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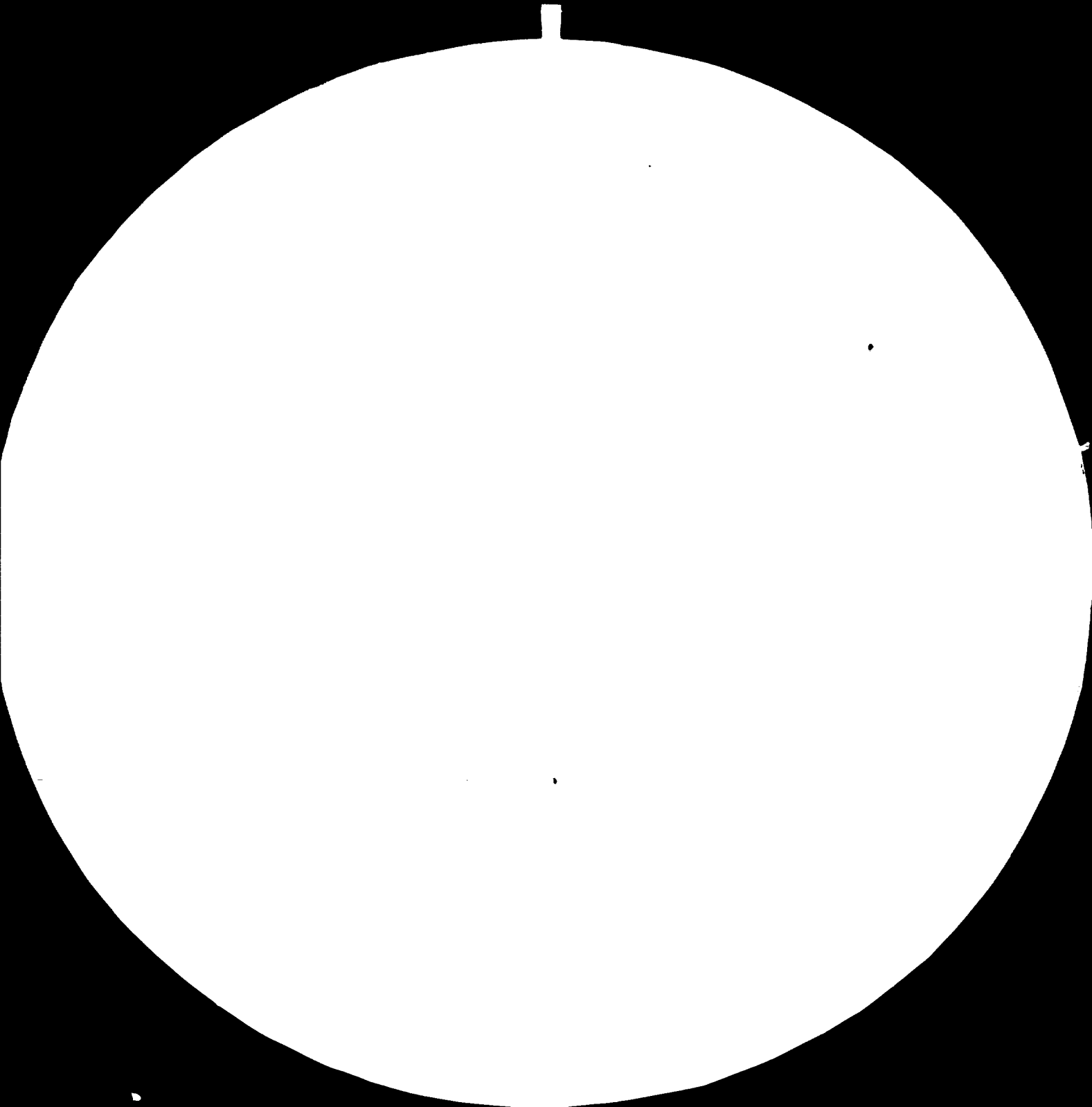

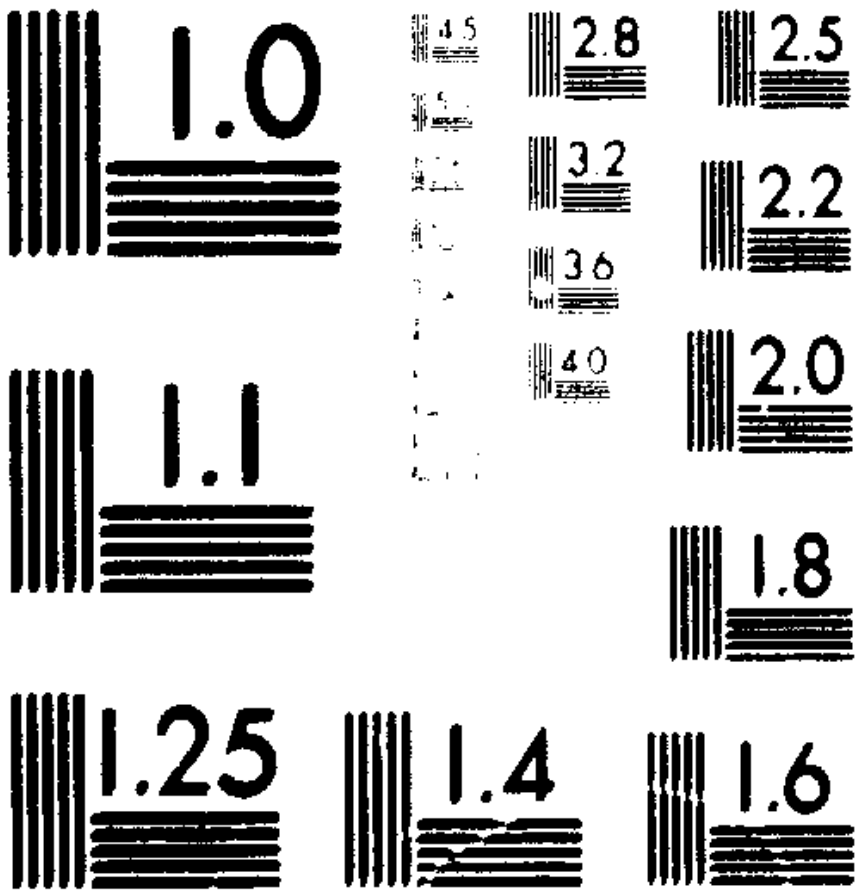

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24 January 1979
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PHARMACEUTICAL EXPERT.

SI/PDY/77/305.

DEMOCRATIC YEMEN.

Terminal report

Prepared for the Government of Democratic Yemen
by the United Nations Industrial Development Organization,
executing agency for the United Nations Development Programme

Based on the work of W. Sobiczewski,
pharmaceutical expert

United Nations Industrial Development Organization
Vienna

Explanatory notes

References to dollars ($) are to United states dollars.

The monetary unit in Democratic Yemen is the dinar (YD). The exchange rate used by the expert in this report was YD 1 = $3.

A slash between dates (e.g., 1975/76) indicates a crop year, financial year or academic year.

