : | |
| | | mg/tablet |
| | A. Uncoated | |
| | -Acetyl salicylic acid | 500 |
| | -Chloroquin phosphate | 150 (Base) |
| | -Paracetamol | 500 |
| | -Mebendazol | 100 |
| | -Isoniazid | 100 |
| | -Co-trimoxazol | 400 + 80 |
| | B. Coated | |
| | -Phenyl butazone | 200 |
| II. | CAPSULES : | mg/capsule |
| | -Tetracycline | 500 |
| III. | ORAL LIQUID : | mg/5ml |
| | -Expectorant | 250 |
| | -Multivitamin syrup | - |
| | -Mebendazol suspension | 100 |
| | -Co-trimoxazol suspension | 220 + 40 |

-These are consumed in the country in fairly large quantities in primary, secondary, tertiary and quarternery levels of NHS, refer table 2-2a. Due to cost reasons the consumption level form of oral liquid dosage (1982-1985) has progressively declined.

Table 2-2a - Consumption volume of the selected products

| Product Dosage Form | 1982 | | 1984 | | 1985 | |
|---|---|---|---|---|---|---|
| | Units Millions | % Consumption | Units Millions | % Consumption | Units Millions | % Consumption |
| Tablets | 265.6 | 69.24 | 239.9 | 62.34 | 88.46 | 52.0 |
| Capsules | 10.8 | 56.25 | 12.2 | 54.25 | 6.66 | 49.0 |
| Oral Liquid | 1.1 | 65.09 | 0.52 | 75.15 | 0.001 | - |

-The estimated minimum country requirements of the selected products in 1990 and 1994 are illustrated in table 2-2b.

Table 2-2b - Long range projected requirement of the 12 selected products in 1990 and 1994

| Dosage Form | Unit | Units in Millions | |
|---|---|---|---|
| | | 1990 | 1994 |
| Tablets | pieces | 768 | 1127 |
| Capsules | pieces | 20 | 30 |
| Oral liquid | bottles | 2.08 | 3.38 |

-The selected product-mix as illustrated in table 2-1 embrace important therapeutic groups. The magnitude of import expenditure for pharmaceuticals within these therapeutic groups in 1980, 1982 and 1984 are indicated in table 2-3 as percent of global pharmaceutical expenditure.

Table 2-3 - Percent expenditure by therapeutic groups.

| Representative Therapeutic Group | % Global Pharmaceutical Import Expenditure | | |
|---|---|---|---|
| | 1980 | 1982 | 1984 |
| 1. Antibiotics and Antiparasites | 45.6 | 47.4 | 36.6 |
| 2. Somatic nervous system | 7.3 | 8.5 | 15.7 |
| 3. Respiratory | 4.2 | 2.2 | 8.6 |
| 4. Nutrition | 11.4 | 6.1 | 3.0 |
| 5. Antirheumatics | 1.9 | 3.6 | 0.7 |

Conclusion : The importance of the selected products within the above therapeutic groups lie in medical, financial and diversity of manufacturing technology. These are basic and indispensible in Mozambique.

## 2.2 Production Program

### 2.2.1 Principle :

-The production volume and the product-mix selected for the pilot plant offers necessary input for dimensioning the plant and fulfilling the following conditions for manufacture :

--Progressive development of manpower in technical, plant management and administration.

--Adherence to WHO good manufacturing practices.

--Possibilities of future expansion and introduction of new formulations within the acquired technology.

--Integrated plant systems and procedures.

2.2.2 The production program is indicated in table 2-4. It is envisaged that the full capacity production in the pilot plant should bereached in second year of operation (refer table 2-7). The products included in the production program represents 5% to 20% of the projected consumption level in 1990.

Table 2-4 - Proposed Production Program

| Product | Production volume Millions of Unit |
|---|---|
| A. Tablets (Uncoated) : | |
| 1. Acetyl Salicylic Acid, 500 mg | 20 |
| 2. Chloroquin, 150 mg | 25 |
| 3. Paracetamol, 500 mg | 5 |
| 4. Mebendazol, 100 mg | 5 |
| 5. Isoniazid, 100 mg | 3 |
| 6. Co-trimoxazol, 400 mg + 80 mg | 6 |
| B. Tablets (Coated) : | |
| 1. Phenylbutazone, 200 mg | 2 |
| C. Capsules : | |
| 1. Tetracycline, 500 mg | 10 |
| D. Oral Liquid : | 000's bottles |
| 1. Multi-vitamin, 100 ml | 350 |
| 2. Mebendazol, 2 g/100 ml | 200 |
| 3. Expectorant, 5 g/100 ml | 200 |
| 4. Co-trimoxazol, 4000mg, 800mg/100ml | 250 |

2.2.3 Oral Liquid Dosage Form :

-The children (upto the age of 14 years) is 46% of population and estimated to be 5.65 millions in 1990. Oral liquid is the preferred administration form for the children.

-In 1982, 26 formulations (in 151,049 litres/ 1.69 million bottles) of syrups, suspensions and emultions were consumed in the country which has declined to 11 formulations in 1984 and 6 in 1985. In 1985, there is a drop of 90% in oral liquid consumption volume over the base year 1982. The reason for the progressive decline in import of the oral liquid is the high import cost of this dosage form.

-Import of selective formulations in compounded bulk form, followed by subdivision and repacking in smaller packs at the country's hospital pharmacies eliminating the unit outer cartons is foreseen to off-set substantially the high import cost of oral liquid. Table 2-5 illustrates the foreign currency component of the current unit price of the selected oral liquids.

Table 2-5 The unit C&F price (1986) of the selected products included in the production program

| Product | Pack size | C&F price per unit US$ |
|---|---|---|
| -Expectorant | 100 ml | 0.50 |
| -Co-trimoxazol | 100 ml | 0.77 |
| -Multivitamin | 125 ml | 0.47 |
| -Mebendazol | 100 ml | 0.86 |

Table 2-5(a) indicates the 1984 import volume, unit cost and expenditures of oral liquid products. The expectorant alone represents 69% of oral liquid import volume and 64% of the import expenditure of total oral liquid consumption in 1984. In 1965 the regular oral liquid import is 11,168 bottles which is 6.8% of donations and cover only three formulations namely, Chloroquin phosphate, Chloramphenicol and Propiliodona suspension.

**Table 2-5(a) : Liquid Imports & Expenditure Level 1984**

| Product | Quantity x 1000 | Unit Cost Meticaise | Import Cost Meticaise x 1000 |
|---|---|---|---|
| 1. Chlorpheniramine, 150 ml | 20.0 | 22.52 | 450.5 |
| 2. Caulina and Rectina, 100 ml | 20.0 | 21.75 | 435.0 |
| 3. Pepsin and Pancreatin, 140 ml | 1.4 | 92.86 | 130.0 |
| 4. Sodium benzoate, 125 ml | 480.0 | 13.22 | 6346.8 |
| 5. Chloroquin phosphate, 75 ml | 60.0 | 12.49 | 749.9 |
| 6. Vitamin B-Complex, 100 ml | 17.5 | 14.72 | 257.3 |
| 7. Multivitamins, 100 ml | 17.5 | 15.75 | 257.6 |
| 8. Defenoxilato, 110 ml | 60.0 | 21.75 | 1305.0 |
| 9. Clomifeno, 60 ml | 20.0 | 10.15 | 203.0 |
| 10. Co-trimoxazol, 60 ml | 22.0 | 14.80 | 325.6 |
| 11. Chloramphenicol palmitate, 60 ml | 60.0 | 15.00 | 900.0 |

## 2.3 Manufacturing Technology

### 2.3.1 Manufacturing Technological Variants :

-Manufacturing here-in referred to as compounding/mixing/encapsulation/tabletting/coating operations in the production cycle of the selected products.

-A description of the manufacturing technological variants by each of the selected products within the three dosage forms is illustrated in table 2-6.

Table 2-6 Manufacturing Technological Variants

| | Technological Variants |
|---|---|
| I. Tablets : | |
| i) Plain | |
| -Acetyl salicylic acid | -Dry granulation |
| -Paracetamol | -Wet granulation |
| -Chloroquin | -Dry granulation |
| -Isoniazid | -Wet granulation |
| -Mebendazol | -Wet granulation |
| -Co-trimoxazol | -Wet granulation |
| ii) Coated | |
| -Phenylbutazone | -Wet granulation + Film coating |
| II. Capsules | |
| -Tetracycline | -Powder filling |
| III. Oral Liquid | |
| -Multivitamin | -Svrup/Emulsion(O/W) |
| -Mebendazol | -Suspension |
| -Expectorant | -Suspension |
| -Co-trimoxazol | -Suspension |

O/W = Oil in water type; Production= Manufacturing + Packaging

## 2.4 Detailed Production Methods : Manufacturing & Packaging

### 2.4.1 Manufacturing

-General

-The suggested manufacturing operations for tablets, capsules and oral liquids are based on semi-automatic equipment and optimum performance will depend on man-machine combination. The individual product within the respective dosage form will follow the process profile characteristic of the product. The outlines of the technical profiles are presented symbolically in Annex 04 through 07.

-The estimated annual manufacturing requirements for tablets, capsules and oral liquid based on the proposed production program are as under :

| Dosage Form | Unit | Blending/ Mixing quantity (at full capacity) |
|---|---|---|
| Tablet -Dry process | Kg | 31,710 |
| -Wet process | Kg | 6,700 |
| Capsule | Kg | 6,500 |
| Oral liquid | L | 105,000 |

-Raw materials dispensing

The materials as specified in the prescribed formulation order of the product are weighed centrally in the designated weighing room in pharmacy and dispensed in the identified containers and waited in the segregated pharmacy area marked as DISPENSED MATERIALS AREA until received by appropriate sections of the production department conforming to GMPs.

-Tablet/Capsule

-Drying

-The powder materials are to be dried in tray dryer and granular materials in fluid bed drier. Depending on product preliminary drying of wet mass is done in tray drier.

-Blending/Mixing

-During blending/mixing operations the materials are sequentially added into the blender/mixer in a pilot/co-pilot concept following standard manufacturing procedure for the specific product.

-Tablet compression/capsule filling

-On completion of mixing the control laboratory approved blend is charged to granulation/tablet compression/encapsulation depending on product type.

-The bulk tablet/capsule is then held until released by quality control/in-process inspectors for subsequent steps in the manufacturing cycle.

-Coating

-Tablet coating operation is performed in a variable speed rotating pan using semi-automatic spray gun. The use of flammable organic solvents should conform to GMP and safety requirements.

-Oral Liquid

-Base preparation

-Sugar solutions, dispersions of suspending aids, thickening agents etc. are prepared in separate vessels with stirring, homogenising, filtration as required.

-Mixing/Compounding/Filtration

-Compounding operations are to be carried out in 1000L and 500L (working capacity) st.st.[1] jacketted vessels equipped with man-door, outlet, gas purging inlets and variable speed propeller type stirring facility. The compounded bulk is filtered depending on product through suitable filter media.

2.4.2 Packaging

-General

-The packaging technology suggested (refer Annex 08 for tablets/capsules) and ease of adaptibility. The suggested pack sizes are economic and suited to the local market. Since the domestic market is not competitive, the importable and sophisticated technology of product presentation by foiling or blister packing has been excluded.

-Tablets/Capsules

-The products produced in the pilot plant will be consumed primarily through hospitals. The bulk packing of tablets and capsules in units of 1000's (an/or in multiples of 1000's) are suggested.

---

(1) stainless steel

-Subdivision operation is carried out by weighing in the sub-division rooms directly connected to the common packaging hall by conveyor belts. The tablets/ capsules are then placed in polythene bags, sealed and put to plastic jar or directly put into cleaned plastic jars. The plastic jars are about 55% cheaper (1986 price) over the local tin containers. The jar is then labelled with pre-printed labels and packed in hard board boxes fabricated locally.

-Oral Liquid

-Bottle wash

--Locally fabricated sodalime amber glass (NP) bottles will be used. These bottles will be washed manually in the wash basins, rinsed with distilled/filtered water and drained inverted on perforated aluminium trays on trolleys in the washing section.

-Filling

-The filling operation with 4 ounce bottles in 100ml fills is suggested to be carried out in semi-automatic filling machine at an estimated effective line rate of 20 bottles per minute by feeding ghe washed bottles manually into the machine. The filling,capping, labelling and boxing operations are performed in a continuous line operation.

-Closing

-Filled bottles will be closed with 25 mm size aluminium screw caps with wads by rotating them on the bottle neck. For reasons of adaptibility with local closures manual closing operation is suggested at initial phase.

-Labelling

-Pre-cut locally printed labels will be glued and pasted manually on each bottle on the conveyor belt.

-Cartoning

-No outer unit cartons are suggested for the labelled bottles.

-Packing

-Each 5x8 labelled bottles will be packed in the locally fabricated card board boxes designed to size specifications (refer table 4.2).

2.4.3 Quarantine :

On completion of packing the goods are initially transported to quarantine store, held until released by quality control and finally removed to the adjacent active finished goods warehouse. The functions of quarantine store should be supervised by quality control section.

## 2.5 Phasing of Product Introduction

### 2.5.1 Adaptation of Technology

-General

-Based on the complexity of formulations and manufacturing technology, the ease of adaptibility of technology for the proposed dosage forms and the need for phasewise development of technical personnel, the following phasing of product introduction is suggested :

| Dosage Form | Phasing | |
|---|---|---|
| | I | II |
| 1. Tablets | | |
| i) Plain | ——— | |
| ii) Coated | | ——— |
| 2. Capsules | ——— | |
| 3. Oral Liquid | | |
| i) Syrup | ——— | |
| ii) Suspension | ——— | |
| iii) Emulsion | | ——— |

2.5.2 Production Phasing

-It is envisaged that about 50% of the installed production capacity should be utilised in the start-up year and the full capacity in second year. The proposed phasing of products is shown in table 2-7.

Table 2-7 Phasing of Introduction of the Selected Products

| PRODUCT | PRODUCTION PHASING Year-I | Year-II |
|---|---|---|
| A. Tablets - in Millions | | |
| -Acetyl Salicylic Acid,500mg | 10 | 20 |
| -Chloroquin, 150mg base | 12 | 25 |
| -Paracetamol, 500 mg | 3 | 5 |
| -Isoniazid, 100 mg | 1 | 1 |
| -Mebendazol, 100 mg | 5 | 5 |
| -Co-trimoxazol, 400mg + 80mg | 2 | 6 |
| -Phenylbotazone(1) 100mg | - | 2 |
| | 33 | 60 |
| B. Capsules - in Millions | | |
| -Tetracycline, 500mg | 5 | 10 |
| C. Oral Liquid - in 000's bottles | | |
| -Multi-vitamin | - | 350 |
| -Mebendazol, 100mg/5ml | 120 | 200 |
| -Expectorant, 250mg/5ml | 160 | 200 |
| -Co-trimoxazol, 200mg+40mg/ml | 150 | 250 |
| | 430 | 1000 |

(1) Film coated tablet

2.5.3 Work Environment

-General

-The purpose of these methods is that the pharmaceutical products should be protected from contamination and the working people from over-exposure to toxic raw materials, accidents and injuries. It is suggested that WHO GMP be implemented in phases with operator's gain in experience in pharmaceutical operations.

-Since the suggested technology is largely manual, the following basic measures of protection by use of protective wear especially in working areas where operators come in direct contact with material and/or products, namely tablet/capsule manufacturing, material dispensing and oral liquid compounding area.

--Aprons/special protective gown
--Nose mask/dust-foe mask/shields for inhalation hazards.
--Protective eye glasses
--Rubber or canvas foot covers

The above protective appliances for operators are to be integrated with the built-in preventive measures, refer Safety Provisions, 4-4.

-The isoniazid hydrochloride is a potent material. The air-borne level of the pharmaceutical raw materials/chemicals especially in tablet/capsule manufacturing area should be monitored in terms of permissible exposure limits (PEL) and threshold

values by periodical air sampling and wipe samplings for inhalation, skin and ingestion hazards respectively.

## 2.6 Production Capacity and Plant Loading

### 2.6.1 -General

-Certain basic assumptions are made on the working conditions for plant operations in order to estimate the plant capacity and plant loading.

The basic assumptions made to standardise the plant operations include :

-annual net plant working days, 229
-gross and net productive time per day(single shift) per direct labour, 7 hours and 6.5 hours respectively.
-net machine running time per day, 6 hours.

