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FEASIBILITY STUDIES ON THE DEVELOPMENT OF PHARMACEUTICAL INDUSTRY IN IRAN

BY:

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UNITED NATIONS DEVELOPMENT PROGRAMME, TAO

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DEPARTMENT OF CHEMICALS AND DRUGS

RESEARCH CENTER FOR INDUSTRIAL AND TRADE DEVELOPMENT

MINISTRY OF ECONOMY

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FINAL REPORT

Feasibility Studies on the Development of Pharmaceutical Industry in Iran

By

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United Nations Development Programme, TAO

September, 1967

This report has not been cleared with the Bureau of Technical Assistance Operations of the United Nations which does not therefore necessarily share the views expressed.

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INTRODUCTION

This is the final report covering the consulting assignment which began upon my arrival in Tehran, Iran on October 22, 1966, and terminated in September, 1967, when I left the duty station. The duties of the pharmaceutical advisor as set forth in the job description I received on my arrival in Iran are listed as follows:

The advisor will be expected to assist the Iranian Government in carrying out feasibility studies on the development of basic drug industry with a view to promoting the co-operation of the three RCD countries (Iran, Pakistan, and Turkey) and possibly setting up joint-purpose enterprises in the field. The advisor is also expected to assist the Iranian Government in carrying out the additional research work necessary in the three countries and in preparing the final feasibility study reports.

For carrying out the project, I am attached to the Ministry of Economy of the Iranian Government and worked with my counterpart, Dr. H. Azarbaijani, Pharmaceutical Expert of the Ministry of Economy. With the generous assistance of Dr. Azarbaijani, opportunities have been provided for intimate contact with many aspects of pharmaceutical activity in Iran. I am especially grateful for the assistance of many Iranian government officials who were interested in our efforts. H.E. Dr. A. N. Alikhani, Minister of Economy, H.E. Dr. M. Yeganeh, Vice-Minister of Economy, provided the dynamic leadership and inspiration for carrying out the programme. Dr. J. Vafa, Acting Director, and Eng. K. Iravani, Head of Industrial Evaluation and Preparation of Projects, Industry Section, Research Center for Industrial and Trade Development, Ministry of Economy, were helpful in the implementation of the plans.

CHAPTER I.

PRESENT SITUATION OF DRUG IMPORTATION & CONSUMPTION IN IRAN

Statistics on the annual importation of pharmaceuticals are made according to the information compiled by the Bureau of Statistics, Ministry of Finance. The imported pharmaceuticals include various forms of pharmaceutical preparations as well as bulky basic drugs for domestic pharmaceutical uses. The classification of pharmaceuticals which was developed by the traditional method of custom is somewhat un-unified. Since some of the pharmaceuticals in the list are classified by articles, such as glucose, phenacetin, plasma, and penicillin etc., and some are classified by categories, such as antibiotics, antimalarials, proprietary drugs and non-proprietary drugs etc. Thus it is rather difficult to get a clear picture for the distribution trends of pharmaceuticals in Iran. The new classification of pharmaceuticals are generally based upon therapeutic and end-use breakdown. It is suggested to make statistics hereafter by adopting new classification system.

Now we try to reclassify the annual importation of pharmaceuticals in brief categories, by value and percentage as shown in Table 1.

Table 1 - Annual Importation of Pharmaceuticals, 1964 through 1966

Source: Yearbooks, 1964-1966, Foreign Trade Statistics of Iran, Bureau of Statistics, Ministry of Finance.

Items	1964 (add 000)	1965 (add 000)	1966 (add 000)
1	2	3	4
Proprietary drugs (1)	Rls.1,730,630(59.2%)	Rls.1,851,722(55.0%)	Rls.2,152,612(59.8%)
Non-proprietary drugs (2)	59,157 (2.0%)	47,571 (1.4%)	41,752 (1.2%)