A hyphen between dates (e.g., 1973-1977) indicates the full period involved, including the beginning and end years.

NDC refers to the National Drug Company.

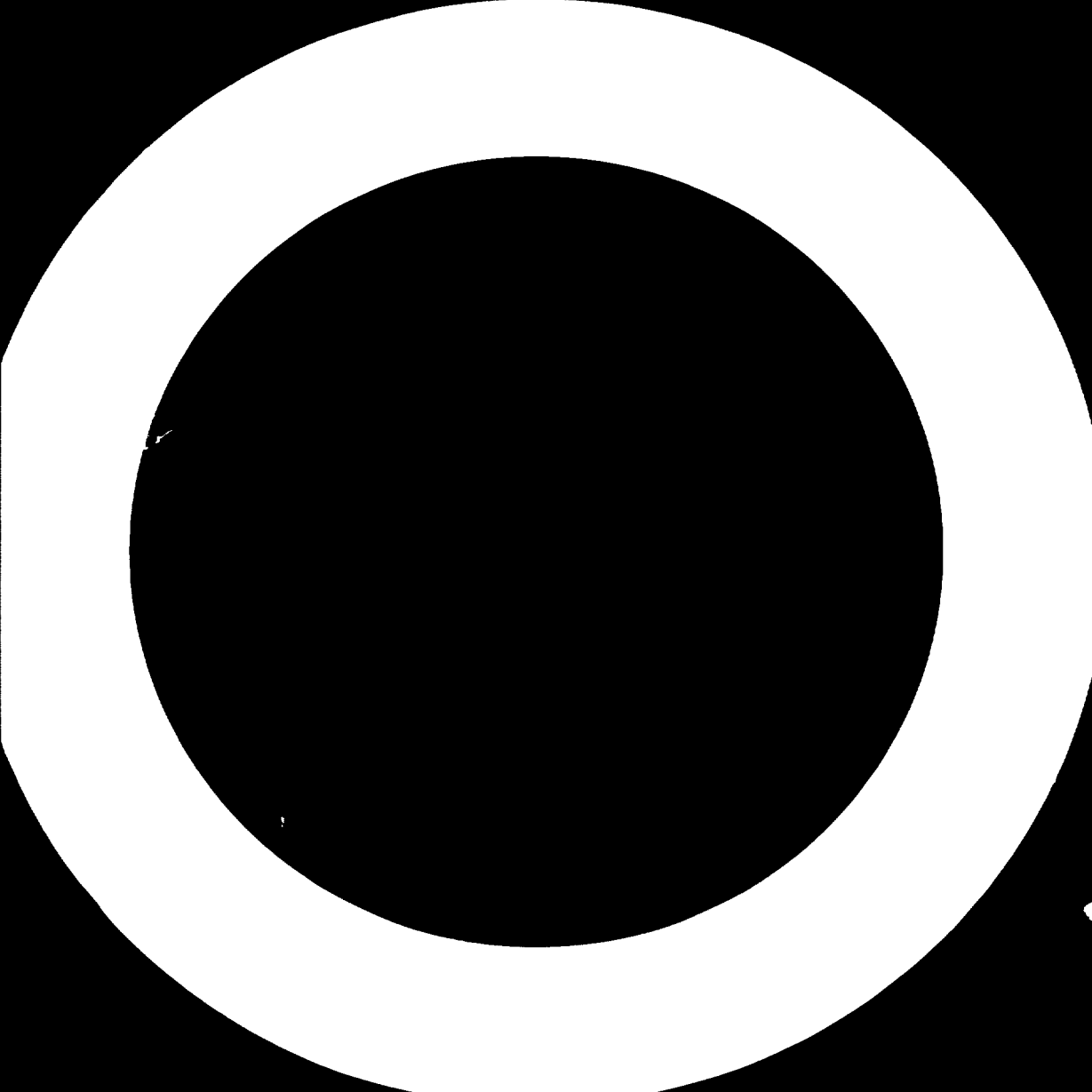
ABSTRACT

On February 1976 the Government of Democratic Yemen requested the Resident Representative of the United Nations Development Programme (UNDP) to provide the services of an expert in pharmaceutical industry for a period of six months. The project "Pharmaceutical expert" (SI/PDY/77/305) was approved by the United Nations Industrial Development Organization, as executing agency for UNDP, on 9 November 1977 and fininanced from Special Industrial Services (SIS) funds. The pharmaceutical adviser took up his assignment in January 1978 and ended it, after an extension of three months, in October 1978.

The report discusses the steps necessary for the establishment of a small scale pharmaceutical industry in Democratic Yemen. In order to establish the quality and quantity of drugs used within the country, a list of all imported medicaments was prepared, including their producers, prices and trade names. The list is a basis for statistical calculations and the selection of sources of importation as well as prices of items. To make planning for the next five years possible, the necessary records and inventory controls must be kept to ensure the utmost economy.

Taking into account the absolute necessity of pharmaceutical industry in Democratic Yemen, a plan of the future manufacturing unit was prepared. A list of machinery and equipment for making liquids, ointments and tablets was also prepared, including prices. The necessity of a quality control laboratory was also presented, and for this purpose, a list of special analytical equipment needed was prepared.

In conjunction with the establishment of the manufacturing unit and the quality control laboratory, a programme for the training of technicians who will be employed at both units was developed.



CONTENTS

Annexes

INTRODUCTION

The United Nations Development Programme (UNDP) set up the project "Pharmaceutical expert" (SI/PDY/77/305) to evaluate the existing aspects of the pharmaceutical industry and to suggest recommendations for improvement and development during the next five years. Initially, an evaluation was made of the existing reports concerning the pharmaceutical industry in Democratic Yemen and of the existing production units. The purpose of the present mission was then determined to encompass the following actions:

(a) To update the quality and quantity of drugs used in the country and to make projections in relation to the needs that will develop during the next five years;

(b) To recommend technological advances which would improve the quality of drugs produced locally for domestic use;

(c) The preparation of a list of machines and equipment needed for the development of existing resources;

(d) The preparation of a technician training programme.

Within the realm of the aforementioned purposes of the mission, a practical plan of action was undertaken. This plan dealt with the following tasks:

(a) The preparation of a list of medicaments which were imported by the National Drug Company last year, including sources, quantities, and prices;

(b) The selection of the sources of imports taking into account the quality of the drugs and the prices;

(c) Taking the necessary steps to establish a control of the distribution of supplies to all stocks and pharmacies with accurate records and inventory controls, therefore making it possible to know how many items have been sold at any given quarter of the year;

(d) The selection of offers from various pharmaceutical companies concerning ready-made products and prices;

(e) Determining the amount of medicaments that are at present in stock-rooms, and the need for importing medicaments. The rising medical services that will be required during the coming years must be calculated;

(f) The preparation of one collective list of the most important medicaments needed for the next years in order to know how many items should be imported in larger amounts;

(g) The preparation of a plan and scheme for the proposed new manufacturing unit to be built in a new structure. The final goal of producing larger amounts of liquids and ointments (stage I) and tablets (stage II) must be taken into account;

(h) The preparation of a list of equipment necessary for the production of liquids, ointments and tablets;

(i) The preparation of a plan of the quality control laboratory as well as the list of special analytical equipment;

(j) The preparation of a programme for the training of technicians for specific functions, for example, the manufacturing and control of certain drugs.