It is suggested that an annual plant shutdown be planned for preventive maintenance to minimise infrequent equipment failures, on-line repairs and optimise plant through-puts. The plant shoutdown may be time with workers annual leave.

Please refer to Annex-09 for details of the basic assumptions and plant working conditions.

2.6.2 Production Batch Size

-Based on the production program, the equipment proposed and the manufacturing technology the suggested production batch size are indicated in table 2-8.

Table 2-8 Production Batch Size

| Dosage Form | Manufacturing | | Packaging(1) | |
|---|---|---|---|---|
| | Unit | Mixing | Unit | Subdivision |
| Tablet -Dry granulation | Kg | 200 | Jar | 300 |
| -Wet granulation | Kg | 200 | Jar | 325 |
| Capsule | Kg | 60 | Jar | 92 |
| Oral liquid | L | 1000 | Bottle | 9900 |

(1) 1000 tablets/capsules per jar and 100 ml oral liquid per bottle.

2.6.3 Based on certain assumptions indicated in Annex-09, the estimated annual capacity is illustrated in table 2-9.

Table 2-9 Estimated Annual Capacity (One shift basis)

| Product Form | Mixing (Kgx1000) | Compression(1)/ Encapsulation (Units x million) | Sub-division (Jars/Bottles x 1000) |
|---|---|---|---|
| Tablet | 50 | 75 | 80 |
| Capsule | 12 | 16 | 80 |
| Oral liquid | 110 | - | 1200 |

(1) Intermediate process : slugging, 25000 Kg and coating, 6000 Kg.

2.6.4 Plant loading

-With the proposed production program, working conditions (Annex-05) and the installed capacity table 2-9, the percentage plant loading at full production is indicated below :

| Product Form | % LOADING | | |
|---|---|---|---|
| | Mixing | Compression/ Encapsulation | Packaging |
| Tablet | 76 | 86 | 83 |
| Capsule | 60 | 65 | 12 |
| Oral liquid | 90 | - | 83 |

2.6.5 The packaging operation for tablet/capsule is essentially manual.

-By addition and/or change of certain manufacturing machines the plant capacity can be increased.

2.7 Quality Control Functions

2.7.1 Bacground

-At present there is no formal drug testing laboratory in Mozambique except limited and specific activity carried out for oralite formulation at Beira. The central National Hygeine Laboratory for Food and Water located at the Ministry of Health, recently initiated formation of a nucleus for limited pharmaceutical analysis.

-In order to ensure that the locally produced finished products meet the acceptable quality standards it is necessary that the production in-puts are judged and the production processes are served with quality control system as an integral part of the production functions.

2.7.2 The quality control system envisaged broadly embrace the following category of functions :

i) Analytical Laboratory Controls
ii) In-process controls.

i) Analytical Laboratory Controls

The analytical laboratories consist analytical chemical laboratory; physico-chemical laboratory; microbiological laboratory.

These covers the followingresponsibilities :

-development and adaptation of the necessary specifications, test procedures, control methods and quality assurance profiles for in-coming raw and packaging materials, semi-finished and finished products.

-analyse raw materials, packaging materials and semi-finished product against specifications for acceptance or rejections following appropriate analytical methods. It will also initiate/co-ordinate corrective actions for deviations from standards.

The outline of the quality control function in relation to materials, products and processes may bedepicted as follows :

-Raw and PackagingMaterials :

-development and co-ordination of local suppliers/ manufacturers of packaging materials

-physical checks and tests of in-comingmaterials

-chemical testing

-microbiological analysis

-Finished Products :

-Physical, chemical and microbiological testing
-Stability studies(1)
-Production batch record analysis and monitoring AOQL.

2.7.3 In-process materials/systems/processes :

-inspection of production processes, sampling procedures and technics, physical checks and documentation.

-validation of processes and equipment

-environment control : house-keeping, safety, production hygeine, monitoring cross-contamination levels.

---

(1) Reference: Accelerated stability studies of widely used pharmaceutical substances under simulated tropical conditions, WHO/PHARM/86.529.

## 2.8 Raw Materials, Packaging Materials & Finished Goods Warehouse

### 2.8.1 Flow of Raw and Packaging Materials :

-Introduction

-The movement of materials adds to the cost of the product while leaving its value unchanged. For safe and efficient operation and orderly and sequential flow of material movement and related activities is suggested. The proposed design of the floor plan of the pilot plant permits unidirectional flow of materials. The size of the raw and packaging material warehouse is based on the assumptions of the inventory profiles of 6 months and 3 months for RM and PM respectively.

-Raw and Packaging Material Warehouse, 374$m^2$

-The flow of materials is designed to prevent back-tracking. The major events in the in-coming materials flow process are indicated in Annex-11 which then moves through manufacturing, packaging, quarantine for unreleased finished goods and finally to active finished goods warehouse.

-Finished Goods Warehouse, 124$m^2$

The finished goods warehouse design primarily consists of :

-segregated storage area for released finished goods at ambient temperature,

-a restraint area for returned goods awaiting analysis and disposal, an area for storage of shippers etc.

-a despatch area including loading dock for finished goods distribution.

-Material Handling and Transportation

-The technology suggested for handling and transportation of materials in the pilot plant is essentially manual with the use of portable carts such as hydraulic trolley, pushing hand trolley etc. in preference to fork lift trucks and palletising.

However, with phasewise increase in plant loading and gain in experience the method of in-house ancillary activities may be progressively up-graded and mechanised to attain favourable cost and efficiency level.

-Heavy materials such a· sorbitol, liquid glucose, glycerine, etc. in jar may be conveniently lifted and stacked with the use of manually operated hoist and crane.

2.8.2 Material Storage, Use and Documentation.

-The recommended system for storage and environment control :

-In the active storage area open "block" stacking (refer Annex-10) utilisingoptimum air space the pre-allotted areas for bulk and large consignments of packaging containers e.g. bottles, jars, maintained in a manner

permitting ready accessibility to the inventory for the operating personnels. To avoid mix-ups adequate spacing should be maintained between stacks.

-"Shelving" in racks for small, lighter and often expensive items. To ensure adequate shelf life of the stored materials, the temperature sensitive materials shall be stored at the predetermined optimum environmental conditions - away from temperature extremes.

-Material use and documentation

-In the management and issue of the RM/PM for use in production area the GMP demand of the FIFO system (first in first out) should be followed using oldest inventory first ensuring expired inventory not being used.

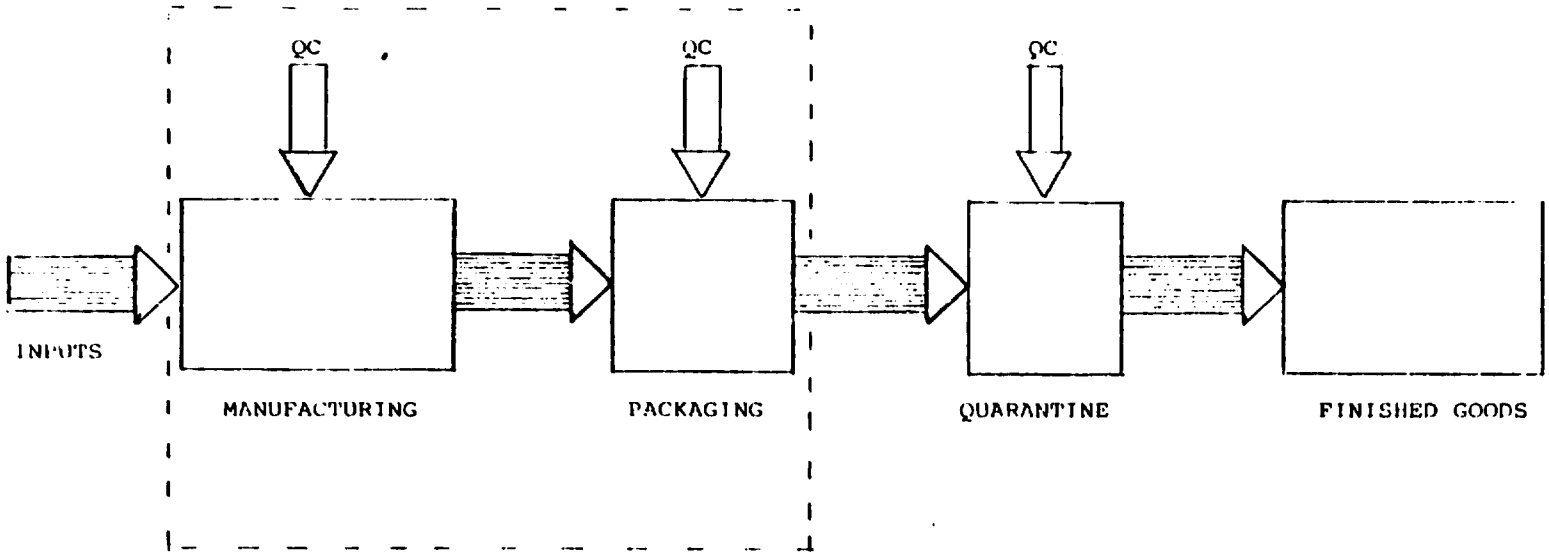
-Perpetual recording through a manual cardex system of materials receipt, issue, returns and retest is suggested.

-The design of flow of the in-coming materials and the paper works at the RM-PM warehouse including dispensing of materials is illustrated in Annex-10.

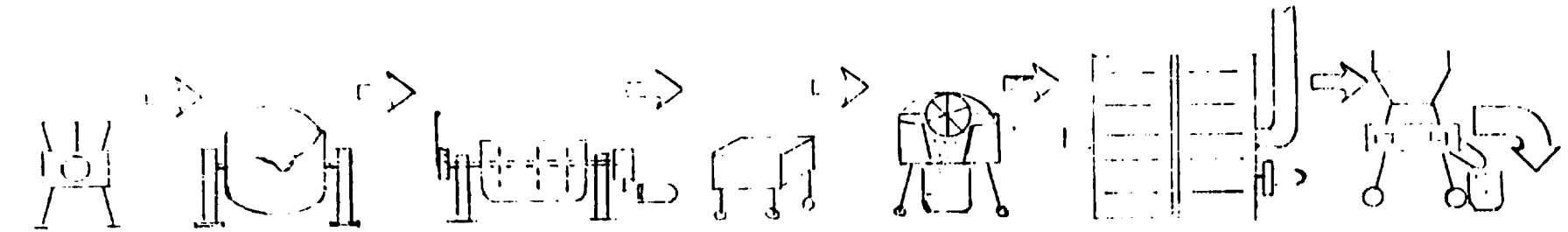
-Re-test dates of formulation materials under the specific storage conditions should be established. Short dated materials are to beretested prior to use as suggested in next page.

| Active Material Dating period | Short dated when |
|---|---|
| 12 months | less than 4 months remain |
| 18 months | less than 6 months remain |
| 24 months | less than 6 months remain |
| 36 months | less than 9 months remain |
| 48 months | less than 9 months remain |
| 60 months | less than 12 months remain |

## PRODUCTION PROCESS FLOW - GENERAL



# FLOW SHEET: TABLETTING - WET GRANULATION & COATING.



GRINDING SIFTING

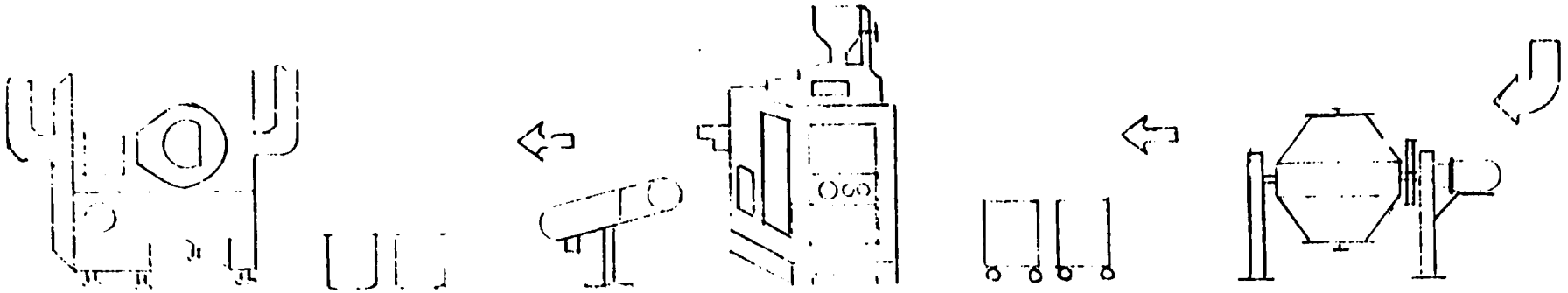
GRANULATION FLUID

WET MASS MIXING

WET GRANULATION

TRAY DRYING

MILLING & SIFTING



COATING

DEDUSTING

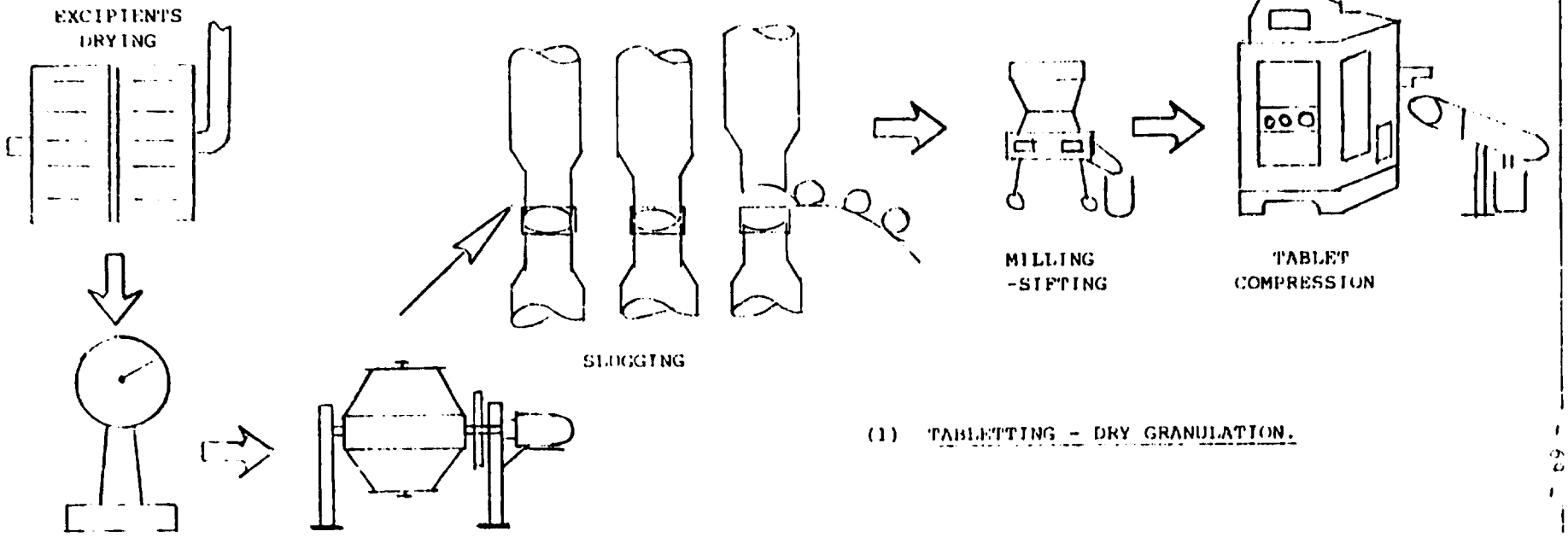
TABLET COMPRESSION

DISPENSING CONTAINERS

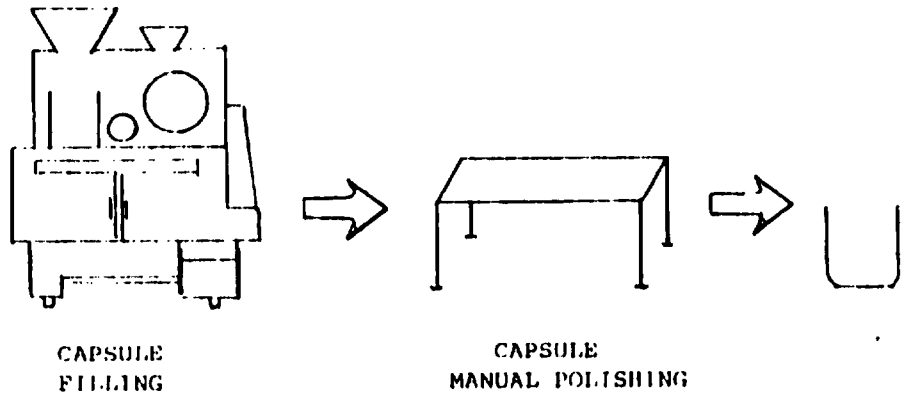
BLENDING

PACKAGING

FLOW SHEET: (1) TABLETTING - DRY GRANULATION, &
(2) ENCAPSULATION.