1	2	3	4
Antibiotics	649,506(22.2%)	963,584(28.6%)	918,458(25.5%)
Excipients (Starch, olive oil, peanut oil, glycerin, lactose, glucose, talc, petroleum, liquid paraffin and paraffin, etc.) (3)	145,720 (4.9%)	118,085 (3.5%)	73,033 (2.0%)
Solvents (methanol, glycols, acetone, & other solvents (3)	31,134 (1.1%)	44,886 (1.3%)	31,436 (0.9%)
Packing materials (empty ampuls)	-	2,878 (0.1%)	2,264 (0.1%)
Sera & vaccines	19,159 (0.7%)	22,863 (0.7%)	22,991 (0.6%)
Antimalarials, antileprosy drugs, bismuth and arsenic compounds, opium alkaloids, etc.	20,283 (0.7%)	16,168 (0.5%)	43,569 (1.2%)
Milk powder and baby foods	257,056 (8.8%)	263,887 (7.8%)	279,940 (7.8%)
Basic drugs for domestic manufacturing and therapy	7,308 (0.3%)	34,968 (1.0%)	32,901 (1.0%)
Total	2,919,953	3,366,612	3,598,956

Note: (1) Proprietary drugs consisting of basic drugs and pharmaceutical preparations bearing the proprietary (trade) names.

(2) Non-proprietary drugs consisting of basic drugs and pharmaceutical preparations bearing the non-proprietary (generic) names.

(3) Excipients and solvents used for the pharmaceutical, chemical and other industries.

Table 2 - Importation of Pharmaceuticals by category: 1965

Source: Ministry of Health

Categories	Items
Anesthetics	51
Antihistamines	124
Antibiotics	575
Antibacterials	359
Antimalarials	14
Antineoplastic agents	7
Anthelmintics	45
Autonomic drugs	123
Cardiovascular agents	257
CNS depressants	346
CNS Stimulants	142
Diagnostic agents	30
Enzymes	22
Gastro-intestinal agents	117
Hematological agents	266
Hormones	637
Renal acting and edema-reducing agents	77
Therapeutic nutrients and substitutes	97
Vitamins	339
Others	883
T o t a l	4,451 items

The total importation of pharmaceuticals amounted to ₨. 3,598,956,000 ($ 47,986,000) in 1966. Comparing to the amount of ₨. 2,916,953,000 ($ 38,932,710) in 1964, the import has risen 23.2% in the past three years. From 1964 through 1966, the import of proprietary drugs ranged between

55.0 and 59.8%. And the import of non-proprietary drugs has decreased from 2.0% to 1.2% in the past three years. For antibiotics, the import has reached 22.2% in 1964, increased to 28.6% in 1965, and decreased to 25.5% in 1966. Besides, the import of milk powder and baby foods (infant feedings and dietary supplements) has ranged to a rather higher percentage between 7.8 and 8.8%. Statistics also indicate that the import of excipients and solvents has reached to 6.0 in 1964; 4.8 in 1965 and 2.9% in 1966. Parts of these substances are used for domestic pharmaceutical processing but the rest are mostly used in the chemical, food and other industries.

In 1965, 4,451 items of pharmaceuticals were permitted to import by licensing. We have noticed in Table 2 that there were too much duplications on the items of imports in each category. For instance, there were 637 items for the hormones, 575 items for the antibiotics, 359 items for the antibacterials and 346 items for the CNS depressants. It would save a large amount of foreign exchange, probably attending to 30-40% of the total imports, if the restriction of the imports of those unnecessary proprietary drugs is effected.

There are no available data concerning the annual consumption of drugs with market prices in Iran. Just upon the wholesale prices, the estimate of the consumption of drugs has been made between Rls. 3,520,000,000 and 3,600,000,000 in 1966.

CHAPTER II.

PHARMACEUTICAL INDUSTRY IN IRAN

The development of pharmaceutical industry in Iran has gone through several distinct phases. Few pharmaceutical plants has been erected thirty years ago. Around ten years from now, more plants were being started. There were about 80% of plants being set up during the period of Second Plan (1955-1966), and about 10% in the period of Third Plan (1960-1966). By 1966, the pharmaceutical plants and laboratories (small-scale plants) reached 65, of which there are about seven plants operating the pharmaceutical production in more large scale with proper technical personnel and adequate machineries and facilities. At least, five domestic plants have allied themselves with foreign firms. These operative ventures will provide many well-known foreign brands to the medical profession and public throughout Iran. Most laboratories produce limited varieties of preparations. Many of their products have not undergone quality tests prior to the sales.