Within the context of this mission a programme of visits, meetings, and discussions was undertaken involving the UNDP, the Ministry of Industry, the Ministry of Health, the Al-Gamhouria Hospital, the Laboratory and Store (Khormaksar) and the National Drug Company (NDC)(Steamer Point) as well as its Laboratory (Crater), Store (Maalla) and the new premises for the Manufacturing Unit (Khormaksar).

I. QUALITY AND QUANTITY OF DRUGS USED IN DEMOCRATIC YEMEN WITH PROJECTIONS FOR THE NEXT FIVE YEARS

A. Importation

The National Drug Company (NDC) imports medicaments and related products for hospitals and pharmacies based on the MIMS Middle East.[1/]

The NDC also imports medicinal products from other pharmaceutical manufacturing company sources, including, Medexport (Union of Soviet Socialist Republics), Medimpex (Hungary), and China National Chemicals. The Research Department of the NDC set up a list of over 160 pharmaceutical companies from which medicaments and related products could be imported. The usual way of purchases of the NDC is by using issue tenders. The tender forms are prepared by the Deputy General Manager of the NDC, and the general conditions of tenders are fixed.

The NDC imports medical preparations for hospitals and people's clinics on the basis of orders, and for pharmacies. The quantities to be ordered are decided upon by the General Manager of the NDC. Products in high demand are imported from many different sources and have different trade names, resulting in confusion and unsatisfactory medical information. As far as the progress in importation of medicaments is concerned, the value of imports in 1973-1977 was:

Year	YD
1973/74	336 237
1974/75	707 542
1975 (nine months)	371 927
1976	1 492 056
1977	1 733 745

1/ The MIMS Middle East is a professionally edited index of ethical preparations available for prescription in the Middle East. Volumes of MIMS are compiled from details supplied by the pharmaceutical manufacturing companies and contain indexes of hundreds of preparations manufactured by many pharmaceutical companies, and in many cases of preparations containing the biologically active compounds, but under different trade names. The volumes of MIMS contain also directories of agents and representatives as well as suppliers of the various products.

According to tenders for hospitals only:

Year	YD
1976	480 395
1977	693 955

In order to facilitate the process of information for doctors and pharmacists interested in the importation of medicaments, a special pharmaceutical list on the basis of MIMS and other materials by the NDC has been prepared. This list contains over 790 different preparations listed under their chemical and trade names which could be available in Democratic Yemen.

The NDC also prepared a list of pharmaceutical preparations which had been imported in 1977 from 43 different pharmaceutical companies, containing data connected with sales balances in the NDC stock and suggested orders for 1978. The above-mentioned list contained also, for about 90 per cent of the preparations, the prices of items. It was of importance to have on one list the quantities of items, their producers and prices in order to be able to compare and select them.

During the first two months of 1978, the NDC prepared about 150 import applications which were sent to approximately 60 pharmaceutical companies. Most of these orders contained a small number of items, and in some cases, the identical orders were sent for the same items to the same suppliers, or orders were sent for the same items to different suppliers. For example:

(a) Ampicillin syrup: manufactured by Beecham Research Int., as Penbritin Syrup - 60 ml bottle - price YD 0.555; and Ampicillin Syrup manufactured by Arab Pharmaceutical Manufacturing - 60 ml bottle - price YD 0.230;

(b) Multivitamin: manufactured by many pharmaceutical companies and imported by the NDC from 13 sources under 20 different trade names and at different prices, for example: Parke Davis (Myadec) - vitamins A, D, C, B_1, B_2, B_6, B_{12}, E + nicotine, iodine, iron, copper, zinc, 30 capsules - price YD 0.735; Leo Pharmaceutical (Miravit) - vitamin A, D, C, B_1, B_2, B_6, B_{12}, E, K + nicotine, iodine, folic acid, calc. panth., biotin, rutin, iron, mang., fluor, copper, zinc, molybd, 30 tablets - price YD 0.450; Rivo Pharmaceutical (Rivo 21) - essential vitamins and minerals, 30 tablets - price YD 0.320.

If the NDC had imported Miravit and Ampicillin Syrup only, it would have saved about YD 3,000 (about $US 9,000), per year; and, if the NDC had imported only Rivo 21, instead of Myadec and Miravit, it would have saved about YD 4,200 (about $US 12,600) per year.

In March 1973, the Research Department of the NDC started preparing special lists of imported medical preparations. These lists contain preparations divided into catagorical groups (decongestants, contraceptives etc.) will be sent to the doctors for their information. It also was agreed that in the future the above-mentioned lists will contain preparations produced by the NDC Manufacturing Unit as well, in order to inform doctors about the products and quantities available. The above-mentioned list should be examined once a year and corrected or reprinted. Doctors should be aware, however, that listed preparations are always attainable on the market under generic trade names.

In order to organize an efficient ordering system, the number of suppliers must be reduced. It should be decided which preparation from which supplier is the most helpful and economical. These medicaments will form the basic drug supply for all hospitals and pharmacies. In addition, small quantities of drugs known to be highly effective against diseases resistant to commonly-used antibiotics must also be stocked, but dispersed only when necessary.[2/]

B. Distribution of drugs and import plans

At present there is no comprehensive legislation governing the distribution and control of pharmaceuticals in Democratic Yemen. Therefore it was also impossible to establish the quantity of drugs that had been sent to hospitals and pharmacies. The NDC only had data concerning the quantity of medicaments in its own stock.

Because of the unorganized ordering practices of medicaments (i.e., the same base product being ordered from a few different manufacturers) the patients are often prescribed one drug and unable to obtain it although a generic equivalent would have been available. Supply does not equal the demand.

In order to establish a control on ordering, importation, and distribution, it was decided that pharmacies would be required to submit a list twice a year

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2/ All drugs should meet the pharmacopoeia requirements and have at least a two year shelf-life. When possible medicaments should be ordered by generic names. The climatic conditions must be taken into consideration and when possible strip packages requested for pharmacies.

indicating the amount of medicaments that had been sold during this time period. These lists would be reviewed in conjunction with the hospital needs. Records would be kept of the quantity of medicaments needed, the amount of medicinal preparations still in stock, and the increases in demand from one period to the next.

On the basis of general tenders for hospitals from 1975, 1976, 1977 and 1978, it was confirmed that during these years, and especially during last two years, the demand for some important medicaments had risen two or three times, while consumption of the other drugs had remained at the same level.

Calculations made on the basis of other developing countries indicate that a steady increase in drug consumption is to be expected with the increase in the gross national product. The Five-Year Plan of Democratic Yemen envisions a nearly 30 per cent increase in the gross national product.