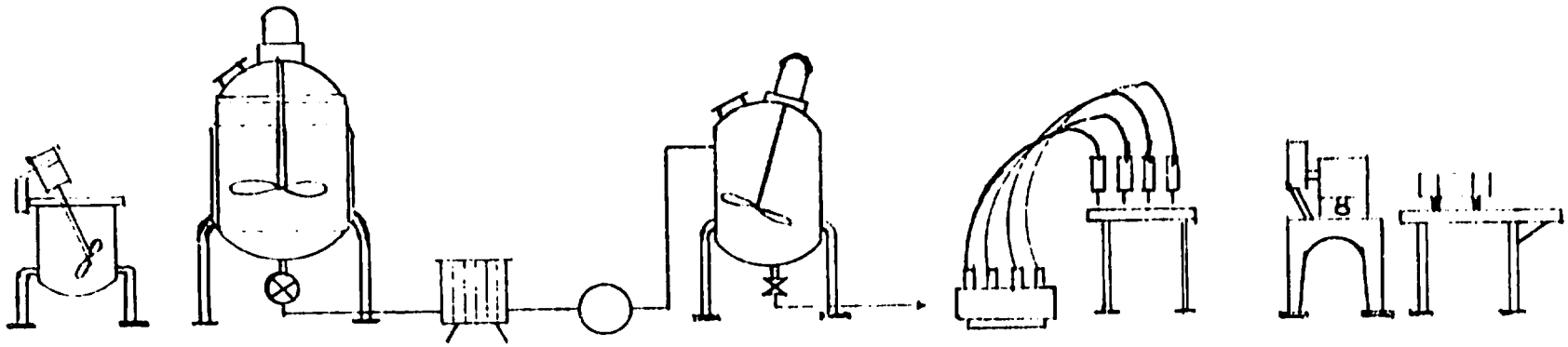



(1) TABLETTING - DRY GRANULATION.




(2) ENCAPSULATION

## FLOW SHEET : ORAL LIQUIDS



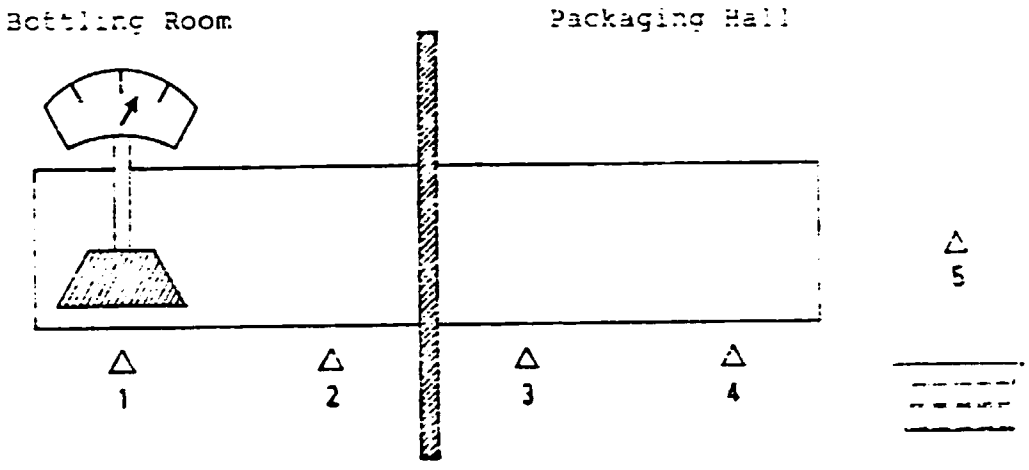

ANNEX-06

ANNEX-0

PACKAGING METHOD SHEET

SUBDIVISION AND PACKAGING OF TABLETS/CAPSULES

PACK SIZE : 1000




| △ Operators | Comments |
|---|---|
| 1 - Count by balance. | 1 - Plastic container with lid. |
| 2 - Opens and arranges plastic containers. | 2 - Label. |
| 3 - Placing the lid and screw capping. | 3 - Shipper/Box. |
| 4 - Labelling manually. | |
| 5 - Arranging & boxing and labelling the box. | |

Pilot plant production capacity are calculated based on certain basic assumptions. These are as follows :

A. Net working days per year: 229 days

| | | |
|---|---|---|
| | Calendar days | 365 |
| Less: | Week-ends | 104 |
| | National Holidays | 10 |
| | Annual Leave | 22 |
| | | 136 |
| | Effective annual working days | 229 |

B. Gross working time per day, per person in single shift; 7 hours

- Stay time in plant ( 8 a.m. - 5 p.m.) : 540 min.
- Breaks (lunch/tea) : 90 min.
- Uniform changes (morning & evening) : 30 min.
- Gross working time per day : 420 min.or 7 hrs.

C. Net productive time per man per day(single shift): 6.5 hours.

Gross working time kper man single shift 420 min.

Less: non-productive (start-up/close-down) time 30 min.

Net productive working time, 390 min. i.e. 6.5 hours.

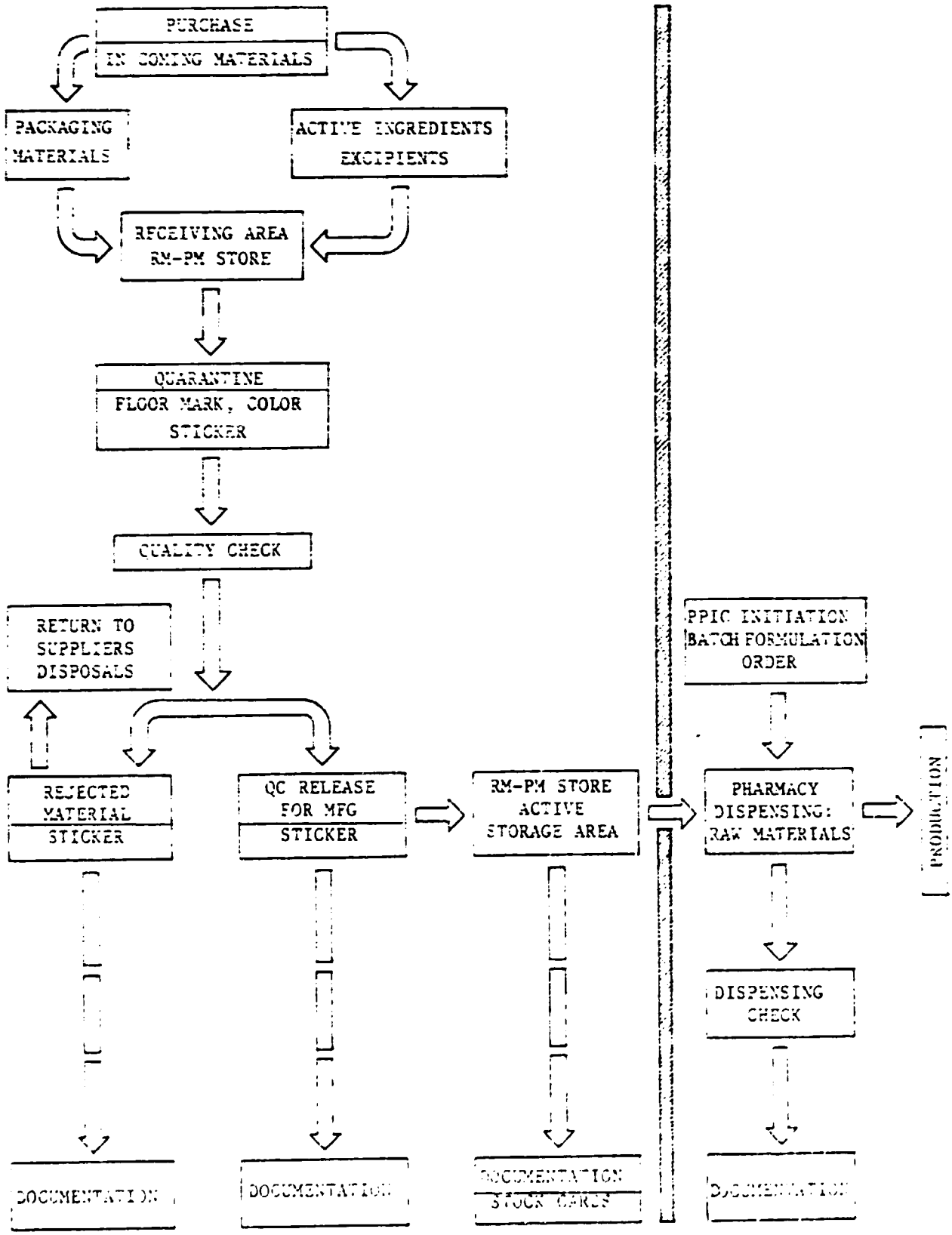
D. Net machine running time, 6.0 hours per day

Average estimated loss time due product change-over .5 hours.

Net machine running time per day = 6.0 hours.

ANNEX-09

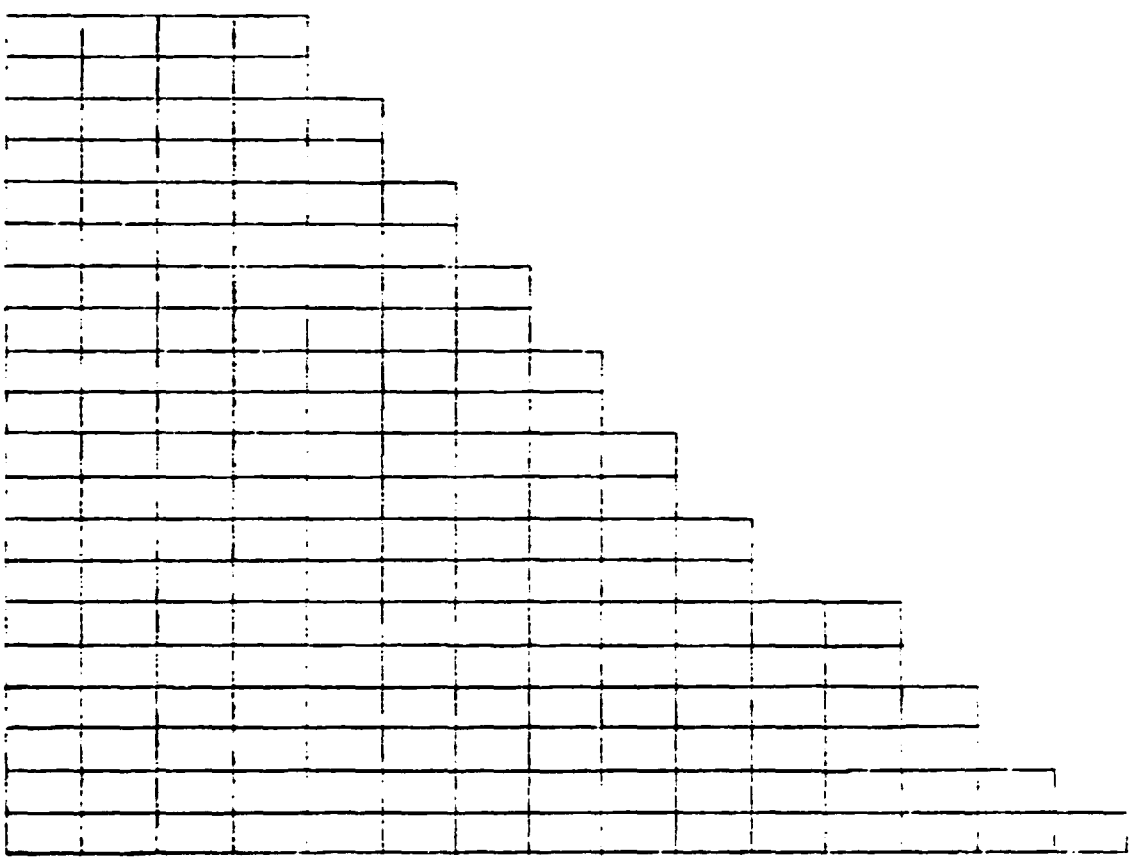
DESIGN OF MATERIAL WORK FLOW: WAREHOUSE



ANNEX-10

OPEN BLOCK

STACKING SYSTEM



## 3.0 MAN POWER

3.1 Plant Manning

3.2 Man Power:

- Requirement/Availability
- Plant manning salary cost

3.3 Man power training

3.4 Plant Organisation Chart

## 3.0 MAN POWER

### 3.1 Plant Manning

#### 3.1.1 General

- The basic estimation of plant personnel at management and various operational levels classified by department at half capacity (Year-I) and full capacity (Year-II) operations is presented in table 3-1. Based on the envisaged plant administrative and functional responsibilities the organization is indicated in Annex-II.

  A total of 69 persons in Year-I and 85 persons, for operating at full capacity is estimated.

Table 3-1 - Plant manning by department

| Functional Level | Number of Persons | | |
|---|---|---|---|
| | Year-I | Year-II | Total |
| - Plant Manager | 1 | - | 1 |
| - Secretary | 1 | - | 1 |
| Sub-total: | 2 | - | 2 |
| Production Department: | | | |
| - Production Manager | 1 | - | 1 |
| - Secretary | 1 | - | 1 |
| - Production Supervisors: | | | |
| - Tablet/Capsules | 1 | - | 1 |
| - Oral liquids | 1 | - | 1 |
| - Process Operators(Mfg.+Packaging): | | | |
| - Tablet/Capsule | 15 | 6 | 21 |
| - Oral liquid | 10 | 5 | 15 |
| Sub-total: | 29 | 11 | 40 |

Table 3-1 (continued)

| Functional Level | Number of Persons | | |
|---|---|---|---|
| | Year-I | Year-II | Total |
| Quality Control Department: | | | |
| - Quality Control Manager | 1 | - | 1 |
| - Quality Control Supervisor | 1 | - | 1 |
| - Analysts (Physical+Chemical+ Microbiological) | 3 | - | 3 |
| - Laboratory attendant | 1 | - | 1 |
| - Inprocess Control Inspector, Sampler | 2 | 1 | 3 |
| Sub-total | 8 | 1 | 9 |
| Engineering and Plant Maintenance Department: | | | |
| - Plant Engineer | 1 | - | 1 |
| - Forman - Maintenance | 1 | - | 1 |
| - Utility | 1 | - | 1 |
| - Maintenance tech./mechanic | 2 | 1 | 3 |
| - Utility | 2 | - | 2 |
| Sub-total | 7 | 1 | 8 |
| Finance and Accounts: | | | |
| - Plant Accountant | 1 | - | 1 |
| - Secretary | 1 | - | 1 |
| - Cost accounts clerk | 2 | - | 2 |
| - Budgetory control clerk | 1 | - | 1 |
| Sub-total | 5 | - | 5 |
| PPIC Department: | | | |
| - Production Planning & Inventory Control Officer | 1 | - | 1 |
| - RM/PM warehouse Supervisor | 1 | - | 1 |
| - Material handlers | 2 | 1 | 3 |
| - FG warehouse[1] supervisor | 1 | - | 1 |
| - Packers/stackers | 2 | - | 2 |
| - Sales Co-ordinator | - | 1 | 1 |
| Sub-total | 7 | 2 | 9 |

Table 3-1 (continued):

| Functional Level | Number of Persons | | |
|---|---|---|---|
| | Year-I | Year-II | Total |
| Personnel/Industrial Relations Department: | | | |
| - Personnel/Industrial Relation Officer | 1 | - | 1 |
| - Drivers | 2 | - | 2 |
| - Site-house keeping and security | 3 | - | 3 |
| - Telephone operator | 1 | - | 1 |
| - Cafeteria | 3 | - | 3 |
| - Clerk | 1 | - | 1 |
| Sub-total | 11 | - | 11 |
| TOTAL PLANT MANNING | 70 | 15 | 85 |

(1) FG = Finished Goods

## 3.2 Man Power Requirement and Availability

-The current availability of the nationals with institutional education engaged in the hospitals and NHS in the country is indicated in Table 3-2(a).