Table 3 Pharmaceutical Plants in Iran

(A) Domestic plants having allied with foreign firms

	Domestic plants	Foreign firms
1.	Daroupakhsh	Imperial Chemical Industries (ICI), UK
		Allen-Hembrius, UK
		Glaxo, UK
		Sharp and Dohme, USA

2.	Tolidaru	Maxon, USA Alkan, USA Vicks, USA Garter Vala, USA Decetine, Germany Baystroff, Germany Phillip Dhar, Holland
3.	Baxter	Baxter, USA
4.	Tehran-Chimie	Grunental, Germany Boringer, Germany
5.	Pars Industrial Co.	Boots, UK

(B) Domestic plants and laboratories

1. Vira	6. Faria	11. Darowgar	16. Wella	21. Wandom
2. Gol	7. Macks	12. Gramy	17. Max	22. Nozak
3. Mycine	8. Park	13. Rash	18. Biochemy	23. Nazin
4. Total	9. Faz	14. Mina	19. Orogal	24. Rosa
5. Abidi	10. Rogeh	15. Ramin	20. Labrano	25. Rita,etc.

(C) Operating Foreign Plants

1.	Lepetit, Italy	With Iranian capital
2.	Bayer-Pharma, Germany	Without Iranian capital

(D) Foreign plants will be erected in near future

1. Squibb, USA
2. Park-Davis, USA
3. Upjohn, USA
4. Pfizer, USA
5. American Cyanamid (Lederle), USA
6. Organon, Holland

Table 4 **Analysis of Some Major Domestic Plants, 1965**

Source: Pharmaceutical Section, Research Center for Industrial and Trade Development, Ministry of Economy

Pharmaceutical plants	Total assets	Total Sales	Scope of Manufacture
Daroupakhsh	Rls.768,000,000	Rls.135,000,000	Injections & other pharmaceutical preparations
Tolidaru	111,000,000	90,000,000	Injections (including repacking of antibiotics), tablets, ointments, liquids & cosmetics, etc.
Lepetit	78,000,000	60,000,000	Tablets, injections, ointments, liquids, etc.
Vira	35,000,000	11,000,000	Various pharm. preparations excluding injections.
Baxter	33,233,000	59,713,000	Injections
Macks	13,000,000	6,000,000	Various pharm. preparations excluding injections.
Mycine	10,000,000	11,000,000	Tablets, ointments and liquids, etc.
Faria	10,000,000	3,000,000	Various pharm. preparations excluding injections.
Park	9,000,000	10,800,000	Various pharm. preparations excluding injections.
Gol	3,000,000	5,230,000	Galenical preparations
Total	Rls. 1,070,233,000	391,743,000	

Among domestic pharmaceutical plants, Daroupakhsh, the biggest one, has its total assets of Rs. 768 million, the next, Tolidaru, Rs. 111 million. Vira and Baxter has its total assets of Rs. 35 million and 33 million respectively. Macks, Mycine, and Faria has its total assets between Rs. 10-13 million. Most laboratories have their total assets of less than Rs. 10 million.

Ten major domestic plants had total assets of nearly Rs. 1,070 million and total sales of Rs. 392 million in 1965. We have noticed that the total sales of some plants as Tolidaru, Baxter, Mycine, Park, and Gol were considerably high but that of the majority were relatively low.

At the present time, the domestic plants produce various items of pharmaceutical preparations but not for basic drugs. The existing foreign plants (some with less than 30% Iranian capital) are all pharmaceutical processing plants. Those Foreign plants which will be erected in near future will also be the processing plants, and they are reluctant to go into the manufacture of basic drugs in Iran.

From November, 1966 to January, 1967, I, accompanied by Dr. Azarbaijani, Technical Expert of Ministry of Economy have made a pharmaceutical plant survey to nine representative plants and one institute in the district of Tehran.

Several large plants affiliated with foreign firms are capable of producing not only standard drug items but also antibiotics (repacking) and sterile preparations. Among those small-scale plants (laboratories), their products are not undergone strict rules of quality control. Because of importance in medicine and the potential danger to public health, the greatest precautions should be taken to control the quality, potency, sterility and therapeutic efficacy of domestic drugs.