The total expenditures spent on medicaments by the NDC in 1975-1977 divided by the population (1.6 million) is as follows:

	Consumption ($)		Increase over 1975 (%)
	Total	Per capita	
1975	3 146 781	1.97	
1976	4 476 163	2.80	42
1977	5 201 236	3.30	68

Taking into account the improvement in health services and the population growth, the annual increase in consumption of medical preparations should be at least 20-25 per cent during the next three to five years.

In order to establish economic sources of importation and quantities of preparations needed during the next years for hospitals and pharmacies in Democratic Yemen, a list was prepared of over 400 of the most important preparations, including their producers, trade names, prices, and foreseen quantities. At the end of this year the list should be examined and corrected taking into account the actual data from pharmacies and from the NDC stock. On the basis of this list the economic sources of importation should be established. The forementioned list of medicaments should be a basis for the establishment of a special up-to-date list of imported pharmaceutical preparations at the NDC. It should contain drugs alphabetically listed on special cards, with producers, trade names, prices and actual quantities in stock.

At present, all imported preparations are stocked on the shelves at the NDC stock according to their producers. For example, a medicament imported from 10 sources and listed under 10 trade names, is stored on 10 different shelves. In order to facilitate the listing and inventory controls, the preparations should be arranged in order on the shelves alphabetically in groups and than the same preparations under their different trade names grouped together on one shelf.

II. EVALUATION OF EXISTING UNITS AND IMPROVEMENT OF THE QUALITY OF DRUGS PRODUCED LOCALLY

A. Laboratory of the National Drug Company

The NDC has at present a small laboratory at Crater, Aden, but no special equipment for manufacturing liquids or ointments in quantity - even as large as 5 kg. The laboratory is inadequate for production as well as unprofitable because of the limited experience of personnel and lack of equipment. In 1976-1977 the laboratory was only able to prepare the following items (refilling, repacking and manufacturing some ointments or liquids):

Preparation	Number of bottles or jars 1976	1977
Acetic acid solution	1 500	-
Benzoic acid compound ointment	1 000	-
Benzyl benzoate	200	11 100
Calamine lotion	2 200	9 200
Castor oil	3 500	-
Cetculex cream	1 000	-
Gentian violet	1 000	5 000
Glycering borax	1 300	9 000
Hair emulsion	7 000	-
Liquid paraffin	10 000	-
Mercurichrome	1 500	5 000
Mixture potassium citrate	3 900	10 000
Spirit methylated	5 200	-
Sulphur ointment	2 200	4 200
Tincture of iodine	7 000	3 000
White soft paraffin	500	-
Zinc oxide ointment	200	3 300

B. Laboratory of the Al-Gamhouria Hospital

During his stay in Aden the expert also visited the Al-Gamhouria Hospital and its laboratory. The laboratory is situated in a normal room and has no special equipment. Some ointments and liquids are made according to pharmacopoeia requirements in small amounts, using laboratory mortars and glassware, and sometimes are sent to other hospitals.

Taking into account the above-mentioned conditions, the improvement of quality and the advancement of existing technology of locally manufactured preparations was not feasible and, therefore, the stress was laid upon the organisation of a new manufacturing unit.

III. EVALUATION OF EXISTING REPORTS ON THE PHARMACEUTICAL INDUSTRY IN DEMOCRATIC YEMEN

A. Report made by specialists from Egypt

The report contained data connected with the specifications of medicinal and perfumery plants growing in abundance, which could be eventually exploited either locally or internationally. An Egyptian survey shows that there are about 190 different kinds of plants in Democratic Yemen, growing naturally in the valleys, deserts, and mountains. Some of these plants, having unknown contents, are used for the traditional treatment by Bedouins and other residents. Many are available in abundance in vast areas, other are scarce. Among these plants, there are a few which are used at the moment in the pharmaceutical industry by the international companies and could be natural sources for preparing ready made medicines; for example, Cassia senna or Datura stramonium. Samples of these plants were sent by the NDC last year to a laboratory in order to examine and determine the effective contents. The NDC received the results of chemical investigations and other information concerning the possibility of exportation of these vegetable raw materials.

The NDC has, at present, no special equipment, laboratory, or skilled personnel that would allow for such research. After the completion of the pharmaceutical industry and laboratory in Democratic Yemen the development of these raw materials for exportation will first be possible.

B. Report made by specialists from Hungary

The report contained data connected with general economic and social trends, drug consumption, as well as the trends in the development of industries in Democratic Yemen. The Hungarian specialists also presented their report suggestions concerning the establishment of the pharmaceutical industry. The following 14 phases of its development, covering a period of about 10-15 years, was included:

Phase	
1-2	Finishing (packing) of 10-20 million tablets/year
3-4	Formulation of 5-10 million tablets (2 items)/year
5-6	Expansion of existing units to the total capacity of 50 million tablets/year
7	Liquids department for 2 million flasks
8-10	Coated tablets department for 5-10 million tablets/year and powders, as well as effervescent granules, for 3 million filled flasks

Phase	
11	Ointment department
12-14	Ampoule filled with distilled water, infusions, vitamins and antibiotics - 2 million ampoules/year

According to the suggestions of Hungarian experts, the locally-manufactured products during that period of time will have to be made in co-operation with companies, utilizing their know-how, technical experience, as well as their materials. At present, there is no further information concerning above-mentioned project.

C. Analysis of the report of the Hungarian experts

In the expert's opinion, the local market is too small for establishing an expanded pharmaceutical industry that would manufacture a great number of tablets and injections in the future. The export possibilities are uncertain and most will probably be highly limited by keen international competition. Therefore, it will be very difficult to achieve the minimum economic size. It should also be taken into consideration that, at present, the related glass, chemical and engineering industries are not developed and pharmaceutical manufacturing units will be highly dependent upon imports. Taking into account the above-mentioned problems, a larger pharmaceutical project (many kinds of preparations) even in about 5-10 years will be very risky.

The expert had been involved with similar projects in a few of the larger countries. Some of these projects failed on account of the considerably high capital investments that had to be made for the equipment needed for installation of the pharmaceutical fabrication facilities, as well as for the highly qualified personnel needed to operate the large production units. The main consideration is that of capacity versus profitableness. A unit large enough to cover the demand of the country would be much too expensive to operate and maintain.

Because of the shortage of domestically produced glass and the minimally developed engineering industry, the pharmaceutical manufacturing unit will have to be almost "self-sufficient". Democratic Yemen will, however, still be dependent upon imports such as chemicals, raw materials, processing vessels, and packages.

The pharmaceutical industry in Democratic Yemen should be established as a small-scale manufacturing unit slowly and carefully, taking into consideration the concurrent development of the other related industries. The proposed small manufacturing unit will certainly not be able to supply the entire nation with all necessary medicaments. The unit will, however, allow for the production of a few highly demanded products therefore partially eliminating the massive importation needs.