Table 3-2(a): Technical Manpower Availability in Mozambique

| Education | Availability(1986) |
|---|---|
| -University graduate | 3 |
| -Pharmacist | 4(1) |
| -Pharmacy technician | 56 |
| -Pharmacy agent | 87 |
| -Pharmacy auxilliary | 201 |

-In addition to these personnels six nationals are stydtubg at the university level in Tanzania, GDR and Brazil to be available in 1990 and early nineties, two more are at planning stage. The plant supervisory, skilled and semi-skilled operator level personnels for training and operation will be identified from these nationals.

-Various levels of plant personnel requirement and availability by function and professional profiles as well as training needs are elaborated in table 3-2(b).

Plant manning annual salary cost is indicated in table 3-2(c).

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(1) 1 national teaching at pharmacy institute and 3 foreign nationals at hospitals.

## Table 3-2(b) : Manpower Requirement/Availability and Training Need

| No.of Personnel | REQUIREMENT | | AVAILABILITY | TRAINING | | REMARKS |
|---|---|---|---|---|---|---|
| | Function | Professional Profile | | In-service | External | |
| 1 | Plant Manager | Personnels<br>Age: Not less than 35 years<br>Experience: Managing Pharmaceutical concerns, management of people and business. | Age: 30-35 years<br>Experience: None<br>Education: University degree pharmac. technology, economy or medical doctors, knowledge of english. | x | x | Limited technical skill available, Managerial skill to be developed. |
| 1 | Production Manager | Education: University degree in pharmacy chemistry, economics, English language<br>Age: 30 to 35 years<br>Experience: Production of tablets, capsules and oral liquids in pharmac industry, practical knowledge of GMP managerial and analytical skill. | Age: 30 - 35 years<br>Experience: Production of tablets, oral liqud, IVP and ointment in industry 2 days/ week, for 3 years.<br>Education: University degree in pharmaceutical technology in Cuba, knowledge of English. | x | x | Technical skill available. Analytical and managerial skill to be developed. |
| 1 | Quality Control Manager | Age: 30 - 35 years<br>Experience: Quality control laboratory in pharmaceutical industry, practical knowledge of GMP, analysis and formulations of pharmaceuticals. | Age: 30 - 35 years.<br>Experience: laboratory analysis of pharmaceutical dosage forms in Cuba.<br>Education: | x | x | Laboratory experience available, quality control systems, Formulations, GMP etc. to be developed. |
| 1 | Plant Accountant | Age: 3 - 35 years<br>Experience: Budget and budgetory control, cost accounting, financial statements etc., in industrial concerns. | Age: 30 - 35 years<br>Experience: Nil.<br>Education: 9 years school, 3 years commercial institute. | x | x | Need of Intensive in service training foreseen, person to be identified for education training. |

Table 3-2(b) continued

| No. of Person-nel | Function | REQUIREMENT Professional Profile | AVAILABILITY | TRAINING NEED In-service | TRAINING NEED External | REMARKS |
|---|---|---|---|---|---|---|
| 1 | Plant Engineer | Age: 30 - 35 years.<br>Experience: Plant maintenance and utility supplies in pharmaceutical production unit.<br>Education: University degree in mechanical engineering | Age: 30 - 35 years.<br>Experience: Nil<br>Education: Secondary school and 3 years in industrial institute. | x | x | Planning for University graduation and long in service supervision by foreign engineer necessary. |
| 1 | Production Planning and Inventory Control Officer | Age: 25 - 30 years.<br>Experience: Plant capacity and PPIC systems.<br>Education: 9 to 11 years school and 3 years tech. institute. | Age: 25- 30 years.<br>Expeirence: Nil.<br>Education: 9 to 11 years school, 3 years tech.institute | x | | Pl[illegible]cy technici[illegible] to be identified, OR planning for education and training. |
| 2 | Production Supervisor | Age: 25 - 30 years<br>Experience: Production of tablet capsule and oral liquid dosage forms, GMP handling of workers.<br>Education: Pharmacist. | Age: Yes<br>Experience: Nil.<br>Education: 9 years school, 3 years chem., and 3 years pharmacy, institutes, 5 years in hospital pharmacy and distribution of drugs. | x | x | Phase-II training in tabletting technology to be completed at Beira training workshop. |
| 1 | Quality Control Supervisor | Age: 25 - 30 years<br>Experience: Practical Laboratory Analysis, Production process controls, GMP.<br>Education: Pharmacist/Chemist | Age: Yes.<br>Experience: 3 months training in France, 1 month seminar in few years in National Lab. Hygeine, Maputo.<br>Education: 9 years school, 3 years chemical inistitute. | x | x | Phase-I completed, further practical training in tabletting workshop at Beira and external training necessary. |
| 2 | Maintenance and Utility Foreman | Age: 25 - 30 years.<br>Experience: Operation, maintenance and supervision of pharmac. plant and machineries.<br>Education: diploma/certificate in engineering. | Age: Yes.<br>Experience: Nil<br>Education: 6 - 9 years school, 3 years industrial institute. | x | x | To be identified/ planned for education and training. |

Table 3-2(b) continued

| No. of Personnel | Function | REQUIREMENT Professional Profile | AVAILABILITY | TRAINING NEED In-service | TRAINING NEED External | REMARKS |
|---|---|---|---|---|---|---|
| 2 | Store/Warehouse supervisor | Age: 25 - 30 years<br>Experience: Systems/procedures pharmac. RM/PM.<br>Education: 9 years school, 3 years technical institute. | Age: Yes.<br>Experience: Nil<br>Education: Yes. | x | | Pharmacy technician to eb identified. |
| | Direct Labour: | | | | | |
| 20 | Skilled operators | Age: 20 - 25 years.<br>Experience: Technical skill in equipment operation and manufacturing processes for tablet, capsule and oral liquid.<br>Education: 4 - 6 years school. | Age: Yes.<br>Experience: Nil.<br>Education: 4 - 6 years school. | x | | Planning education, training, estimated 10-15 skilled operators shall be trained in tabletting facilities at Beira by 1989. Further training need in the pilot plant foreseen. |
| 16 | Semi-skilled operators | Age: 20 - 25 years.<br>Experience: Nil.<br>Education: 4 - 6 years school. | Age: Yes.<br>Experience: Nil.<br>Education: 4 - 6 years school. | x | | Tablet jar packaging operators can be trained at Beira, need for limited in service training foreseen for these packaging operators. |
| 3 | Laboratory analyst | Age: 25 - 30 years.<br>Experience: laboratory exp. physical, chemical and microbiological analysis of raw and packaging materials, intermediates and finished pharmacedutical products.<br>Education: 6 - 9 years school, 3 years chem. institute. | Age: Yes.<br>Experience: Nil.<br>Education: 4 - 6 years school. | x | | To be identified, edcucation to be planned. Foreseen by 1989, 2 to 3 experienced lab.analyst trained in, (i) training workshop EMOPAR Beira and (ii) National Hygeine Laboratory, Maputo will be available. |

Table 3-2(b) continued

| No. of Person-nel | Function | REQUIREMENT Professional Profile | AVAILABILITY | TRAINING NEED In-service | TRAINING NEED External | REMARKS |
|---|---|---|---|---|---|---|
| 3 | QC in-process inspector/ sampler | Age: 20 - 25 years.<br>Experience: Statistical sampling, GMP, safety, production hygeine in pharmaceutical plant.<br>Education: 6 - 9 years school. | Age: Yes.<br>Experience: Nil.<br>Education: 6 - 9 years school. | x | | By 1989 estimated 3 technician (in-process) will be available - trained in tablet manufacture in EMOFAR workshop at Beira. |
| 2 | Laboratory attendant | Age: 20 - 25 years.<br>Education: 4 years school. | Age: Yes.<br>Education: 4 years school. | | | |
| 3 | Maintenance mechanics/ technicians | Age: 25 - 30 years<br>Experience: repair, maintenance paharmaceutical plant machineries.<br>Education: 9 years school, 2 years industrial institute. | Experience: None | x | | Planning for education and training, need of long in service training foreseen. |
| 2 | Utility technician | Age: 25 - 30 years.<br>Experience: Operation and maintenance of boiler, power generator, air conditioning system, power supply etc.<br>Education: 9 years school, 3 years industrial institute. | None. | x | | Planning for education. Need pf long in service training foreseen under supervision. |
| | PPIC: | | | | | |
| 3 | RM/PM Handlers (semi-skilled) | Age: 20 - 25 years.<br>Experience:<br>Education: 4 years school. | Age: 20 - 25 years.<br>Experience:<br>Education: 4 years school. | x | | |
| | Finished goods Picker-Packer (semi-skilled) | Age: 20 - 25 years.<br>Experience:<br>Education: 4 years school | Age: 20 -2 5 years<br>Experience:<br>Education: 4 years school. | x | | |

Table 3-2(b) continued

| No. of Personnel | Function | REQUIREMENT Professional Profile | AVAILABILITY | TRAINING NEED In-service | TRAINING NEED External | REMARKS |
|---|---|---|---|---|---|---|
| 1 | Plant and Medimoc Purchase Co-ordinator | Age: 25 - 30 years<br>Experience:<br>Education: 9 years school, 3 years tech. institute. | Age: 25 - 30 years<br>Experience: Distribution of Essential drugs, clerical job in Medimoc imports.<br>Education: 9 years school, 3 years tech.institute. | x | | |
| 4 | Accounting Clerk | Age: 25 - 30 years.<br>Experience: Cost/accounting, book-keeping and budgetory controls in Manufacturing.<br>Education: 4 years school, 5 years commercial school. | Age: Yes.<br>Experience: Nil.<br>Education: To be planned. | x | | To beidentified/ planned for education and training. |
| 1 | Personnel/ Industrial Relations officer | Age: 30 - 35 years.<br>Experience: Handling of peoples inter-personnel skills.<br>Education: 9 years school. | Age: Yes.<br>Experience: Nil<br>Education: 9 years school. | x | | To be identified/ planned for education. |
| 3 | Site, Housekeeping and security | Age: 35 - 45 years.<br>Experience: Ex-army or police man.<br>Education: 4 - 6 years school. | Age: Yes.<br>Experience: Ex-police man. | | | |
| 3 | Cafeteria | Age: 20 - 25 years | Age: Yes. | | | |
| 3 | Vehicle and telephone operator | Age: 25 - 35 years.<br>Education: 4 - 6 years school. | Age: Yes.<br>Education: 4 - 6 years school. | | | |
| 1 | Office Clerk | Age: 20 - 25 years.<br>Experience: Typing<br>Education: 6 years school. | Age: Yes.<br>Experience: Yes.<br>Education: 6 years school. | | | |
| 3 | Secretary | Age: 20 - 30 years<br>Experience: Typing/shorthand<br>Education: 6 - 9 years school, English language. | Age: Yes.<br>Experience: Nil.<br>Education: 6 - 9 years school | x | | To be identified/ planned for development. |

External training means training in foreign industry.

Table 3-2(c) Plant Manning Cost

| Rank/Category of Personnel | No.of Personnel | Annual Salary MT x 1000 per person | Total Annual Salary MT x 1000 | |
|---|---|---|---|---|
| 1. Administration | | | | |
| -Plant Manager | 1 | 540 | 540 | |
| -Production Manager | 1 | 450 | 450 | |
| -Quality Control Manager | 1 | 450 | 450 | |
| -Plant Accountant | 1 | 450 | 450 | |
| -Personnel and Industrial Relations Manager | 1 | 360 | 360 | |
| -Secretary | 1 | 270 | 810 | |
| | | | | 3060 |
| 2. Supervision | | | | |
| -Production Supervisor | 2 | 324 | 648 | |
| -Quality Control Supervisor | 1 | 324 | 324 | |
| -Maintenance and Utility Foreman | 2 | 324 | 648 | |
| -Warehouse Supervisors | 2 | 198 | 396 | |
| -Medimoc(sales) Co-ordinator | 1 | 198 | 198 | |
| | | | | 2214 |
| 3. Direct Labour | | | | |
| -Skilled Operator | 20 | 234 | 4680 | |
| -Tablet 13 | | | | |
| -Capsule 3 | | | | |
| -Oral Liquid 4 | | | | |
| -Semi-skilled | 16 | 162 | 2592 | |
| -Tablet/Capsule 6 | | | | |
| -Oral Liquid 10 | | | | |
| 4. Other Plant Personnel | | | | |
| -Mechanics, Electricians, Utility technicians | 5 | 270 | 1350 | |
| -Laboratory Analysts | 3 | 270 | 810 | |
| -Laboratory Attendant | 2 | 162 | 324 | |
| -QC Inspector | 3 | 162 | 486 | |
| -Accounts Clerk | 5 | 180 | 900 | |
| -Picker-Packer | 5 | 108 | 540 | |
| -Cafeteria, site house-keeping and security etc. | 10 | 90 | 900 | |
| | | | | 5310 |
| TOTAL | 85 | 5526 | 17,856 | |

(Equivalent US$89,280)

## 3.3 MANPOWER TRAINING

### 3.3.1 General

-The availability of skilled manpower is the important element in successful operation of the pilot plant laying emphasis on selection and phase-wise training and development of the different levels of technical and management personnel.

3.3.2 -The training and development is suggested to beaccomplished primarily in 2 stages :

-Stage-I

The training workshop at Beira with the tabletting facilities should be optimally utilised to train and develop technical and management personnel in production, warehousing and quality control functions on a planned basis. Table 3-3 indicates the category and numbers of the national personnel that are foreseen to be trained in initial 2 years of establishment of the workshop under the supervision of foreign experts for placement in the pilot plant.

Table 3-3 Projected Training and Development of Nationals in Tabletting at the Tabletting Workshop at Beira in initial 2 years.

| FUNCTION | CATEGORY OF PERSONNEL | NO.OF PERSONNEL TO BE TRAINED | |
|---|---|---|---|
| | | YEAR-I | YEAR-II |
| I. Production, Tablets | | | |
| A Management | Production Manager | - | 1 |
| B. Direct Labour | | | |
| -Equipment Operation | Skilled | 4 | 4 |
| -Process Operation | Skilled | - | 3 |
| -Packaging Operation | Semi-skilled | 1 | 1 |
| C. Supervision | | | |
| -Manufacturing and Packaging supervision | Foreman supervisor | 1 | 1 |
| II. Quality Control | | | |
| -Laboratory Analysis | Analyst | 1 | 1 |
| -In-process control | Technician/in-process inspector | 1 | 1 |
| -Sampling of RM/PM | Sampler | 1 | 1 |
| III. Production Planning and Inventory Control : | | | |
| -Warehouse (RM/PM/FG(1) Receipt, Storage and issue of RM,PM & FG. | Warehouse supervision | - | 1 |
| IV. Engineering services | | | |
| -Maintenance | Mechanic/technician | - | 1 |

(1) RM = Raw material; PM = Packaging material; FG = Finished goods

Stage - II :

This stage is planned to be implemented in 2 phases.

-Phase - I

External training for key management and supervisory personnel in a foreign experienced pharmaceutical plant timed during the construction phase or at the beginning of the machineries installation. The following persons should receive the training for the approximate period shown in table 3-4.

Table 3-4 External trainingcost for key and supervisory personnel

| Rank of Personnel | No. of Personnel | Approx. duration Manmonths | Total Salary $ | Travel & Housing $ | Total Cost $ |
|---|---|---|---|---|---|
| -Plant Manager | 1 | 1 | 220 | 4500 | 4720 |
| -Production Manager | 1 | 3 | 549 | 8500 | 9049 |
| -QC Manager | 1 | 3 | 549 | 8500 | 9049 |
| -Plant Engineer | 1 | 3 | 549 | 8500 | 9049 |
| -Maintenance Foreman | 2 | 6 | 792 | 15000 | 15792 |
| -Production Supervisor | 2 | 4 | 528 | 10500 | 11028 |
| TOTAL | 8 | 20 | 3187 | 55,500 | 58,687 |

-Phase - II

In-service local training to be time during running-in of the plant in presence of foreign experts for the approx. period of 24 man-months as indicated in table 3-5.

Although the contents of theindividual training program, will have to be worked depending on specific needs and adapted to individual precondition, the suggested personnels and the time period is a guide line in nature.