During the recent years, while the domestic pharmaceutical industry expanded in numbers of plants and potential output, no much reduction in the cost of production or improvement in the quality of drugs was attained. Most physicians and the public still not trust to the domestic drugs. That is why the domestic drugs are not competitive with imported foreign drugs. To rectify this situation, it advocates taking the following steps:

1. To modernise existing manufacturing facilities and introduce the latest techniques;

2. To convert small and medium size enterprises of uneconomical size into more economical production;

3. Temporary moratorium on the establishment of new small-scale domestic plants and foreign pharmaceutical processing plants should be declared;

4. More large-scale domestic manufacture of pharmaceuticals especially basic drugs should be encouraged under the Government protective policy;

5. Domestic manufactured drugs should meet required standards of quality. Strict quality control inspection of all pharmaceuticals plants should be established;

6. Importation of foreign proprietary drugs (pharmaceutical preparations) should be reduced to a certain extent from now on year by year without depriving the medical profession of essential life-saving drugs;

7. A modern drug control law should be enacted with provision for regulating the manufacture, distribution, and sale of drugs.

It is noteworthy that certain packing materials are not available in Iran. High quality glass ampuls, vials (neutral, hard glass), bottles, gelatin capsules, plastic caps and seals are not being produced until present time. Establishment of these auxiliary plants is very helpful for the development of pharmaceutical industry, and may be carried out under the co-operation of pharmaceutical plants.

An academic institute, Pasteur Institute, Teheran, a branch of Pasteur Institute of Paris, provides a certain amounts of sera and vaccines for human uses. Another academic institute, Razi Institute (Institut Razi d'Etat des Serums et Vaccins) of the Ministry of Agriculture which was established thirty five years ago in Hessarak, North of Teheran, also produces a certain amounts of sera and vaccines for human and veterinary uses. For meeting the increasing demands of biological products in this country, it will be wise that the Iranian Government give to Razi Institute more financial supports for encouraging its increasing production on those anti-infective agents against human and animal diseases. The importation of sera and vaccines amounted nearly Rls. 23 million in 1966 (cf. Table 1). It may be partly substituted by the domestic products.

A central drug control laboratory has been established in 1966 under the auspices of Ministry of Health. This laboratory is not only responsible for the control of medical supplies, but also for their standardization. The Director, has made an effort for carrying the responsibility. In the laboratory, they

are working under great handicaps of lacking suitable working space, adequate equipment and sufficient technical personnel. Drug control laboratory work was significantly encouraged by the UN-WHO-sponsored program of Dr. H. Sarbart. Under his guidance, the drug assay works were carried out more efficiently at the beginning period of the laboratory. The central drug control laboratory should be reinforced for carrying its responsibility to examine and test different batches of imported and domestic drugs.

As to the standards of pharmaceuticals, national pharmacopoeia is a collection of well-recognized basic drugs and formulas with given standards, methods of preparation, test and assay etc., usually served as a guide book for drugs in medicine and pharmacy. The National Iranian Pharmacopoeia Committee should be organized under the auspices of Governments in preparing and issuing the first edition of Iranian Pharmacopoeia as soon as possible.

In the medical profession, there is now a trend that most physicians prescribe proprietary drugs (new drugs or preparations of multiple-components bearing trade names). Only a very low percentage of prescriptions are needed for compounding in the pharmacies. The over use of proprietary drugs resulted the higher costs of medicament charges to the patients. In the infancy of domestic pharmaceutical industry, it is hard to expect the domestic plants producing hundred of specialties. The basic drugs and formulas in the national pharmacopoeia are "Official drugs". The use of official drugs for prescription should be enccuraged.

The Iranian drug industry must create new and expanding markets. A public relations program should be started to establish confidence among the medical profession, the pharmacist, and the public in the quality of domestic manufactured drugs. The pharmaceutical plants should spend more money on their selling affairs in introducing quality products to the medical profession. In advertising and promotion, new marketing methods with more selective method should be adopted.

It is suggested that the Iranian Government provide a fund to establish a national pharmaceutical research institute, or otherwise to ask the collaboration of pharmacy colleges for carrying out the pharmaceutical research works. The research project will cover: (a) basic pharmaceutical research; (b) domestic manufacturing of basic drugs; (c) new drug research; and (d) new pharmaceutical products development, etc. Domestic pharmaceutical plants should allocate a sum to search for new and improved drugs.

There is a desire for first hand knowledge of drug control methods among the Government personnel working in the pharmaceutical administration areas. For this reason, I would recommend that the Ministry of Economy send the national counterpart of my programme to the U.S.A. by the United Nations fellowship grant for a period of one year to study at first hand the regulatory operations including the pharmaceutical factory registration and inspection system etc.