As far as the problem of profitableness of such a small manufacturing unit is concerned, the expert stressed that it would be economic only if one million tablets a month were produced and sold. The manufacturing of drugs within Democratic Yemen and the feasibility of progressive manufacturing operations will depend upon a multiplicity of factors leading to viable marketing operations. During the first years, the manufacturing of some liquids, ointments and a maximum of two items in tablets will be possible. Aspirin, or other single items, may not be able to be produced in a volume sufficient to justify an economic manufacturing operation.

It must be remembered at all times that a small production volume results in higher costs and inflated product prices. During the first years of production a special endowment and rate of import allocation will have to be made to support this developing pharmaceutical unit. The economic advantages to domestic production of medicines will be highly dependent upon the initial cost of imported materials and ready-made products.

According to suggestions from Hungarian experts, it might be possible, as a first step, for the NDC to import some items (for example aspirin tablets) in bulk rather than in packages and to wrap them in suitable packages locally, printing the name, form etc., as the information appears on imported packages. For these purposes, the agreement of producers would be necessary, and repacking would have to be made by special personnel in special premises equipped with a dehumidifier, because the tablets would otherwise deteriorate quickly under Democratic Yemen's climatic conditions. An expensive strip packing machine would have to be imported. It is known, however, that the producers can usually agree neither to the utilization of their original packages for legal reasons, nor to the utilization of their brand name due to trade-mark reasons; and therefore, these problems too would have to be solved. In the opinion of the expert, this arrangement would not be profitable. The NDC could purchase tablets in larger and more suitable packages for hospitals and pharmacies directly from selected producers.

Hungarian experts also suggested the production of liquids as a seventh step, and ointments as an eleventh step. This means that it would take at least 10 years before their production could begin. However, the expert felt that refilling and manufacturing some liquids, pastes and ointments, which could be used in larger amounts within the country, should be taken into consideration as the first stage. Such production, excluding eye ointments, does not require more complicated machinery or the special training of personnel, but needs only to be well organized.

IV. THE NEW NDC MANUFACTURING UNIT (NATIONAL DISPENSARY CHEMIST AT KHORMAKSAR)

A. Premises

The manufacturing unit will be housed in new premises at Khormaksar (about 150 m^2). In the expert's opinion, the premises would be adequate for the establishment of a small manufacturing unit after suitable restoration and large enough for the necessary equipment which will have to be contained. During a conversation with the Director of the Pharmaceutical Department of the Ministry of Health, the expert was informed that in about three years the necessary steps would be taken in order to erect a new building for the establishment of a larger manufacturing unit. In the expert's opinion, there is adequate area at Khormaksar, close to the existing premises, for the erection of an additional one level building covering about 150 m^2. It would be very practical if the NDC had that area at its disposal.

The existing premises, after suitable restoration, would be large enough for the installation of machinery for tablet production, but there would only be a very small place for raw material supply and the packing area. The tablet making area must meet special requirements, especially taking into account climatic conditions in Democratic Yemen. Tablets should be formulated at maximum 55 per cent relative humidity, and, therefore, that area should be suitably isolated and equipped with an efficient dehumidifier. The equipment for making liquids and ointments should be at present placed in the existing premises, but the necessary steps should in any case be taken as soon as possible to erect the special one level building for production and packing of tablets and storage of raw materials. The future addition of the first floor of the building for the quality control laboratory will be possible with minimum additional investments. As far as the special equipment for the manufacturing unit is concerned, during the first weeks of the present mission letters were sent to some manufacturers of chemical and pharmaceutical machinery (including, Manesty Machinery Ltd (United Kingdom), Cadmach Machinery Company and Sunderji Kalidas Manufacturing (India)), in order to determine the actual prices, technical details and delivery periods. On the basis of this correspondence as well as other materials already on hand, the list of machinery was prepared. It was taken into consideration that the machinery listed below must be useful

both for laboratory work and smaller charges in the actual manufacturing process, as well as for training of personnel in the basic methods of producing liquids, ointments and tablets, including granulates for tabletting under industrial conditions. The same machines will be useful in the future for manufacturing larger amounts of preparations in a larger scale when the manufacturing unit is sufficiently developed.

B. Equipment for the liquids and ointments department

Water still (Cadmach, Barnstead Type)

Made of stainless steel. Output: 20 l/h
14 kW, 440 V, 50 Hz

Tank: 1,000-litre capacity with stirrer

Made of stainless steel.

Cadmach colloid mill (Model CMC M5)

This machine is useful in emulsifying, homogenizing, dispersing and extracting. It is suitable for small, medium, or large scale production. Output: 150-1,500 kg Motor: 5 hp, 2,850 rev/min; 440 V, 50 Hz, 3 phase. Floor space: 43 x 76 cm

Cadmach gravity-operated filling machine

The machine is simple to operate and designed for the rapid and clean filling of free flowing liquids into any container. Containers may have a small or large opening and a capacity from 15 millilitres to 5 litres. No electricity or other power is required (a very desirable feature in filling flammable liquids). The tank incorporates a flow-control supply valve which maintains a constant level of liquids in the tank over the filling valve to ensure accurate filling. The output depends upon the viscosity and volume of the liquids to be filled, but it can be generalized that a maximum of 1,800 to 2,000 containers of 100 ml, and 900 to 1,000 containers of 450 ml can be filled per hour. Floor space: 46 x 93 cm.

Cadmach triple-roller mill type CTR-100 HS

The machine is useful for the grinding of ointments, both for laboratory work and smaller charges, in the actual manufacturing process.

Output: 35 kg
Roller diameter: 110 mm
Roller length: 230 mm
Motor: 2 hp, 1440 rev/min, 3 phase, 440 V, 50 Hz
Floor space: 114 x 64 cm (height: 137 cm)

Piston-type filling machine for tubes

10-l capacity. Manually operated.

Tube-closing machine

Manually operated. Output: 600-300 tuber/per hour

Sterilizing oven (Gallenhamp Cataque)

Useful for the sterilization of heat-resistant powdered medical substances as well as oils, fats and waxes in containers. Dimensions: internal, 46 x 61 x 46 cms, overall, 112 x 79 x 81 cm. Maximum temperature: 250°C. 220/240 V, 50 Hz.

C. Equipment for tablet department

Single-stroke tabletting machine (Cadmach)

The machine is an electrically driven press for tablets up to a maximum of 18 mm in diameter. The speed of the machine is 45 to 60 tablets per minute with single punch fitted. It can take up multi-punches as per the diameter of the punches.

Maximum tablet diameter: 13 mm
Depth fill adjustable: 15 mm
Maximum operating pressure: up to 5 tons
Output: 45-60 tablets per minute
Motor: 1 hp, 1,440 rev/min; 440 V, 3 phase, 50 Hz
Height: 155 cm ; floor space: 46 x 74 cm

The following table gives an approximate indication of the maximum number of round punches that can be incorporated in one die

Diameter of the tablets (mm)	Punches per die
3	7
5	5
6	4
7-8	3
9-12	2
13-18	1

Cadmach mixer

Useful for the mixing of dry or damp materials.