Table 3-5 Training in Mozambique by external experts and cost estimates.

| Rank of Personnel | No.of External Experts | Estimated duration months | Salary $ | Est.Cost Travel & Housing $ | TOTAL COST $ |
|---|---|---|---|---|---|
| -Production Manager | 1 | 3 | 15000 | 8800 | 23800 |
| -Quality Control Manager | 1 | 3 | 15000 | 8800 | 23800 |
| -Plant Engineer | 1 | 6 | 15000 | 8800 | 23800 |
| -Plant Accountant | 1 | 2 | 10000 | 6700 | 16700 |
| -Quality Maintenance Foreman | 2 | 2+2 | 16000 | 10900 | 26900 |
| -Process Technician | 2 | 3+3 | 18000 | 13400 | 31400 |
| TOTAL | 7 | 24 | 89,000 | 57,400 | 146,400 |

- The estimated cost of $ 205 for stage-II external training and experts for in service training is considered as investment cost.

- A qualified plant engineer is not readily available, the development need is critical and suggested to plan for university education followed by industrial training. Until a suitable national is available, it is foreseen that a foreign engineer shall have to be placed in the plant.

- The development of laboratory analysts through practical training in physical, chemical and microbiological analysis of pharmaceuticals for quality control functions is an institution building process.

- It is suggested that early plant operations especially during the phase-II training certain key, supervisory management and technical functions are carried out under the umbrella of foreign experienced technical persons for a limited period to enable adopting and integrating an array of defined plant systems and procedures.

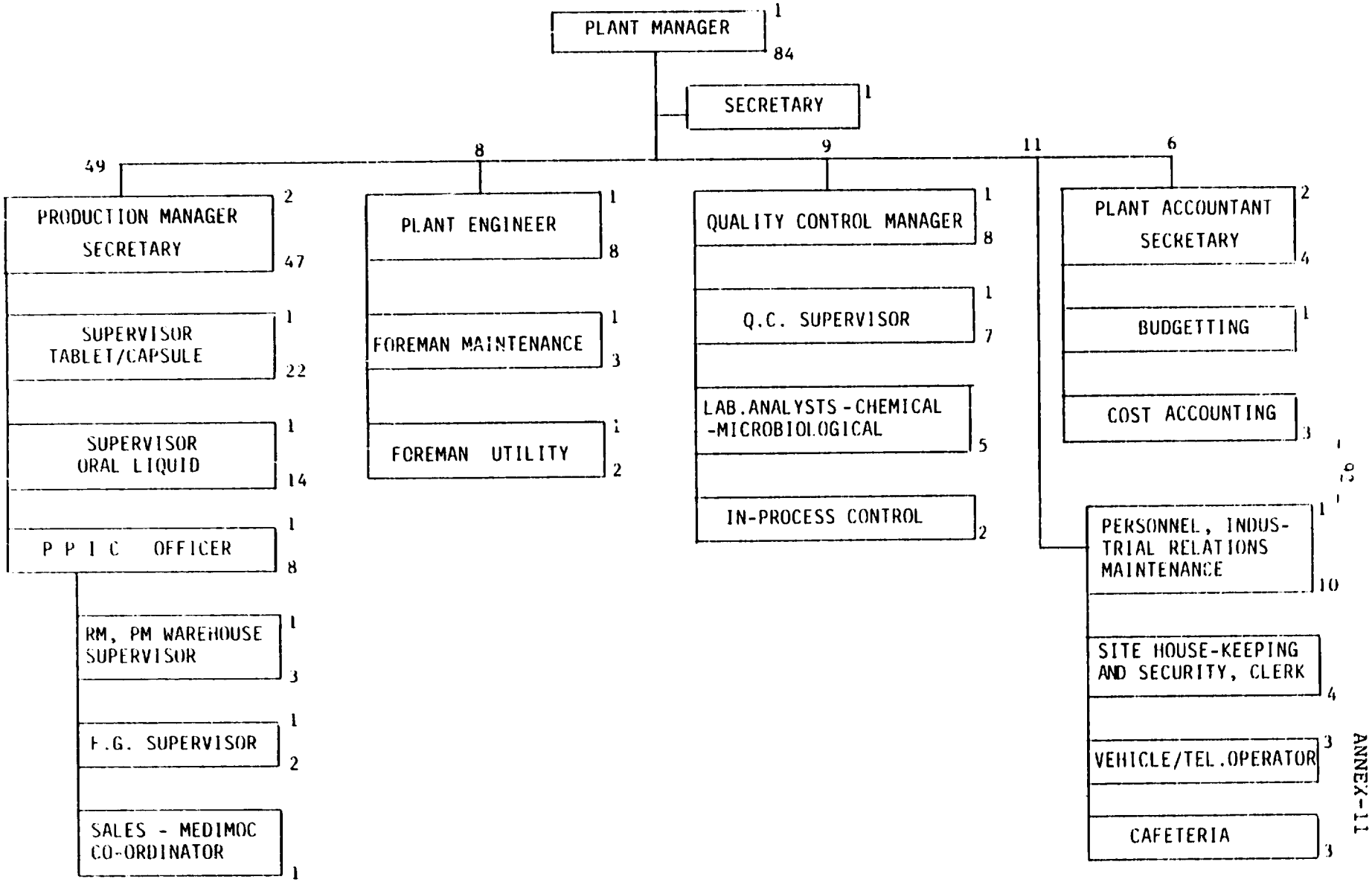
## 3.4 Plant Organisation

-Production Planning and Inventory Control (PPIC) functions are suggested to be initially under the supervision of production management.

-Materials management will be administered by Medimoc through a co-ordinator under PPIC located in plant.

-The administrative distribution of 85 plant personnel is indicated in Annex -11.

# PLANT ORGANISATION CHART




ANNEX-11

# 4.0 PRODUCTION IN-PUTS AND COST ESTIMATES

## 4.1 MATERIALS

### 4.1.1 Indigenous Raw Materials

### 4.1.2 Indigenous

- Domestic Ancillary Industries
- Sources and Specifications
- Cost Estimates

### 4.1.3 Importable Raw Materials, Sources and Cost Estimates.

## 4.2 EQUIPMENT

### 4.2.1 General

### 4.2.2 Specifications and Cost Estimates

# 4.0 PRODUCTION IN-PUTS AND COST ESTIMATES.

## 4.1 Materials : Indigenous and Importables

### 4.1.1 Raw Materials (Indigenous)

**-General**

At present all formulation materials except water has to be imported. On a long term perspective however Mozambique has endowed potentiality of indigenous sources of sugar, corn, maize and potato starch as well as caramel colour.

**-Sugar**

The current production samples of white and brown sugar have been tested locally and does not meet compendia specifications for use in pharmaceutical. Special purification steps should be undertaken by local industries to upgrade the level of purification to meet pharmaceutical specifications. The presently declining output of sugar industries (1982 production 175,000 M.tons and 1985 production 20,000 M. tons[1]) shall have to be rehabilitated/revitalised. Once quality sugar is ensured, the projected import requirement of 14,418 Kg of 70% liquid glucose for the oral liquid formulations can be favourably substituted with 30% to 40% indigenous sugar solution.

For the local pharmaceutical plant the indigenous production of the above raw materials should be encouraged.

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(1) Source: Directorate of Sugar Institute, Maputo, Mozambique.

### 4.1.2 Packaging Materials (Indigenous)

-General

At the initial phase of the implementation of this (1986), a predesigned structured survey was undertaken to evaluate the status of domestic packaging material industries in Maputo, the capital city, and Beira, the port city that are essentially complementary to pharmaceutical manufacturing unit.

Table 4-1 - Summarises the current 'State of Art' of the domestic ancillary industries as revealed by the survey.

Although at the present outlook there are common deficiencies in the country's industrial fabric, the supporting ancillary industries, such as, glass and plastic containers, cardboard, printing, closures are potential. In order to create and develop a favourable infra-structure base for a pharmaceutical plant, it is suggested that packaging materials are sourced locally. Since these supporting industries are dependant on foreign sources for primary materials, back-up assistance in financial or with primary materials is an expressed condition for contractural agreements with the local suppliers contacted.

Table 4-1 : Domestic Ancillary Industries Sample Survey - 1986

| A. Containers/Closures Type of Material | Supplier/Location (Ownership) | Size/operational difficulties | Conditions for Supply |
|---|---|---|---|
| A. Containers/Closures | | | |
| -Tin containers, Aluminium closures | Metal Box/Maputo (Private, UK subsidiary) | Employees-250, RM, Machine breakdown and spare parts | Assistance for primary RM, minimum 30 days lead time. |
| -Plastic bottles and closures | Unidade de Direccao de Plasticos., E.E./ Maputa (State owned) | Consists of 5 i.u./ Plastic granules, Engineering services, Spare parts. | Prior contract, Financial support, 90 delivery time, mouldto be supplied. |
| | Plastic : SOPLAS/ Beira (State owned) | 3 i.u. in Beira, each about 80 employees/spare parts. RM, Maintenance. | Technical staff, RM. |
| -Aluminium containers | Aluminium de Mozambique/Beira, subsidiary factory of Maputo (State owned) | Employees-65, annual capacity 15,000 pcs., RM availability. | (1) |
| -Cardboard box | Carbeira/Beira (Subsidiary of Carmoc (State owned) | Employees-120, Spare parts, Adhesive glue. | 60 days prior notice contract, RM. |
| -Amber glass bottle | Vidreira/Maputo (State owned) | 1986 cap.-99 MT/day, 1989 cap.-174MT/day; Power supply, Technical staff. | 9 months lead time for new mould fabrication for 25mm neck size. |
| B. Printing Materials: | | | |
| -Labels and Cartons | Spanos Graphica, LDA,/ Maputo (Private, partly (State support). | Employees-103 cap.-label per Mo.-90 m, 3 size carton, per Mo.-25,000/paper board and Ink. | Art paper and boards to be supplied, 3 months delivery time, Minimum order 3 million labels, contractual agreement. |
| | Cetibel/Beira (Private enterprise) | Employee-50 Cap.ann.-19,300cm² paper surface. | |
| C. Formulation Materials: | | | |
| -Sugar | Institute Nacional de Sugar/Maputo (State owned) | 6 factories (3 in operation) Technical manpower, Finance, Importable materials for sugar purification. | Brown sugar (1) |

Abbreviations: (1) Unsuitable for pharmaceutical use.
RM= Raw materials; i.u= Industrial Units
MT= Metric ton, Cap.= Production Capacity, mil.= Millions
MO= Month, ann.= annual.

The recommended local packaging materials, specifications and manufacturers are presented in table 4-2.

**Table 4-2: Packaging Materials, Manufacturers & Specifications**

| Material | Specification | Local supplier | Product to be packed |
|---|---|---|---|
| 1 -Glass bottles | USP:NP sodalime round & amber color. size 120ml. | Vidreira de Mozambique, Maputo | Oral liquid |
| 2 -Metallic roll on screw cap | Al-cap, Diameter 25 mm | Metal Box, Maputo | Oral liquid |
| 3 -Plastic jar with lid | H D P E, size, 106x92mm | Unidade de Direccao de Plasticos Maputo | Tablets & Capsules |
| 4 -Cardboard box | T/C:100x38x11cm OL: 40x25x12.5cm | Carmoc, Maputo/ Beira | Plastic jars containing tablets/capsules |
| 5 -Label for contain | | | |
| - glass | 64x88mm, GSM-80 | Spanosgraphica, Maputo | |
| - plastic | 64x88mm, GSM-80 | -do- | |
| - cardboard | 104x80mm, GSM-50 | -do- | |

T/C = Tablet/capsule; GSM = Gram per square meter; OL = Oral liquid

-Containers

**Plastic**

- The plastic industries appear to be historically well based. At present these industries are largely engaged in fabricating domestic containers, utensils, pipes, varieties of containers for consumer goods with imported granules. Polypropylene or PVC granules are currently not in use. BDPE granules are used by local manufacturers. The quoted price (1986) for plastic jars for 1000's tablets/capsules appear to be cheaper by about 55% over the corresponding glass jars.

**Glass**

- The glass manufacture appeared to be well-based, enjoying technical assistance of Portugal and Italy. The industry plans for capacity expansion in 1987 and 1988 to reach 150 ton per shift (current level, 75 tons) of amber glass, soda lime, NP-USP grade. The production capacity and quality of the glass bottles fabricated by vidreira the single glass industry available are acceptable for the proposed oral liquid formulations. The sample bottles (1986) were found to be free of cracks, warts, folds, mould seams, blisters etc. Annual o- quantities of a minimum of 2 million bottles .s preferred by this glass industry.

  Howerver the existing neck size of 22mm of the 4-ounce bottles fabricated by Vidreira will have to be upgraded to 25mm size with a new mould and adapted to the closures fabricated by Metal Box. An important institutional co-ordination activity is foreseen to be necessary between the two suppliers - Vidreira and the Metal Box co-ordinated by Pharmaceutical quality control.

-Closures

Both metallic cap and plastic cap are being produced by local industries. Currently both 22mm and 25mm size metallic closures are produced by Metal Box.

-Card board boxes

The cardboard boxes fabricated locally by Carmoc in Maputo and Carbeira at Beira are presently used to pack country's exportable product and are of acceptable quality. The requirements is estimated for (5 x 8) bottles of oral liquid per box and 4 x 10 jars for tablets and capsules per box.

-During the survey the overall production capacity utilization in the local packaging material industries were found to be significantly low. In order to ensure that the production of these supporting industries are consistently of acceptable quality and that their deliveries are timely, they have to pass through a distinct technical development phase integrated with the pharmaceutical quality control department. In addition some rehabilitation/revitalisation support should facilitate the development and reliability of the local suppliers.

**Quality Control Facilities in Local Ancillary Industries**

- Since none of the packaging industries except the Vidreira glass industry has distinct quality control facility, the need for a distinct development phase of the local packaging material suppliers would be unavoidable to ensure that the physical and chemical quality specifications consistently meet the requirements for pharmaceutical products. The necessary fine tuning of the local suppliers will have to be co-ordinated with the quality control department of the envisaged pharmaceutical plant through initial small scale deliveries. The fine tuning development phase should be timed when investment decision is made or well ahead of the deliveries required.

- For technical reasons of compatibility of the product-pack combination initial productions with local supplies should be checked through adequate concurrent accelerated stability studies by pharmaceutical quality control laboratory[1,2].

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(1) Reference: Accelerated stability studies of widely used pharmaceutical substances under stimulated tropical conditions. WHO/Pharm/86.529

(2) WHO Technical Report series No. 645, 1979.

**Cost Estimate of Indigenous Packaging Materials**

- The cost of the local packaging materials were quoted by the domestic suppliers in February 1987. The packaging materials are illustrated by annual quantity, unit cost and annual cost in local currency in table 4-3.

  The distribution of the total cost of packaging materials by dosage form is indicated below:

| Packaging Material | US$ x 1000 |
|---|---|
| - Tablet | 6.34 |
| - Capsule | 1.01 |
| - Oral Liquid | 62.50 |
| Total cost: | 70.00 |

**Table 4.3 Cost of Indigenous Packaging Materials**

| PACKAGING MATERIALS | | | COST |
|---|---|---|---|
| Material | Annual Quantity Pieces x 1000 | Unit Cost Meticais | Annual Cost Meticais x 1000 |
| -Glass bottle | 1050 | 6.95 | 7,297.50 |
| -Aluminium seal | 1030 | 2.31 | 2,379.30 |
| -Plastic jar with lid: | | | |
| - Tablet | 68 | 17.85 | 1,213.80 |
| - Capsule | 10.3 | | 183.85 |
| -Cardboard box: | | | |
| - G B | 25.50 | 44.10 | 1,124.55 |
| - P J T | 1.80 | 35.00 | 63.00 |
| - P J C | 0.26 | | 3.46 |
| -Label for glass bottle | 1050.00 | 1.58 | 1,659.00 |
| -Label for plastic jar: | | | |
| - Tablet | 69.30 | 1.58 | 109.49 |
| - Capsule | 10.50 | | 16.59 |
| -Label for cardboard box[1]: | | | |
| - G B | 26.25 | | 41.48 |
| - P J T | 2.00 | 1.58 | 3.16 |
| - P J C | 0.30 | | 2.21 |
| | | | Total: 14,095.39 |

(1) GB = glass bottle, PJT = plastic jar for tablets
PJC = plastic jar for capsules.