The total importation of pharmaceuticals in Iran reached Rls. 3,598,956,000 (US$ 47,987,080) in 1966. The domestic pharmaceutical production amounted to Rials 157,154,000 in 1963, Rls. 207,675,000 in 1964 and Rials 179,758,000 in 1965, ranging between 6.5 - 8.1% against the imported products, 91.9 - 93.5% in 1963 through 1965.

The processing capacity for pharmaceuticals is slightly short in Iran at the present. Domestic pharmaceutical plants should be encouraged in producing more quality pharmaceuticals, and also bringing their production up to the full capacity. It is recommended that four or more larger scale pharmaceutical processing plants, with the capital cost of Rls. 187,500,000 (US$ 2,500,000) for each plant may be planned to set up for meeting the full demands. If the total value of input of those sanctioned processing plants reach an amount of Rls.750,000,000 ($ 10,000,000), the total value of output is expected to be Rls. 750,000,000 - 900,000,000 ($10,000,000 - 12,000,000).

CHAPTER III.

FEASIBILITY STUDIES ON THE ESTABLISHMENT OF SOME BASIC DRUG PLANTS IN IRAN AND OTHER RCD COUNTRIES

Iran, Pakistan and Turkey, the three RCD countries are in little different stages as regards development of the pharmaceutical industry. In all these countries, the pharmaceutical industry started as a processing industry based on imported bulk basic drugs. Some of basic drug manufacturing have been started in recent years.

The extent to which manufacture of basic drugs from primary raw materials is being undertaken has also been dependent on the state of development of chemical industry in these countries. Where the chemical industry itself is in the backward state, it has well-nigh been difficult for the pharmaceutical industry to switch over to basic stages of manufacture. There are disadvantages as the lack of adequate demand, and also the higher costs of imported raw materials which make such manufacture less competitive to the imports.

BASIC DRUG MANUFACTURING

The pharmaceutical industry of basic drug manufacturing can be classified into five main groups:

(1) Antibiotics and other products obtained by fermentation techniques;

(2) Chemical synthetic drugs;

(3) Drugs of vegetable origin;

(4) Drugs of animal origin;

(5) Sera, vaccines and other biological products.

(1) Antibiotics and Other Products Obtained by Fermentation Techniques

In modern therapy, antibiotics are widely employed against infectious diseases. Penicillin is the leading antibiotic, streptomycin and dihydrostreptomycin take second place and the tetracyclines and chloramphenicol third place. Neomycin, bacitracin, polymyxin, erythromycin, fumigallin and tyrothricin are produced on a much smaller scale. The antibiotics comprise a new and very large segment of pharmaceutical industry. It far exceed in economic value, any other single portion of pharmaceutical chemical industry.

The first antibiotic to be produced on a large scale was penicillin. Streptomycin, chloramphenicol and various tetracycline compounds are produced by another genus of micro-organisms, several species of Streptomyces. But chloramphenicol is now produced chiefly by chemical synthetic method.

The raw materials of the antibiotics industry consist of nutrient media required for fermentation. Important among these are sucrose, lactose, glucose, corn steep liquor, fat and oil, and some protein-rich substances, such as soya bean, cotton seed cake, and yeast, etc. The other raw materials are chemicals, solvents required for the extraction and purification. The established starch, glucose, and sugar industry as well as units for the production of some necessary chemicals and solvents are therefore essential to supply the required materials. A start can be made, however, by importing the items which are not locally available in the RCD countries. The condition might be improved in reducing the cost of production until the raw materials required are mostly self-sufficient.

In Iran, the establishment of some plants of antibiotics and other products by fermentation may be under consideration:

Table 5 - Sanctioned Plants of Antibiotics and Other Products by Fermentation

Sanctioned Plants	Annual Productive capacity		Estimated Total Assets
Penicillin plant	Penicillin G Potassium Procaine-Penicillin G Banthazine Penicillin G	20 million mega units or 15,000 kg.	US$ 2,600,000
Tetracycline plant	Chlortetracycline Tetracycline	10,000 kg.	US$ 1,200,000
Streptomycin plant	Streptomycin Dihydrostreptomycin	10,000 kg.	US$ 1,400,000
	Vitamin B_{12}	8 kg.	
Yeast plant	Yeast (medical yeast, yeast extract and vitamin B complex etc.)	5,000 tons	US$ 1,200,000
	Total		US$ 6,400,000

(2) Synthetic Drugs

To provide the required experience and training in the manufacture of synthetic chemical drugs, the establishment of production units starting initially from imported intermediates should be taken up. Basic stages of synthetic drug manufacturing should be introduced subsequently, after the necessary experience has been gained and domestic raw material supplies has been organized.