Capacity: 50 kg

Speed of stirrer: 32 rev/min

Motor: 3 hp, 1440 rev/min; 440 V, 3 phase, 50 Hz

Floor space: 175 x 78 cm

Height: 105 cm

Cadmach granulator

Suitable for granulating damp and dry materials. Hopper, the granulating blades both for dry and wet materials, sieves, and all other parts which come in contact with the material to be granulated, are made of stainless steel.

Hopper steel: 20 cm

Motor: 1 hp, 1,440 rev/min; 440 V, 3 phase, 50 Hz

Floor space: 46 x 30 cm

Height: 145 cm

Cadmach drying oven

Electrically heated and thermostatically controlled hot-air oven fitted with a timer to facilitate day and night operation.

Aluminium trays: 30 x 40 x 3.5 cm

Temperature indicator: Dial type, 0°–100°C with thermostatic control 5°C

Temperature span: 30°–100°C

Electric heaters: 3 heaters each of 2 kW

Exhaust fan motor: 1 hp; 440 v, 3 phases, 50 Hz

Floor space: 192 x 100 cm

Tablet-hardness tester

The instrument records on a dial indicator the hardness; reading with accuracy from plus or minus 0.5 kg to 20 kg.

One single punch tabletting machine, simple in construction and inexpensive, will be capable of producing about 60 tablets per minute, i.e., about 3 million tablets per year, working eight hours per day, for 300 working days a year. This will produce a sufficient amount of one or two items in tablets during the coming years. The training of personnel and time needed for tablet testing must be calculated into the production quantity. Hopefully it will be possible to totally eliminate the importation of preparations that will be locally produced.

During the first years, large amounts of raw materials will have to be imported. They must then be tested and stored under suitable conditions. In order to produce acetylsalicylic acid tablets, for example, the following materials will have to be imported: 1,000-2,000 kg of acetylsalicylic acid, starch and talc. The anticipated production quantity for the first few years is 2-4 million tablets per year. Having suitable premises and skilled production personnel, the NDC will then be able to purchase a second single punch tabletting machine. However, larger production will depend upon the technical aptitude of the manufacturing unit. Two single-punch tabletting machines would be capable of producing about 18 million tablets per year (8 hours per day for 300 working days). Working, however, in two or three shifts, the two machines would be capable of producing up to about 50 million tablets per year. Taking into consideration the necessity of periodical maintenance and conservation and repair of these machines, it would be safer and more convenient to have two such machines instead of one. Refer to annex I for a price list of machinery and equipment and to annex II for the proposed scheme for the national dispensery chemist.

V. QUALITY CONTROL LABORATORY

The establishment of a quality control laboratory will be necessary to carry out the following functions:

(a) Testing of all imported raw materials for locally manufactured preparations, especially for manufacturing tablets, in order to have a minimum of production troubles;

(b) Testing of manufactured preparations, especially tablets, according to pharmacopoeia requirements, including making a determination of disintegration time, mechanical strength etc.;

(c) Testing of some imported preparations after a determined storage time, in order to test their stability during the storage-life declared by producers.

At present, the premises NDC (two rooms about 70 m^2, at Crater) will be adequate for the establishment of the laboratory intended for chemical analysis. It must, however, be furnished with the necessary equipment. There is one smaller room which should be intended for special research and development involving the use of toxic or inflammable organic solvents and other toxic or corrosive chemicals. It must be furnished with an efficient fume cupboard that practically eliminates the hazards of fire, poisoning and corrosion.

Actual prices of equipment for the quality control laboratory based on UNIDO information

Analytical equipment (present)	Cost (dollars)
Water still or demineralizer (3 kW; 220 V; made of stainless steel; output: 3,3-4,5 l/h)	600
Laboratory pH meter	1 500
Laboratory analytical balance (optical scale; 200 g capacity; 1.0 mg sensitivity)	1 000
Melting-point apparatus: (220 V; temperatures up to 350°C)	
+ 3 thermometers, 0°C-150°C	
3 thermometers, 140°C-190°C	
3 thermometers, 0°C-360°C	
10 packs x 100 capillary tubes	300
Polarimeter with lamp, angular and sugar scales, and three tubes	900

Analytical equipment (present)	Cost (dollars)
Thin-layer chromatography apparatus completely outfitted for carrying out experiments	300
Water bath (25 cm diameter)	135
Refrigerator (143 l capacity)	800
Oven, 200°C (220/240 V, power rating: maximum 750 W)	400
2 Dessicators	150
Analytical equipment (future)	
Spectrophotometer	2 500
Refractometer	800
Centrifuge	400
Hot plate	200
Vacuum pump	1 500

VI. PROGRAMME FOR TECHNICIAN TRAINING

The health education and training in Democratic Yemen comes under the jurisdiction of the Ministry of Health and the domain of the World Health Organization (WHO).

At present, there are two courses of study: doctors, at the Aden University; and pharmacists and technicians at the Institute of Health Manpower Development, Aden. There are no faculties of chemistry and pharmacy in Democratic Yemen. The pharmacists and technicians have academic training in pharmacognosy, pharmacology, pharmaceutical chemistry and pharmacy. The present local education, however, does not produce specialized pharmaceutical analysts or technologists.

During discussions at the Ministry of Health and the NDC. it was agreed that the programme for the training of technicians should be intended to cater to approximately six selected persons only. Upon successful completion of this programme all would be employed at the quality control laboratory and manufacturing unit.

A. Quality control laboratory personnel

At the quality control laboratory at least one pharmacist skilled in chemical and pharmaceutical analysis should be employed. He will be responsible for the results of all investigations undertaken, and for the training of technicians. All necessary methods for the testing of drugs and raw materials are given in the pharmacopoeia, or in special norms. These norms should be used without exception. However, because the testing must be accurate it is necessary to have well-trained technicians.

As a first step, the tablet department of the manufacturing unit should start on the production of acetylsalicylic acid tablets. Technicians must be trained to analyse imported aspirin and also to test the raw materials which will be used in aspirin production.

For these purposes only, taking into account the technological requirements for acetylsalicylic acid, starch and talc, the personnel should be trained in following methods:

Determination of free salicylic acid

Determination of the melting point, chlorides, sulphates, iron and calcium

Determination of ash, sulphated ash and heavy metals

Determination of solubility, acidity or alkalinity

Determination of loss on drying or on ignition (talc)

Determination of acid soluble or water soluble matters

Determination of specific rotation

The personnel of the quality control laboratory should also be trained in such commonly used and necessary methods as:

Colorimetric and potentiometric determination of pH

Titration and preparation of standard solutions as well as buffer solutions (and checking of volumetric vessels)

Determination of the density of liquids, solid fats and waxes

Determination of acid number, iodine number and saponification number

Quantitative determination of alcohol in pharmaceuticals

Thin layer chromatography

Special methods, e.g.: colorimetry, spectrophotometry, fluorometry or viscosimetry

As far as the last point is concerned, during a conversation with the WHO lecturer for the pharmacist technicians at the Institute of Health Manpower Development, and the research manager of the NDC it was agreed that, if necessary, the instruments at the Institute's disposal could be used for analysis as well as for the training of the quality control laboratory personnel.