### 4.1.3 Importable Raw Materials, Sources and Cost Estimates

-Introduction

- The raw materials source and cost indicated are primarily based on competitive price quotes. The quality specifications considered are USP, BP, NF and EP. The unit price of raw materials are largely dependant on the quality of materials to be procured. Some of the cost of small quantity items were collected from the users in the region. No local import duty has been assumed in agreement with Medimoc, 10% handling charge for raw materials is to be charged as against 33.4% mark-up currently charged for the imported pharmaceutical finished products.

-Raw material cost

- The raw material in-puts, quantity, cost and manufacturer/supplier is indicated in table 4-4. The cost is expressed in US$ and the conversion rates of various currencies are illustrated in Annex-12. The raw material import cost by dosage form is illustrated below:

| | | |
|---|---|---|
| Tablets | - | $320,537 |
| Capsules | - | $162,349 |
| Oral Liquid | - | $201,986 |
| Total | | $684,862 |
| Plus local charge 10%, | | |
| Grand Total | | $809,000 |

Table 4.4 Raw Materials: Source, Quantity and Cost

| Material | Recommended supplier/ Manufacturer | Quoted price C&F per Kg | Quantity of Material | Cost of Material |
|---|---|---|---|---|
| | | | Kg. | US$ |
| Acetyl salicylic acid (Crystals 20 mesh) | Biochemie Gessellschaft, Kundl, Austria | 1.90 | 10,200 | 19,380 |
| Chloroquin phosphate | (1)Biochemie, Austria (2)Medimpex, Hungary | 26.00 | 6,250 | 162,500 |
| Sulfamethoxazole | Biochemie, Austria | 17.50 | 3,400 | 59,500 |
| Trimethoprim | (1)Biochemie, Austria (2)Dong Wha Pharma. S. Korea | 29.00 | 680 | 19,720 |
| Isoniazid | (1)Bayer A.g., Germany (2)Yuki Gosei Kogyo Co.Ltd. Japan | 9.50 | 110 | 1,045 |
| Mebendazole | Setra s.r.l. Bergamo, Italy | 50.50 | 900 | 45,450 |
| Paracetamol | Ribbon s.r.l. | 7.00 | 1,625 | 11,375 |
| Phenylbutazone | Amsa Spa, Milano, Italy | 21.00 | 400 | 8,400 |
| Tetracycline HCl | (1)Biochemie, Austria (2)Farmitalia, Carlo Ebra Export, Italy | 24.00 | 5,250 | 126,000 |
| Corn starch | Holland comp. Products Co. Denmark | 0.93 | 158,607 | 14,750 |
| Avicel pH 101 | Setra, Italy | 5.50 | 2,090 | 11,495 |
| Magnesium stearate | (1)Nippon Oil & Fats Co., Japan (2)Unilever Emery NV.,Holland | 2.50 | 220 | 550 |
| Lactose | Setra s.r.l., Bergamo, Italy | 1.40 | 1,170 | 1,638 |
| Alginic acid | Alginate Industries, London, UK | 26.70 | 210 | 5,607 |
| Talcum | E. Merck, Germany | 2.00 | 25 | 50 |
| Colloidal silicon dioxide (Cab-O-Sil) | Degussa, Post-fach Frankfurt, W.Germany | 7.00 | 65 | 455 |
| Sodium lauryl sulfate | Tama Enterpirse, Japan | 3.30 | 20 | 66 |
| Dibasic calcium phosphate | C.F. Budenheim, G.Germany | 2.10 | 210 | 441 |
| Methylene-chloride | (1)Rotex Pharma, FRG (2)Dow Chemicals Europe, Switzerland | 0.70 | 500 | 350 |
| Denatured spirit | BP Chemicals, UK | 7.00 | 220 | 1,540 |
| Methocel HG 60 | Colorcon Ltd., UK | 14.65 | 25 | 366 |

Table 4.4 (continued)

| Material | Recommended supplier/ Manufacturer | Quoted price C&F per Kg. | Quantity of Material | Cost of Material |
|---|---|---|---|---|
| | | | Kg. | US$ |
| EHG Capsules, Size 'O' | (1) Capsugel, Basel, Switzerland<br>(2) SU Heung Caps Co.Ltd. S. Korea | 3.36/1000 EHG<br>1.17/1000 " | 10,100,000pcs. | 33,936 |
| Vitamin-A Palmitate 1.7 mu/g. | F.Hoffman-La Roche & Co. Basle, Switzerland | 61.50 | 329.45 | 20,261 |
| Calciferol 40mu/g | F.Hoffmann-La Roche, Switzerland | 1.69/g | 1,925 | 3,253 |
| Thiamine HCl | Hoffman-La Roche & Co.Switzerland | 35.20 | 61.25 | 2,156 |
| Riboflavin-5-phosphate sodium | Hoffman-La Roche & Co. Switzerland | 147.30 | 20.79 | 3,062 |
| Ascorbic acid | Hoffman-La Roche | 10.90 | 560 | 6,104 |
| D-Panthenol | F.Hoffman-LaRoche | 18.85 | 105 | 1,979 |
| Niacinamide | Hoffman-la Roche | 7.35 | 154 | 1,132 |
| Pyridoxine HCl | Hoffman-La Roche & Co. | 41.15 | 8.4 | 346 |
| Sodium bicarbonate | (1) China National Chemicals Exp. & Imp.Corp. China<br>(2) E.Merck, Germany | 1.85 | 1,848 | 3,419 |
| Citric acid monohydrate | Fluka Ag., Switzerland | 6.0 | 745 | 4,470 |
| Sodium benzoate | China National Chem.Exp. & Imp. Corp., China | | | 190 |
| Sodium saccharine | China National Chemicals Exp. & Imp.Corp. China | 5.0 | 49.2 | 246 |
| Glycerine | (1) Lever Brothers, UK<br>(2) Unilever Export B.V. Rotterdam, Netherlands | 2.6 | 28,289 | 73,551 |
| Tween 80 | (1) E.Merck, Germany<br>(2) Rotex pharma, FRG | 10.62 | 720 | 7,646 |
| Sodium CMC | Tama Enterprises Ltd. Japan | 5.00 | 35 | 175 |
| Methyl paraben | Emerck, W.Germany | 11.50 | 15 | 173 |
| Propyl paraben | Nipa, UK | 12.00 | 5 | 60 |
| Sodium citrate | Boehringer Ingethin, FRG | 4.30 | 750 | 3,225 |
| Pharmacol, SG (Guar Gum) | Hanekl KGA, FRG. | 20.14 | 90 | 1,813 |
| Polyvinyl pyrrolidone (DUP K-30) | BASF A.G, W. Germany | 14.00 | 40 | 560 |

Table 4.4 (continued)

| Material | Recommended supplier/ Manufacturer | Quoted price C&F per Kg. | Quantity of Material | Cost of Material |
|---|---|---|---|---|
| | | | Kg | US$ |
| Sorbitol solution 70% | Roquette Frerace,France | 0.70 | 14,416 | 10,091 |
| Banana flavour | (1)Bush Boak Allen, UK (2)Fire menich SA Switzerland | 7.45 | 25 | 186 |
| Antifoam AF | Rotex Pharma, A.G. F.R.G. | 16.00 | 10 | 160 |
| Guaifenazine | Fermion OY, Finland | 11.50 | 420 | 4,830 |
| Povidone | BASF , A.G. Germany | 14.00 | 12 | 168 |
| Lecithin | (1)E.Merck, Germany (2)Arnold, F.R.G. | 131.11 | 50 | 6,556 |
| Veegum regular | Vanderbilt World Trade Corp. USA | 28.00 | 126 | 3,528 |
| Alcohol, 95% | BP chemicals, U.K. | 0.72 | 650 | 468 |
| Lemon flavor | (1)IFF (GB) Ltd., UK (2)Feremenich SA Switzerland | 22.00 | 20 | 440 |
| | | TOTAL | US$ | 684,862 |

## 4.2 EQUIPMENT

### 4.2.1 General

- The equipment chosen are semi-automatic based on the adaptibility and degree of mechanisation foreseen. Manufacturing operations are dependant on equipment while the proposed packaging operations are largely manual. Prices are based on competitive quotes(1986) and no import duty has been assumed in the indicated prices, refer table 4.5. In most cases spare parts as recommended by suppliers are included for 1 to 2 years of preventive mainteance are included.

4.2.2 - The estimated investment cost in equipment is US$1,242,000 including 20% on C&F for insurance, inland freight and installation.

| | C&F ($) |
|---|---|
| Tablet/Capsule | 474 |
| Oral Liquid | 63 |
| Quality Control Laboratory | 89 |
| Maintenance and Utility | 295 |
| Warehouse/Pharmacy | 31 |
| Others | 83 |
| | $ 1035 |

**Table 4.5 : Equipment, Capacity and Cost Estimates**

| Equipment Description | Capacity | Quantity | C&F Cost US$ in 000's |
|---|---|---|---|
| **A. PRODUCTION EQUIPMENT** | | | |
| **Capsules/Tablets section:** | | | |
| - Tray drying unit | 100 Kg. | 1 | 8 |
| - Powder sifter | - | 1 | 6 |
| - Fluid bed dryer (including flame-proof fittings) | 200 L | 1 | 110 |
| - Milling machine (+screens) | Upto 500Kg/hr. | 1 | 10 |
| - Drum mixer | 200 L | 1 | 15 |
| - Wet mass mixer/Planetory mixer | 500 L | 1 | 10 |
| - Y Mixer | 20 CFT | 1 | 8 |
| - Steam heated kettle with stirrer | 100 L | 1 | 6 |
| - Floor scale | 300 Kg | 1 | 6 |
| - Control scale | 0 - 160 g | 2 | 6 |
| - Coating pan (including accessories) | 36 inch dia | 1 | 9 |
| - Tri-Homo Colloid mill (Homogeniser) | 3 - 10 gph | 1 | 10 |
| - Coat prepartion vessel with stirrer | 60 L | 1 | 3 |
| - Stirrer | - | 1 | 2 |
| - Rotary Tablet Press (including 1 set punches & dies for slugging 7 sets for tab. compression) | 300 to 500 | 4 | 180 |
| - Tablet deduster | - | 3 | 7 |
| - Oscillating granulator (with 6 sets of screens) | 50 - 500 Kg/h (wet material) | 2 | 25 |
| - Table scale for tablet subdivision | 0 - 5 Kg | 3 | 5 |
| - Capsule filling and closing Machine | 12 - 15000 cph | 1 | 20 |
| - Assorted containers and tools | - | 3 | 5 |
| - Cabinets | 3 | - | 5 |
| - Supporting equipent/conveyor, and accessories | - | Various | 18 |

**Table 4.5 (continued)**

| Equipment description | Capacity | Quantity | C&F Cost US$ 000's |
|---|---|---|---|
| Oral liquid section: | | | |
| - Mixing vessel (jacketted, fixed propeller type stirrer, dip stic, gas purging inlet, airtight lid), st. st. | 1000 L | 1 | 10 |
| - Storage vessel (with stirrer), stainless steel | 1000 L | 1 | 5 |
| - Mixing vessel (jacketted, with stirrer) stainless steel | 500 L | 1 | 6.5 |
| - Vessel (Pre-mixing tanks), stainless steel | 100 L | 2 | 1 |
| | 50 L | 2 | 1 |
| | 10 L | 3 | 0.5 |
| - Silverson mixer/emulsifier (with hydraulic lifter) | | 1 | 4 |
| - Transfer pump | 250 - 500L/h | 1 | 2 |
| - Multiplate filter | 400 L per hr. | - | 2 |
| - Wash basins | - | 2 | 1 |
| - Semi-automatic liquid filler | 20 - 40 p.m. | 1 | 7 |
| - Portable stirrer | - | 1 | 1 |
| - Conveyor belt | - | 1 | 2 |
| - Bottle wash tanks | - | 3 | 1 |
| - Tray trolleys | 10 trays | 10 | 3 |
| - Cabinet | - | 1 | 1 |
| - Shelf/Rack | - | 2 | 1 |
| - Miscellaneous equipment/utensils | - | - | 2 |
| - Set of furniture | - | 1 | 3 |
| - Pall water filter/Deioniser | - | 2 | 6 |
| - Semi-automatic batch printer | 50-60 per min. | 2 | 3 |

Table 4.5 (continued)

| Equipment description | Capacity | Quantity | C&F Cost US$ 000's |
|---|---|---|---|
| **B. QUALITY CONTROL LABORATORY:** | | | |
| In-Process control laboratory: | | | |
| - Tablet hardness tester | - | 1 | 5 |
| - Tablet friabulator | - | 1 | 1 |
| - Tablet/capsule dissolution tester | - | 1 | 3 |
| - Moisture determination apparatus | - | | 1.5 |
| - Viscometer with accessories | - | 1 | 5 |
| - pH meter | - | 1 | 2 |
| - Precision balance | - | 2 | 3 |
| - Disintigration tester | - | 1 | 1 |
| Physico-chemical labortory: | | | |
| - Spectrophotometer UV-M, 200 - 1000 nm | - | 1 | 7 |
| - Polarimeter | - | 1 | 4 |
| - Melting & Boiling point apparatus | - | 1 | 1.5 |
| - Top loading balance | 0-1200g | 1 | 2 |
| - Analytical balance | 0-160 g | 1 | 3 |
| Micro biological laboratory: | | | |
| - Refrigerator | 0.2 cu.m | 1 | 1 |
| - Autoclave | - | 1 | 6 |
| - Microscope | | 1 | 3 |
| - Incubator | | 1 | 3 |
| - Zone reader | | 1 | 0.5 |
| - LAF unit/clean air bench | | 1 | 3.5 |
| - Turbidimeter/Spectronic-20 | | 1 | 2 |
| - Bench centrifuge | | 1 | 1.5 |
| - Top loading balance | 0-200 g | 1 | 1 |

Table 4.5 (continued)

| Equipment description | Capacity | Quantity | C&F Cost US$ 000's |
|---|---|---|---|
| General laboratory instruments: | | | |
| - Fumehood | | 1 | 3 |
| - TLC and accessories | | 1 | 1.5 |
| - Water distillation still | | 1 | 0.5 |
| - Vacuum oven | | 1 | 1 |
| - Set of sieves | | 1 | 1 |
| - Calliper gauge, scoops, spatula etc. | | various | 1 |
| - Water bath with thermostat | | 1 set | 2 |
| - Muffle furnace | | 1 | 2 |
| - Analytical balance | 0-160 g | 1 | 2 |
| - Drying oven | | 1 | 2 |
| - Hot plate and magnetic stirrer | | 2 each | 2 |
| - KF apparatus and accessories | | 1 set | 1 |
| - Calculating machines | | 3 | 1 |
| - Vacuum pump | | 1 | 3 |
| - Cabinets | | 2 | 0.5 |
| - Laboratory benches | | 4 | 3 |
| - Miscellaneous | | | 3 |
| C. PHARMACY/WAREHOUSE: | | | |
| - Scales: Table top precision | 1-5 Kg | 1 | 1 |
| Table top pecision | 1-10 Kg. | 1 | 2 |
| Floor balance | 0-250Kg | 1 | 4 |
| - Scales, Top Loading Digital Precision | | 1 | 4 |
| - Bench Stone Top (antivibratory) | | 1 | 2 |
| - Hydraulic trolley | | 4 | 4 |
| - Shelves, Racks | | 3 | 3 |
| - Miscellaneous scoops, containers, utensils | | | 3 |
| - Protective equipment | | | 3 |
| - Supporting equipment & accessories | | | 3 |
| - Wooden pallets | | 20 | 2 |

Table 4.5 (continued)

| Equipment description | Capacity | Quantity | C&F Cost US$ 000's |
|---|---|---|---|
| **D. MAINTENANCE & UTILITY SUPPLY:** | | | |
| - Standby Power Generator, 400/230 Volt, 50 cycles | 250KVA | 1 | 35 |
| - Reciprocating water Chiller | 50 ton | 1 | 50 |
| - Centrifugal water pump | 5 HP | 2 | 1 |
| - Water cooling tower | | 1 | 3 |
| - Airhandling unit | 60 Cu.M | 3 | 10 |
| - Air filtering unit | | 2 | 2 |
| - Duct Dampers and Diffusers | | Lot | 2 |
| - Dehumidifier | | 1 | 3 |
| - Temperature & Humidity recorder | | 2 | 2 |
| - Dust control units | | 2 | 2 |
| - Steam generator, Fuel - Furnace/ Diesel oil | 450Kg/Hr. at 8Kg/cm² | 1 | 20 |
| - Feed water treatment unit | | 1 | 5 |
| - Steam pipes and Valves fittings | | Lot | 5 |
| - Water Still | 100L/hr. | 1 | 30 |
| - Air compressor, 1 Cu.M at 12 kg/cm² | | 1 | 25 |
| - Distribution system and installation: | | | |
| - Piping for Hot and Cold water | | | 30 |
| - Piping for Compressed air | | | |
| - Electrical distribution system: | | | |
| - High tension switch as per requirement | | | |
| - Step-down Transformer | | | 50 |
| - Power distribution Panel | | | |
| - Lighting distribution Panel | | | |
| - Maintenance workshop equipment | | | 20 |
| **E. OFFICE AND MISCELLANEOUS:** | | | |
| - Office furniture | | Various | 10 |
| - Canteen equipment, furniture | | Various | 10 |
| - Lockers | | 4 | 5 |
| - Vehicles | | 4 | 25 |
| - Miscellaneous | | - | 33 |

4.2 2 Conversion rates

The currency expressed for the local and importable materials and equipment are in US$. The conversion rate used is as follows:

1.00 US$ = 200 MT (Mozambique)
= 37.50 BEC(Belgium Franc)
= 2.15 Korea(DPR) (South Korea)
= 2.25 Merck (Federal Republic of Germany)
=£0.625 Sterling (U.K.)
= 1296 Lira (Italy)
= Rs.12.75 (India)
= SFr. 1.53 (Switzerland)
= 2.06 Dfl (The Netherlands)
= ¥ 145 (Japan)
= AS 16.6 (Austria)
= 6.45 FF (France Franc)

# 5.0 SITE PLANNING

5.1 Site Planning

5.2 Building Design, Plant Layout

5.3 Utilities

5.4 Safety and Ecological provision

5.5 Cost Estimates: Building and Civil works

5.6 Time Schedules

# 5.0 SITE PLANNING, BUILDING DESIGN, ROOM LAYOUT & TIME SCHEDULES

## 5.1 Site Planning

5.1.1 Site selection is not within the scope of the present study. The Ministry of Health in principle selected Chimoio as the location for pharmaceutical industry in Mozambique in 1979/1980. In the selection process the consulting firm, ASTRA AB of Sweden participated.