Some plants of synthetic drugs may be considered to set up in Iran and other RCD countries. Estimated total assets of these plants are shown in the following table:

Table 6 - Estimated Total Assets of Some Pharmaceutical Plants of Synthetic Drugs, Complete with Technical Know-how

Pharmaceutical plants	Annual productive capacity	Estimated total assets	Suggested place for the plant	Remarks
1	2	3	4	5
Chloramphenicol plant	Chloramphenicol and its esters 6,000 kg.	US $ 500,000	Iran	
	30,000 kg.*		Pakistan	Sanctioned project
	19,000 kg.		Turkey	
P-Aminosalicylic acid plant	PAS 40,000 kg.	US $ 300,000	Iran	
	180,000 kg.	US $ 850,000	Any one RCD country	
	PAS/INAH, 25,000 kg.		Pakistan	Sanctioned project
Isoniasid plant	Isoniazid (INAH) 30,000 kg.	US $ 250,000	Any one RCD country	
	PAS/INAH, 25,000		Pakistan	Sanctioned project
Sulfa drugs plant	Sulfa drugs, various 200,000 kg.	US $ 950,000	Iran or any one RCD country	
Ascorbic acid plant	Ascorbic acid (Vit. C) 70,000 kg.	US $ 600,000	Iran or any one RCD country	

1	2	3	4	5
Calciferol plant	Calciferol (Vit.D_2) 100 kg.	US $ 80,000	Iran or other RCD country	
Phenacetin plant	Phenacetin, 50,000 kg.	US $ 240,000	Any one RCD Country	
	8,000 kg.		Pakistan	Sanctioned project
Aminopyrin plant	Aminopyrin 25,000 kg.	US $ 180,000	Iran or any one RCD country	
Barbital plant	Barbitals, 15,000 kg.	US $ 200,000	Any one RCD country	
Meprobamate plant	Meprobamate, 29,000 kg.		Pakistan	Sanctioned project
Acetylsalicylic acid plant	Acetylsalicylic acid, 250,000 kg.) Salicylates, 150,000 kg.)	US $ 250,000	Any one RCD country	
	Acetylsalicylic acid 120,000 kg.		Pakistan	Sanctioned project
	" 240,000 kg.		Turkey	"
Procaine plant	Procaine HCL 10,000 kg. (Penicillin/procaine plant)		Iran	
	50,000 kg.	US $ 410,000	Any one RCD country	

1	2	3	4	5
Piperazine plant	Piperazine Salts,	12,000 kg.	Pakistan	Sanctioned project
		10,000 kg.	Turkey	"
Vitamin B_{12} plant	Vitamin B_{12} (Streptomycin/Vitamin B_{12} plant)	8 kg.	Iran	
		4 kg.*	Pakistan	Sanctioned project
		10 kg.	Turkey	"

* Actual basic drug production in Pakistan, 1965
Chloramphenicol and its esters, 11,000 kg.
Vitamin B_{12}, 7.7 kg.

For manufacturing of basic drugs in bulk, one has to take into consideration a suitable economic size of production. In any RCD country, the demand may not be sufficient to maintain an economic unit. For instance, the demand of acetylsalicylic acid (aspirin) in Iran is estimated to be 80,000 kg. per year. Considering the present circumstances of the world market, the establishment of a plant with the production capacity of 80,000 kg. per year is not economical, because the countervalue of manufacturing machinery is too high as compared to the production value. Same in the case of Sulfa drugs, as an estimate of Sulfa drugs consumption is 50,000 kg. in Iran, it is not economical to establish a plant with a production capacity of less than 200,000 kg. per year.