It is understood that the training of technicians in some of these analytical methods will be dependent upon the needs and possibilities of the laboratory and undertaken step by step.

B. Manufacturing unit personnel

The technicians employed at the manufacturing unit should know the basic theoretical information concerning methods of sterilization under laboratory and industrial conditions, as well as technological methods of manufacturing liquids, paste, ointments, and tablets with the use of special large scale equipment (pharmaceutical technology). A special emphasis should be put upon the methods of manufacturing tablets, including technical requirements (machinery), as well as the methods of investigation of ready-made products (hardness, time of disintegration, friability value, mechanical strength, and all pharmacopoeia requirements).

VII. RECOMMENDATIONS

1. A pharmaceutical industry should be established in Democratic Yemen. This will prove to be financially advantageous to the country and fulfill the urgent needs of hospitals and pharmacies.

2. The first step in the organization of the pharmaceutical industry should be the establishment of government regulations controlling the production, quality, and distribution of medicaments. A new food and drug administration should be constituted encompassing the following topics:

(a) Drugs: approval and registration of drugs; free sale certificate with price control; quality speculations and control of pharmaceuticals; information concerning the distribution, dispensing, and prescription of various drugs; and the advertising of drugs;

(b) Manufacturing: special requirements and an industrial licence for the premises, manufacturing licence including quality specifications and price controls for each preparation;

(c) Trade: special requirements should be established and a licence to buy, stock, and sell pharmaceuticals.

3. The pharmaceutical industry may be organized in the first few years as a small-scale manufacturing unit divided into a liquid and ointments department and a tablet department.

4. The manufacturing unit should start with the production of some selected preparations in a semi-technical scale. The first phase should be the refilling and manufacturing of liquids, pastes and ointments. The second phase should be the production of one or two tablet items.

5. Before, or at least simultaneously with the manufacturing unit, a quality control laboratory should be established.

6. The realization of this pharmaceutical project will be dependent upon efficient managerial guidance and a skilled technical staff, in conjunction with technical and commercial organization. Therefore, it is recommended that specially selected personnel (2 pharmacists and 6 technicians) should be assigned. They will be divided into two teams, the analytical team and the technological team, and will be responsible for the organization of the quality control laboratory and manufacturing unit, and, in the future, will be the backbone of manpower of the pharmaceutical industry in Democratic Yemen.

The above-mentioned group of pharmacists and technicians should receive information on general industrial problems, and especially the problems of the pharmaceutical industry, on systematic work organization, administrative and financial management, marketing, quality control, and safety. Such information should be received at special courses organized by the Ministry of Industry. The people must learn how to prepare for production and to carry out the different operations with the effective utilization of raw materials, machines, and manpower.

Both analytical and technological teams should receive a training conducted according to the special needs in Democratic Yemen. Therefore, it is recommended that they get acquainted with the basic theoretical information concerning pharmaceutical technology, methods of sterilization as well as methods of manufacturing liquids, ointments and tablets under industrial conditions. Both teams should be assigned as soon as possible in order to become familiar with the procedures. A special stress should be placed on the pharmacopoeia requirements as well as all necessary analytical methods which the quality of produced preparations will be dependent upon.

A. Analytical team: 1 pharmacist and 2 technicians

Recommended responsibilities and functions

1. To supervise the preparation of the premises for the quality control laboratory.

2. To obtain equipment listed in chapter V as well as needed chemicals and laboratory glassware.

3. To determine some pharmaceutical preparations according to the Pharmacopoeia requirements, in order to get acquainted with the methods which will have to be used in the future for the testing of manufactured preparations.

4. To be responsible for all investigations carried out and tests where the quality of preparations will be dependent upon.

5. To closely co-operate with the technological team.

B. Technological team: 1 pharmacist and 4 technicians

Recommended responsibilities and functions

1. To supervise the restoration and suitable preparation of the premises for the manufacturing unit according to the scheme in annex II.

2. To supervise the importation and installation of machinery and special equipment for making liquids, ointments and tablets as listed in chapter IV, sections B and C.

3. To prepare the list of raw materials and chemicals needed which will have to be imported, and to prepare the premises for storage under suitable conditions.

4. To closely co-operate with the analytical team.

7. Many developing countries have already built up a considerable amount of experience in the formulation and packaging of drugs and in the production of equipment for this industry. Egypt, India, Iraq and Parkistan, together with other developing countries, should be considered for help in establishing such a programme for the training of Democratic Yemen personnel.

In the case of such co-operation (under technical co-operation among developing countries (TCDC)), the analytical and technological teams should spend a minimum of three to four months at the co-operating pharmaceutical company in order to get acquainted with the technology, machinery, and all analytical requirements, and then to transfer them to the manufacturing unit in Democratic Yemen.

All divisions of the pharmaceutical industry (quality control laboratory, the manufacturing unit, and the personnel training section) will then be interdependent upon each other.

8. After all needed raw materials and machinery are available the expert suggests that the production of liquids and ointments using special equipment with a larger output capacity be initiated. The following medicinal products were determined to be the most important preparations to be manufactured in larger amounts:

Liquids	Ointments
Calamine lotion	Benzoic acid ointment
Castor oil	Salicyl acid ointment
Liquid paraffin	Sulphur ointment
Paracetamol mixtures	Zinc ointment

When all personnel are trained and necessary starting materials imported, the manufacturing unit could gradually begin to produce some of the following preparations. The end result would be to supply hospitals and pharmacies with

sufficient quantities so that the importing of these medicaments would no longer be necessary. All manufacturing should be undertaken in conjunction with the evaluated needs of the hospitals and pharmacies. The preparations to be considered for production are:

Acetic acid solution
Aluminium acetate solution
Ammoniated mercury, coal tar, and salicylic acid ointment
Ammoniated mercury and coal tar ointment
Benzocaine ointment compound
Benzoic acid ointment, compound
Benzoic acid solution
Benzyl benzoate
Calamine and coal tar ointment
Calamine lotion
Calamine ointment
Calcium hydroxide solution
Castor oil
Capsicum ointment
Cetrimide solution
Chlortetracycline skin ointment
Coal tar and salicylic acid ointment
Coal tar and zinc ointment
Codeine phosphate syrup
Ephedrine elixir
Gentian violet
Glycerine borax
Hamamelis ointment
Hydrocortisone and elioquinol ointment
Isoniazid elixir
Liquid paraffin
Mercurichrome
Methyl salicylate ointment
Mixture potassium citrate
Paracetamol elixir, paediatric
Piperazine citrate elixir
Salicylic acid and sulphur ointment
Salicylic acid ointment
Simple ointment
Spirit, methylated

Sulphur ointment
Tincture of iodine
Zinc ointment

9. A major problem to be confronted is that of obtaining an ample supply of bottles, jars, and tubes for packaging manufactured goods. Importing such items would be highly unprofitable. The expert suggested the introduction of a glass recycling plan. All glass bottles and jars would carry a deposit and this would encourage people to return all glass products.