However, in the present context the Ministry of Health likes to reconsider involving relevant government institutions the earlier decision for the establishment of pilot plant.

5.1.2 The following criteria are suggested for the site selection process:

- topography, size, shape and soil conditions
- water and power sources
- communications
- expansion possibilities
- pollution
- political and/or socio economic strategy of the location.

5.1.3 Site utilization

Foreseeing the need for future expansion of the pilot plant, the selected site should permit the site-covered-area utilization of about 50%.

## 5.2 Building Design and Plant Layout

5.2.1 The plant activities are proposed to be carried out in the same building based on a "through flow" to prevent back-tracking thus avoiding possibilities of mix-ups. The process layout follows the room layout in respect of movement of raw materials to finished goods. The flow of working personnel is designed to prevent personnel - originated contaminants from contaminating the products.

### 5.2.2 Building and Room Layout

Without considering the RM, PM and FG warehouses located at the opposite ends of the plant, the suggested building internally is composed of about 3 modules separated by corridors, refer Annex-13 for the proposed floor plan.

The modules incude the following areas:

- the management and services area
- the dry tablet, capsules manufacturing and subdivision area. The pharmacy/material dispensing, oral liquid compounding and subdivision area. Both the manufacturing core areas(dry and wet area) leads to the common packaging hall.

The RM, PM warehouse is directly connected to the manufacturing area, the packaging hall to the FG warehouse via the FG quarantine.

Please refer to table 5-1 for the occupancy of different operational rooms in the planned covered site area of 1352 $m^2$, refer Annex-13.

### 5.2.3 Foundation and Structure

- Foundation will be chosen according to site soil testing which should be carried out priot to selection of construction site. Base of footing of concrete directly on the existing soil or piling may be necessary depending on soil condition.

- The conventional concrete construction is primarily suggested over the pre-fabricated steel construction because the technology is indigenous and favourable local cost considerations. All elements of the pre-fabricated steel structure are import dependant.

  However in view of substantial gain in construction time consequently early start-up of the plant it is suggested that the overall financial returns be evaluated for steel structure at the implementation phase.

- The basic modules suggested is 5.2m x 5.2 m.

- For the waste water drainage, a drainage blanket is suggested to be laid out below the concrete plant floor.

- **Warehouses:**

  - The suggested design of the raw materials(RM) and packaging flow eliminating back-tracking, mix-ups and GMP considerations. It icludes the following:

    - an initial RM-PM receiving area. This area permits unloading of consignment, storage of pallets, etc., and in a manner buffers the warehouse.

    - a quarantine area where the in-coming materials must be held until sampled, tested and released by quality control for final placement in the designated active storage area. Although except for labels, the use of physically segregated

(walled-off) quarantine area is meaningful, it makes large demands on space, investment and in a manner less flexible operation. Although alternative method of identification by floor marking and use of specified colored stickers on material stacks to indicate the relese status are possible, with gain in operational skill and experience an effective system of administrative control is suggested.

- specifically designated active storage areas for RM and PM are provided with appropriate environmental conditions, namely airconditioned space including material weighing room, dispense area and cold storage (at 6°-8°C for storage of temperature sensitive materials as a part of the raw material warehouse here in referred to as pharmacy (60 $m^2$).
- a restraint,"Reject area" to permit safe temporary storage eliminating chance of mix-ups of the rejected materials until disposition is determined.
- a fenced corrosive material storage area.
- a secured segregated area for storage of pre-printed labels with access to authorised persons.
- a bonded, temperature controlled room with explosionproof fixtures for flameable solvent storage.

Based on the inventory profile (RM 6 months, PM 3 months, FG 2 months), the space and loading requirement, is estimated to have,

- RM, PM warehouse (including quarantine space) 190 $m^2$
- FG Warehouse (including quarantine store) 180 $m^2$
- Free height 6.5 m
- Loading 1.5 - 2.0 ton/$m^2$
- FG warehouse is designed to have a netted 'shipping dock' and the RM, PM warehouse with a suitable "off-loading" truck dock.
- the warehouses is designed to have self ventilation system.

**Manufacturing and Packaging area:**

- The GMP considerations built into the over all design for the core area include prevention of cross contamination, mix-ups and dusty operation by providing :
  - unit operation in cubicles
  - dust extraction facility milling/granulation rooms
  - airconditioning system
  - the covered areas for manufacturing is 225 $m^2$ and for packaging 83 $m^2$.
  - free room height 4.5 m
  - loading 0.8 - 1.0 ton/$m^2$
  - a technical floor, exists on top of the production area with a free height of about 2.0 m to enable housing of airconditining ducts, steam, water and electrical net work.

**Management and Services modules:**

This consists of office, laboratory, cafeteria, reception, lockers/change room and maintenance workshop. It occupies a floor space of 124 $m^2$.

The useful load bearing (except the utility and workshop area) is 0.4 ton/$m^2$.

**Utility Supply and Maintenance workshop:**
Housing of water distillation plant, steam generating plants, air compressor, water treatment system, emergency generator, maintenance workshop and the transformer room are suggested in a corner of the building occupying 91 $m^2$ floor space.

- Free height 6.5 m
- Loading 2.0 - 2.5 ton/$m^2$.

**Floor, wall and partitions:**

- Warehouse, utility/maintenance workshop area floor are heavy duty concrete.
- Bricks are locally fabricated in four sizes, 20x20x30 cm, 15x20x30 cm, 10x20x30 cm and 7x12x22 cm and brick wall is preferred.
- The exterior walls are hollow concrete blocks and the walls of the core area rooms shall be composed of brick-work, plastered and painted, glassed and brick work again. The wall between the packing and the bottling/subdivision rooms will also be glassed.

**Window:**

The internal windows are permanently closed permitting visual communication only. Manufacturing area windows, size about 1.0 x 1.8 m, must be flushed with the inner side of the wall to minimize dust settlement and ease of cleaning, windows in facade are suggested to be dimensioned (height not more than 90 cm) to shield against sun radiation.

- For finishing and application of coating materials on walls, floor and ceiling, plese refer Table 5-2.
- The supportive entities of guards room, incenerator, car parking lot, are included in the civil works while the dwelling and laundry facilities are excluded.

**Table 5-1: Distribution of the Floor Space to Operational Rooms**

| Covered Site Area | 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 | 6.5 |
| Lockers, sanitary & medical services | 85 | 6.5 |
| Cafeteria | 60 | 4.5 |
| | 1352 | 100.0 |

**Table 5-2: Finishing And Application Of Coating Materials On Walls, Floors and Ceiling**

| AREAS | Walls[1] | Floors | Ceilings |
|---|---|---|---|
| Tablet-Capsule | Plastered and epoxy painted, smooth joint free surface. | Concrete with mosaic stone. | Epoxy resin coating and non-porus. |
| Oral Liquid | Welded PVC sheet or ceramic tiled | Concrete with non-skid tiles | Epoxy resin-coating. |
| Office, Laboratories, canteen, change rooms | Plastered and epoxy resin coating. | Mosaic stone on concrete | Plastered epoxy resin painted |
| Corridor | Plastered and painted | Mosaic stone on concrete | Plastered and epoxy resin |
| Packaging Hall | Epoxy Coating | Mosaic stone on concrete | Plastered and epoxy resin, inner corridor of tablet, capsule processing area |
| Pharmacy/Material dispensing | Plastered and epoxy painted | Concrete with stone top | False ceiling with P.V.C. shooks |
| Warehouses | Lime white wash | Cement finish | False ceiling of PVC shooks |
| Cold storage | Insulated walls with moisture protection on outside of the wall | Insulated floor with concrete and stone top | Lime white wash insulated ceiling |

(1) All floors, walls and ceiling junctions should be rounded and filled.

## 5.3 Utilities

**Warm Water:**

Warm water is required in the following areas:

- Oral liquid compounding
- Equipment and bottle wash area
- Laboratories
- Lockers and sanitary area

Installation of a heat-exchanger on the technical floor is foreseen:

- temperature 50°C - 60°C
- pressure 4 - 5 bar; estimated requirement 1 - 2 $m^3/h$.

**Fresh Water:**

Depending on quality of raw water, at site, pre-treatment may be necessary prior to use in boiler or in production area. The water consumption is estimated to 30-40 $m^3$/day.

**Steam Supply:**

A steam generator (oil fired) to produce dry steam at 4.5 - 5 bar pressure steam required for the fluid bed drier oral liquid compounding, water still and other process work area is included.

**Distilled Water Supply:**

The distillation unit, water still, is provided with water and steam which is then evaporated and then condensed. The distillation rate of 200 - 250 L per hour is foreseen. Water is stored at 90° - 95°C in stainless steel insulated vessel to avoid microbial contamination. The need for deionization of boiler feed water is to be determined based on the quality of plant site water-source.

**Water Pipe Lines:**

| | | |
|---|---|---|
| - Fresh water | ... | Copper, Steel, Synthetics |
| - Warm water | ... | Steel pipes |
| - Steam | ... | Steel pipes (Insulated) |
| - Distilled water | ... | Stainless steel |
| - Oxygen and Nitrogen gas | ... | Copper pipes. |

For ease of identification, the standard color code on pipe lines should be used.

**Utility distribution networks/electrical system:**

The whole detail network of the utility distribution and electrical systems should be authenticated by competent engineers prior to implementation phase.

- Air conditioning and ventilation:
  - Centralised air conditioning unit backed up by air-handling units (with dust control units) and automatic temperature and humidity control system is foreseen for production core area and packing hall only.
  - The tablet/capsule manufacturing core area are supplied with filtered, conditioned/dehumidified air as products will come in direct contact with room air. Metallic prefilters be provided at the manufacturing area room ceilings.

- The recommended conditions of air within the plant are as follows:

| Plant Areas | Temperature °C | Rel.Humidity % RH | Air-change Vol./h |
|---|---|---|---|
| Warehouse: Normal outdoor climatic conditions: | | | |
| - Cold Storage | 8 ± 1 | - | - |
| - Laboratories | 24 ± 2 | 60 ± 10 | - |
| - Manufacturing: | | | |
| • Tablets | 25 ± 3 | 50 ± 10 | 3 - 5 |
| • Capsules | 28 ± 5 | 30 ± 5 | 3 - 5 |
| • Oral Liquid | 25 ± 3 | 50 ± 10 | 3 - 5 |
| • Packaging | 25 ± 3 | 50 ± 10 | 4 - 6 |

Laboratory and offices can be conveniently furnished with window and console type room airconditioning units.

All fittings e.g., light fixtures, switches, etc. shall be explosion-proof in the tablet coating drying and solvent storage room. The duct should be fire-insulated.

- Ventillation is foreseen for areas, such as, equipment wash room, bottle wash room and other hot and high humid areas e.g. social facilities, cafeteria where the conditioning of air is not suggested.

- Compressed Air:

  Non-lubricated reciprocating compressor, air-cooled silent box type at discharge pressure 6-7 bars is suggested.

- **Gas:**

  Nitrogen and oxygen gases are needed in small quantities in production and workshop. The gas cylinders should be located outside the building of consumption.

  Nitrogen gas used directly for manufacturing and packaging of the oral liquid products must be filtered to remove particulate matters at pint of use.

- **Electrical System:**

  The working voltage is 380-410 volt, 3 phases, 50 cycles and 220 V, 1 phase, 50 cycles. The distribution of utilization points will be carried out by cables. The electric switch boards for production departments may be locate there or on the walls of the respective corridors. Branches to utilization points and switches for each room will be fitted in the walls.

- **Lighting system:**

  The illumination level in above floor of the different plant areas should be as follows:

| | |
|---|---|
| Production and laboratory | 800 lux |
| Packaging area | 800 lux |
| Corridor | 400 lux |
| Offices, Canteen | 600 lux |
| Exterior | 15 - 20 lux |

  Approximate annual power consumption is 450,000 units (KWH/Unit). The capacity of the connection should be 350 KW/h.

- **Power Generator:**

  A stand-by diesel driven 250 KVA generator is recommended to continue power supply during interruptions.

## 5.4 Built-in Safety and Ecological provisions

### 5.4.1 Safety provisions - equipment installations

- Guarding projecting shafts, exposed moving parts etc.
- Safety fenced interlocking device for blenders.
- Static eliminators: preventive measure for built-up of static electricity in the flow of powder, liquid and moving belts.
- Explosion-proof measures for dusty operations, combustible solvent storage, fluid bed dryer, coating room.

**Miscelleneous provisions**

| | | |
|---|---|---|
| - Emergency exits | - | Yes |
| - First Aid at conspicuous places | - | Yes |
| - Fire extinguishers (different types) | - | Yes |
| - Lightning arrestor | - | No |
| - Water hydrants | - | Yes |
| - Laboratory safety showers with pull chain/foot valves | - | Yes |
| - Laboratory eye wash fountains with foot or hand operated valves | - | Yes. |

### 5.4.2 Protection of equipment

- Rain, sewage and plant waste water:

  The rain water will be drained through open cemented drains covered with concrete slabs. Provisions are included to handle the production waste (originating from production, laboratory, bottle wash area) as well as the sanitary waste (toilets, showers, wash basins and kitchen area) through two independent sewage lines. The line handling the sanitary sewage is suggested to be treated to coagulate and separate the solids by sedimentation. The sanitary sewage line should be treated biologically in septic tanks to decompose the organic wastes. The production waste line is treated similarly, in addition neutralisation of the liquids is suggested prior to biological treatment. Depending on topography of the plant site connecting the two lines may be done far from the plant.

- No spent air should escape into outside without efficient filtration from contaminated rooms primarily in manufacturing area. Washable metallic filter at room ceiling followed by air mat filter (7 ply paper, about 10 micron pore size) is suggested. The filtered discharge air should be filtered through air mat filter not to contain particulate matter exceeding 5 mg per $m^3$.

- The incinerator is included in the infra structure to ensure protection of the environment from solid waste.

## 5.5 Cost Estimates: Building and Civil works

- In agreement with the local architects in Maputo and Beira and based on the concrete construction ratings in Mozambique 1986, the cost estimates for completion of the pilot formulation plant is indicated in table 5-3. Most of the construction materials including the electricals are to be imported and therefore the cost estimates should be checked at the implementation time.