For the manufacture of synthetic organic chemical drugs, most raw materials required are not available in Iran or other RCD countries at the present time. The coal-tar industry in Iran will start to produce benzene, xylene, and phenol, etc. by 1970. In the gap of this period, by using higher priced imported raw materials or intermediates in the manufacturing, the cost of production of finished drugs are sometimes higher than the world price that makes the domestic pharmaceutical industry difficult to compete with the imports. There is only fairly protection which would permit the joint venture manufacture of basic drugs in the RCD countries. Exemption or cutting down of customs tariff on those imports of pharmaceuticals and raw materials from other RCD countries should be undertaken into consideration.

(3) Drugs of Vegetable Origin

The pharmaceutical plants or factories processing basic drugs of vegetable origin can be manifold, depending on the medicinal plants grown in the respective country. In such factories, processing is generally based on extraction, the active substances are extracted from the medicinal plants. In Iran, there are massive production of vegetable drugs, such as glycyrrhiza (licorice), asafoteda, and gum tragacanth, etc. These drugs are partly provided for domestic consumption, and it has also a surplus amount for the exportation.

Table 7 - Quantity and Value of Exports of Vegetable Drugs, Iran

1966

Items	Quantity	Value
Licorice root (glycyrrhiza)	17,685,657 kg.	Rls. 92,578,784
Gum tragacanth, ribon and other grade	2,902,750 kg.	319,701,844
Asafetida, bitter and sweet	112,919 kg.	7,250,400
Other plants, for scent-making and medical purposes	348,116 kg.	6,159,778
Total	21,049,442 kg.	Rls. 425,690,816 ($ 5,675,877)

Iranian gum tragacanth which has earned a high reputation in the world market, is the top item of vegetable drugs for exportation. All licorice roots are exported in the form of crude drug at a price of about Rls. 5.2 per kg. It is recommended that the licorice roots are better to be processed into the extract or fluidextract of licorice. It will be much more profitable from the higher costs of those licorice products.

In Pakistan, Santonin, ephedrine, and rauwolfia alkaloids are extracted from the crude drugs. Some narcotic drugs, such as morphine hydrochloride, codeine phosphate etc. are the important analgesics and sedatives used in the therapy. It is recommended that the manufacture of morphine, codein, and other opium alkaloids might be undertaken in Turkey, by extracting and processing these drugs from the Turkish opium.

(4) Drugs of Animal Origin

Most importants are those processing various animal organs by extracting the active substances of healing effect. These are, pepsin, pancreatin, insulin, thyroid, peptone, heparin, liver extract, and adrenal cortical extract etc. Basic materials of such manufactures are animal organs available for the plants as by-products of slaughter-houses. No such plants can be established until the large-scale slaughter-houses are available for collecting and storing of those animal organs without any risk of deterioration and contamination.

(5) Sera, Vaccines and Other Biological Products

Many infectious diseases in men and animals are prevented, treated or cured by sera, vaccines and other biological (microbiological) products. In Iran, there are two institutes producing those biological products for human and veterinary uses under the restrictive control of manufacturing. These products are including antidiphteric serum, antitetanic serum, antianthrax serum, antirabies serum, antisnake-bite serum, as well as diphteric and tetanic toxoids, various vaccines and diagnostic antigens, etc.

For meeting the increasing demand in Iran, and also for the demands of other RCD countries, the expansion project of biological products manufacturing for the existing institutes in Iran may be undertaken into consideration. Otherwise, the new sera and vaccines plant may be set up in producing more biological products for human and veterinary uses.

According to the customs figures, a big item of imports under pharmaceuticals is baby food, chiefly milk powders. The imports amounted to Rls. 263,887,000 in 1966. It is suggested that the manufacture of baby food in Iran from locally-produced milk and other accessories may be started at an early date.

Table 8 - Sanctioned Plants of Biological Products

Sanctioned plants	Annual productive capacity		Annual outputs	Total assets
Sera & vaccines plant	Various sera and vaccines		US$ 400,000	US$ 300,000
Baby food and milk powder plant	Baby food (milk powder enriched with sugar, vitamins and minerals)	5,000 tons	US$ 3,800,000	US$ 3,000,000
	Milk powder			
		Total		US$ 3,300,000

1. MANUFACTURE OF PENICILLIN AND PROCAINE

In modern therapy, the most important group of antibiotics is the penicillins. The annual consumption of penicillins is estimated to be 20 million mega units (MMU) or 15,000 kg. in Iran, and about 50 MMU in the three RCD countries. According to the adequate demand of penicillins in Iran, it is suggested to set up a plant with an annual production capacity of about

20 MMU or 15,000 kg. of penicillins, in addition with 10,000 kg. of procaine hydrochloride, of which 2,650 kg. are used for manufacturing procaine-penicillin and the rest, 7,350 kg. are provided in the form of powders and injections. Procaine is one of the least toxic and most widely employed of the local anesthetics. It is therefore worth to have a penicillin/procaine combined plant for meeting the demands of both penicillin and procaine.