10. The production of tablets will be a more difficult problem and, therefore, should be undertaken and organized as the second phase. Because of the shortage of skilled personnel at present, only a small department for tablet production should be established. For such a venture, starting from machinery and raw materials and ending in the training of manpower, special requirements will be needed. Tablet production, even one or two items, will not be possible unless the NDC has its own efficient quality control laboratory. Every batch of tablets produced will have to be analysed before being sent to hospitals or pharmacies, meet all the pharmaceopoeia requirements, and have suitable hardness, time of disintegration and content of active compounds. For these purposes, trained and skilled personnel as well as special equipment will be needed. Production troubles take place even in well established pharmaceutical manufacturies. A small mistake or inacuracy in the weighing or the mixing of ingredients in the preparation of tablets or granulate for tabletting, or insufficient drying may sometimes lead to the change of colour and deterioration of tablets. Taking into account the manufacturing of many kilograms of tablets, miscalculations would result in a great waste of raw materials and money. Therefore, every completed batch of tablets produced as well as the base ingredients will have to be laboratory investigated.

11. As far as the manufacturing of tablets is concerned, it was agreed upon that following items had to be given preference as the most needed preparations:

Acetylsalicylic acid tablets
Paracetamol tablets
Chloroquine sulphate tablets

12. It is suggested that a UNIDO expert be available in Democratic Yemen for a minimum of 12 months, even if pharmacists and technicians have been trained abroad under technical co-operation among developing countries. The organization of manufacturing liquids, ointments and tablets, as well as the organization of quality control and marketing operations, should be carried out with UNIDO expert assistance. This will be necessary for the efficient organization of a small scale pharmaceutical industry in Democratic Yemen within a reasonable time period.

13. The importation of drugs must be organized in an efficient manner. Ordering, storage and distribution controls must be initiated in order to assure an economic operation. The following suggestions should be implemented:

(a) On the basis of the list of imported preparations prepared during the present mission, a special list of drugs should be established. All drugs should be listed alphabetically, according to the generic names of medicaments;

(b) Sources of importation for medicinal preparations should be selected and reduced to a maximum of two to three, taking into account the quality and prices. Importation of the drugs from many sources and under many trade names leads to confusion;

(c) Minimally twice a year the pharmacies should prepare and send to the NDC lists of pharmaceuticals needed as well as preparations which have been sold within that period of time. On the basis of these orders, the statistical calculations concerning the demand of individual preparations for outdoor treatment will be facilitated;

(d) In order to facilitate listing and inventory controls all imported preparations should be stored and arranged in order on the shelves at the NDC store alphabetically in groups. The same preparations imported from different sources and under different trade names should also be grouped together on one shelf.

Annex I

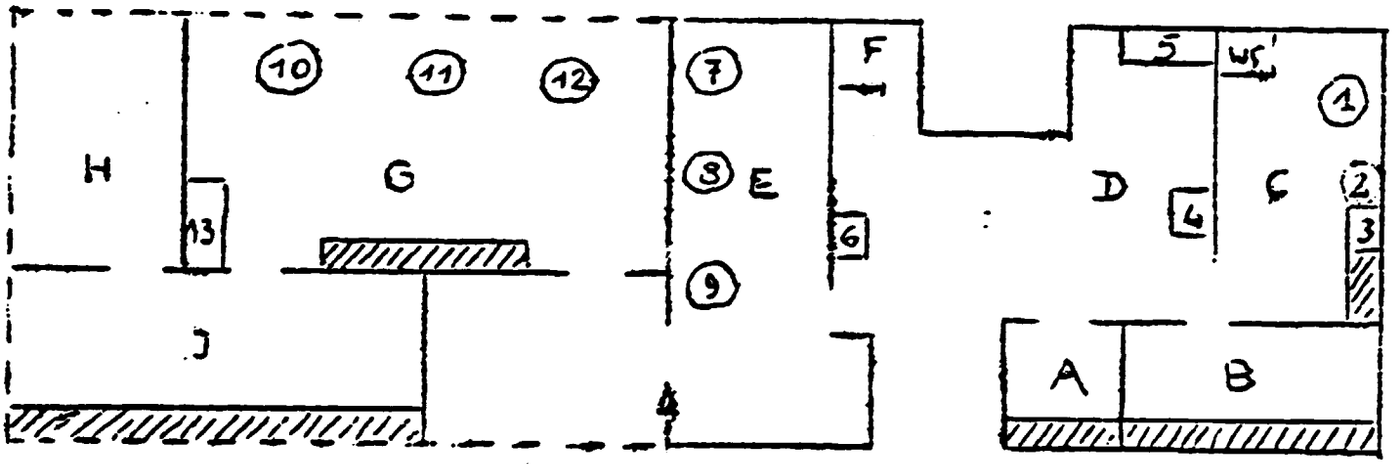
PRICE LIST OF MACHINERY AND EQUIPMENT

Production equipment (present)	Dollars
Demineralizer	5,000
Mixing tank, 1,000 l with stirrer	4,500
Filling machine (liquids)	2,500
Triple-roller mill	6,000
50-l electrically heated container for ointments	2,000
Tabletting machine	3,500
Planetary mixer, 50 kg	2,000
Drying oven	5,000
Granulator	6,000
Hardness tester	200
Tube filling and closing machine	5,400
Production equipment (future)	
V-type mixer	4,000
Capsule filling machine	5,000
Distilled water unit	7,000
Ampoule filling machine	4,500
Seitz filter	3,000
Autoclave	2,000
Bottle-washing machine	6,000

Prices are based on a quotation received by UNIDO.

Annex II

SCHEME OF PREMISES OF THE NATIONAL DISPENSARY CHEMIST



Key: Rooms

A	Staff
B	Ointments
C	Ointments
D	Water still
E	Liquids
F	Washing
G	Tablet
H	Raw materials
J	Storage and packing

Equipment

1	Triple-roller mill
2	Tube-filling machine
3	Tube-closing machine
4	Sterilizing oven
5	Water still
6	Drying oven for bottles
7	Tank with stirrer
8	Colloid mill
9	Filling machine for bottles
10	Mixer
11	Granulator
12	Tabletting machine
13	Drying oven

Annex III

MATERIAL LEFT WITH THE RESEARCH DEPARTMENT OF THE NATIONAL DRUG COMPANY

1. Methods of sterilization under laboratory and industrial conditions. The following information was included: the use of hot air, saturated steam, and flowing steam; tyndallization; bacterial filtration with tests for sterility and exposure to gaseous ethylene oxide.

2. Tables with the time and temperature needed for the sterilization of: dressing materials; glass and metal objects; heat resistant powdered medical substances; and mineral or vegetable oils, fats, and waxes.

3. Materials concerning the methods of manufacturing ointments (including some methods of their investigations) pastes, liniments, solutions, syrups, elixirs, and emulsions with 55 examples, as well as the quantities of starting materials needed.

4. Materials concerning the methods of manufacturing and testing tablets. Included are 35 examples and full prescriptions for the preparation of many tablets and granulates, as well as special mixtures for grounding, basic coating, colouring, smoothness of a surface and polishing of coated tablets.