**Table 5-3: Cost Estimates**

| Sections | Size, m² | Estimated Cost/m² US$ | Cost x 1000 US$ |
|---|---|---|---|
| - Production core packaging and laboratory area | 458 | 600 | 275 |
| - Corridors, raw, packaging and finished goods warehouse | 534 | 350 | 187 |
| - Offices | 124 | 300 | 37.2 |
| - Utility and maintenance workshop | 91 | 300 | 27.3 |
| - Social facility area | 145 | 500 | 72.5 |

| | | |
|---|---|---|
| - Site preparation and development | ... | 51 |
| - Auxiliaries: Drainage, guard house, vehicle parking, incinerator | ... | 40 |
| - Sewage system | ... | 10 |

**Total building and Civil works :** $700,000.00

Specific building cost is US$517.7/m²

## 5.5 Time Schedules

5.5.1 Certain major activities for the implementation of the project is presented in terms of estimated time - need in Annex-14 for concrete type of construction.

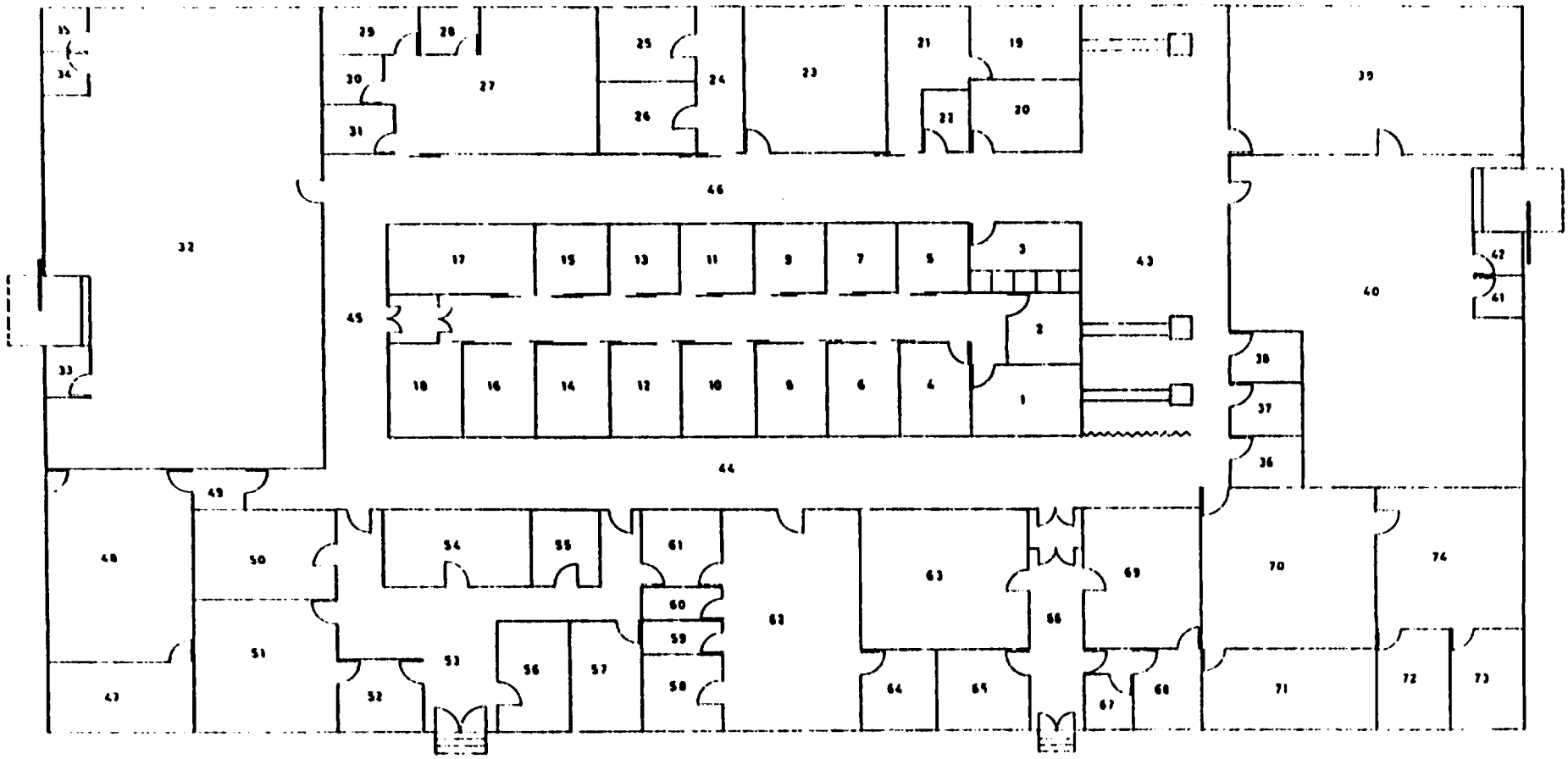
The estimated time - need is about 27 month for the start-up of production after the investment decision and the site selection have been made.

The time schedule foreseen is however dependent on timely completion of the civil works and utility installations. Currently most of the construction materials are imported in Mozambique. It is suggested that all construction materials are collected & stored prior to start-up of the job to enable efficient completion of the plant under supervision of the foreign engineers.

The pre-fabricated steel construction has not been considered.

## IDENTIFICATION OF ROOMS

| Room No. | Identification | Room No. | Identification | Room No. | Identification |
|---|---|---|---|---|---|
| 1 | Tablet/Capsule sub-division | 26 | Tray Dryer | 51 | Plant Manager |
| 2 | Tablet/Capsule subdivision | 27 | Pharmacy/Dispensing | 52 | Secretary |
| 3 | Printing | 28 | Weighing Room | 53 | Passage |
| 4 | Inprocess store | 29 | Cold Storage | 54 | Finance |
| 5 | Capsules Polish | 30 | Controls | 55 | General Office |
| 6 | Milling | 31 | Dispensed Material | 56 | Reception |
| 7 | Capsules Filler | 32 | RM Warehouse | 57 | Toilet |
| 8 | Tablet Press | 33 | Warehouse Superivsor | 58 | Instrument |
| 9 | Tablet Press | 34 | Solvent Store | 59 | Sample |
| 10 | Slugging | 35 | Reject | 60 | Laboratory Bench Reference |
| 11 | Blender/Mixer | 36 | Engineer's Office | 61 | QC Manager |
| 12 | Wetmass mixing | 37 | Secretary | 62 | Laboratory Bench |
| 13 | Tablet Press | 38 | Production Manager | 63 | Women Toilet/Change room |
| 14 | Sifter | 39 | Quarantine | 64 | Bio Test |
| 15 | Coating | 40 | FG Store | 65 | Medical Officer/Dispensary |
| 16 | Blender | 41 | Return Goods | 66 | Corridor |
| 17 | Inprocess Tablet/Capsule | 42 | Store Supervisor | 67 | Time Keeper |
| 18 | Tray Dryer | 43 | Packing Hall | 68 | Uniform Store |
| 19 | Oral Liquid Fill | 44 | Corridor | 69 | Men's toilet/Change room |
| 20 | Inprocess Oral Liquid | 45 | Corridor | 70 | Engineering workshop/Plant |
| 21 | Bottle Wash | 46 | corridor | 71 | Utility Equipment |
| 22 | Bottle Un-pack | 47 | Kitchen Store | 72 | Power Sub-station |
| 23 | Oral Liquid Manufacturing | 48 | Canteen | 73 | Pump House |
| 24 | Corridor | 49 | Buffer | 74 | Generator House |
| 25 | Fluid Bed Dryer | 50 | Conference room | | |



PILOT PLANT LAYOUT
FOR PHARMACEUTICALS

PEOPLES' REPUBLIC OF
MOZAMBIQUE

# TIME SCHEDULE

| ACTIVITIES/MONTHS | 1 2 3 4 5 6 7 8 9 10 11 12 YEAR-I | 1 2 3 4 5 6 7 8 9 10 11 12 YEAR-II | 1 2 3 4 5 6 7 8 9 10 11 12 YEAR-III |
|---|---|---|---|
| 1 Architechtural Drawings, Prel. Bills of Quantities, Specs., Cost Estimates | | | |
| 2 Civil works Contracting | | | |
| 3 Site Preparations and Development | | | |
| 4 Excavations, Foundations, Construction and other Civil works | | | |
| 5 Installation of Utilities and other Technical Facilities | | | |
| 6 Erection of Production Equipment and Machinery | | | |
| 7 Start-Up Production | | | |
| 8 TRAINING: | | | |
| - PHASE-I (EXTERNAL) | | | |
| - PHASE-II (IN-SERVICE) | | | |

# 6.0 ECONOMICS

The studies on economics primarily aims at the estimation of production cost.

## 6.1 Investments

### Fixed Investment

**-Land**

In agreement with the Ministry of Health, the land cost is not included. The land is considered as free if Mozambique builds the industry on her own and will have value when if foreign investers participate.

**-Civil Works & Building**

Based on the local availability of technology & minimum of foreign currency expenditure, only in-situ concrete construction has been evaluated. The pssible alternatives of pre-fabricated steel construction and combination of concrete and steel constructions has not been considered. However it is suggested that at the implementation phase a comparative economic evaluation be done for construction alternatives.

**-Machinery and Equipment**

Table 4-5 (Chapter 4) indicates the cost of production, laboratory, utility & maintenance workshop and office equipment. The total fixed investment is shown in table 6-1. The total investment sum inclusive of the estimated working capital is $3,527,000, refer table 6-2. The depreciation of building, machinery & equipment and pre-production capital expenditure is shown in table 6-3. The pre-production capital expenditure is elaborated in table 6-3(a). The total plant overhead is estimated to $194,000 consisting of 49% variable and 51% fixed portion, refer table 6-4 & 6-5.

The cost of raw & packaging materials by dosage form and the cost of direct manpower by product line split into foreign & local components is indicated in table 6-6 & 6-7 respectively.

The total production cost of $1,039,000 excluding depreciation and interest and its split by foreign and local currency portions is shown in table 6-8. The estimated total assets and the total investment schedule is shown in table 6-9 & 6-10 respectively.

**-Working capital & GP.**

The estimated working capital of $856,000 (when operating at full capacity) is based on accounts receivable 30 days, Inventory - materials 120-180 days, finished goods 60 days, cash in hand 30 days and accounts payable 30 days. The annual net sales with the planned volume of production of 12 products at 21.2% gross profit level is estimated at $1,890,000. Thus the local production cost will be slightly higher over the 1986 import cost. For the annual trade account at full plant capacity operation, refer table 6-11.

The calculated pre-tax profit is $400,000. This should be treated as acceptable level of gross profit. The possible source of finance are the share capital, long term, mid-term and short term loans. The interest rate on loans is assumed 10%.

In respect of the foreign exchange impact, when operated at full capacity, the pilot plant should allow an estimted annual saving of hard currency to the tune of US$565,000, approximately 70% of which is foreseen to be contributed by oral liquid formulations.

**Table 6-1: Total Fixed Investment (000 US$)**

| Item | Foreign currency | Local currency | Total cost |
|---|---|---|---|
| a. Land | | | |
| b. Civil works & Building | 560 | 140 | 700 |
| c. Machinery and Equipment | 993 | 248 | 1241 |
| Initial Fixed Investment | 1553 | 388 | 1941 |

**Table 6-2: Total Investment (000 US$)**

| Item | Foreign currency | Local currency | Total costs |
|---|---|---|---|
| a. Initial Fixed Investment | 1553 | 388 | 1941 |
| b. Pre-production capital expenditure | 615 | 115 | 730 |
| c. Working Capital (at full capacit) | 532 | 324 | 856 |
| Total Initial Investment | 2700 | 827 | 3527 |

**Table 6-3: Depreciation (000 US$)**

| Items | Depreciation years | Start-up | Full Capacity |
|---|---|---|---|
| -Civil works and building | 25 | 28 | 28 |
| -Machinery and equipment | 10 | 124 | 124 |
| -Pre-production capital expenditure | 5 | 146 | 146 |
| Total Depreciation | | 298 | 298 |

**Table 6-3(a) : Pre-production Capital Expenditure (000 US$)**

| Item | Foreign currency | Local currency | Total Cost |
|---|---|---|---|
| a. Consultant Fees Engineering and Management during implementation | 100 | | 100 |
| b. Training | 145 | 60 | 205 |
| c. Running-in Expense | 50 | | 50 |
| d. Interest during construction | 110 | | 110 |
| e. Preliminary Expenses | | 50 | 50 |
| f. Site supervision | 120 | | 120 |
| g. Process Fees | 50 | | 50 |
| h. Additional Costs(1) | 40 | 5 | 45 |
| Total pre-production capital expenditure | 615 | 115 | 730 |

(1) Additional costs: estimated lump sum amount for soil test, survey fees, special consultants etc.

**Table 6-4: Variable Overhead (000 US$)**

| Product Form | Foreign currency | Local currency | Total |
|---|---|---|---|
| - Tablets | 27 | 24 | 51 |
| - Capsules | 5 | 5 | 10 |
| - Syrups | 18 | 16 | 34 |
| Total | 50 | 45 | 95 |

**Table 6-5: Fixed Overhead (000 US$)**

| Product Form | Foreign currency | Local currency | Total |
|---|---|---|---|
| - Tablets | 22 | 32 | 54 |
| - Capsules | 4 | 6 | 10 |
| - Syrups | 13 | 22 | 35 |
| Total | 39 | 60 | 99 |

**Table 6-5: Cost of Raw and Packaging Materials (000 US$)**

| Product Form | Foreign currency | Local currency | Total Costs |
|---|---|---|---|
| - Tablets | 320 | 8 | 359 |
| - Capsules | 163 | 3 | 166 |
| - Syrup | 202 | 82 | 284 |
| Total | 685 | 124 | 809 |

**Table 6-7: Cost of Direct Manpower (Full Capacity) : (000 US$)**

| Product Line | Foreign currency | Local currency | Total costs |
|---|---|---|---|
| - Tablets | | 19 | 19 |
| - Capsules | | 4 | 4 |
| - Syrup | | 13 | 13 |
| Total | | 36 | 36 |

**Table 6-8: Total Production Cost(Excluding Depreciation & Interest): (000 US$)**

| Cost Components | Foreign currency | Local currency | Total |
|---|---|---|---|
| - Raw and Packaging materials | 685 | 124 | 809 |
| - Direct Manpower | | 36 | 36 |
| - Variable Overhead | 50 | 45 | 95 |
| - Fixed Overhead | 39 | 60 | 99 |
| Total | 774 | 265 | 1039 |

**Table 6-9: Total Assets (000 US$)**

| Items / Year | Construction 1 | Construction 2 | Start-up 3 | Full capacity 4 |
|---|---|---|---|---|
| - Initial Fixed Investment | 720 | 865 | 356 | |
| - Pre-production expenses | 321 | 347 | 62 | |
| - Current Assets | | | 478 | 956 |
| Total Assets | 1041 | 1212 | 896 | |
| - Cumulative Fixed Assets | 1041 | 2153 | 3049 | 3049 |
| - Cumulative Current Assets | | | 478 | 1434 |

**Table 6-10: Total Investment Schedule (000 US$)**

| Type of Investment | Construction | | Start-up | Full Capacity |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| - Initial Fixed Investment | 720 | 865 | 356 | |
| - Pre-Productin Capital Expenditure | 321 | 347 | 62 | |
| - Working Capital | | | 378 | 478 |
| Total Investment | 1041 | 1212 | 796 | 478 |
| Cumulative Investment | 1041 | 2253 | 3049 | 3527 |

Table 6-11: Trade Account (Full Capacity):(000 US$)

| Item | Foreign currency | Local currency | Total |
|---|---|---|---|
| a. Net Sales | | 1890 | 1890 |
| b. Variable Costs: | | | |
| b1 Raw & Packaging Material | 685 | 124 | 809 |
| b2 Direct Manpower Cost | | 36 | 36 |
| b3 Variable Overhead | 50 | 45 | 95 |
| c. Fixed Costs: | | | |
| c1 Fixed Overhead | 39 | 60 | 99 |
| c2 Depreciation | | 298 | 298 |
| c3 Interest | | 153 | 153 |
| | 774 | 716 | 1490 |
| Gross Profit | | | 400 |
| % of Net Sales | | | 22.1% |