The penicillin/procaine plant should consist of: (a) a biosynthesis department for manufacturing penicillin by fermentation; (b) a synthetic department for manufacturing procaine hydrochloride, procaine-penicillin G and benzanthine penicillin G and (c) a pharmaceutical processing department for manufacturing various pharmaceutical preparations such as tablets, capsules and injections of penicillins and of procaine.

The total assets (capital expenditure) of the sanctioned penicillin/procaine plant is estimated to be Rials 193,000,000 (US $ 2,600,000). It might not be possible for local private entrepreneurs to take up such project, and the setting up of this plant under government management and financed by the government should be considered.

Since the production of penicillin is carried out on the world today in a tremendous large scale that makes the cost of production considerable low. A production capacity of 15,000 kg. of penicillins in the sanctioned plant is still not an economical production, and most of the raw materials required for the manufacture are not available in Iran today, thus, the resulting cost of production of penicillin might be

little higher than the world price. In the sanctioned plant, the cost of production of 1 million units vial of penicillin G potassium is estimated to be Rls. 4.0 ($ 0.054) and of 400,000 U. vial is Rls. 1.8 ($ 0.024). The lowest selling price of imported 1 million units vial of penicillin G potassium is Rls. 6.5 ($ 0.086) and of 400,000 U vial is Rls. 2.5 ($ 0.033). The dumping prices of imported penicillin products are so low that make the local industry rather difficult to compete. The protective policy of restricting imports to the amount required to supplement local production or of increasing the customs tariff should be applied on those imported penicillin preparations.

The annual total sales of penicillins and procaine are estimated to be Rls. 211,407,060 (US $ 2,818,760) (Table 9-4). The value of yearly output (total sales) will be greater than that of input (total assets). A gross profit is estimated to be Rls. 59,220,710 ($ 789,605) per year. If we count 20 % of total sales as the net profit, it will have an amount of Rials 42,281,400 ($ 563,752) of net profit per year (Table 9-4). It will yield a pay-out for the plant in 3 years and 5 months (Table 9-5).

Procedure of Penicillin Production

The name "penicillin" now designates a number of antibiotic substances produced by the growth of Penicillin chrysogenum or produced by other means. Many penicillins, natural and semisynthetic, are now known. Penicillin of commerce is largely pure crystalline penicillin G, known as benzylpenicillin. It occurs in fermentation liquors together with variable amounts of others, and is separated from the other penicillins

during purification. Commercial practice suppresses to a certain extent the natural tendency of the mold to form penicillins other than the desired G form by adding a precursor of G, namely phenylacetic acid or phenylacetamide to the culture medium during the fermentation. Dozens of semi-synthetic penicillins have been prepared by reacting penicillin with some chemical agents. Among them, the procaine-penicillin G, and benzathine penicillin G (N,N'-dibenzylethylenediamine dipenicillin G) are the more important penicillins introduced into the therapy.

When a good strain of penicillin chrysogenum is bred by fermentation in a nutrient medium, penicillin is originating. The selected strain bred continuously, are added to the well prepared and sterilized medium. Here, the molds are propagated in a large quantity suitable for large industrial production. When the propagation of the mold has reached the suitable level in the inoculum and the laboratory test proved them apt for production, the mixture is introduced under sterile conditions to the medium, prepared in the fermentors. The fermentors are fitted with a special stirrer and aerating installations. The Sterile air needed for the fermentation is provided by a compressor.

During the fermentation process, various penicillins are originating. By adding a precursor, phenylacetic acid to the culture medium, mainly the most active benylpenicillin (penicillin G) can be produced. Maximum penicillin potency is obtained in approximately 50-60 hours at 23-25°C. The proceeding of the fermentation is controlled by taking samples. After finishing the process, the fermented liquid is cooled to 5° and the mycelia are filtered off by passing the rotary drum filter. The penicillin is extracted in acid medium from the filtered liquid

by butyl acetate. The solvent phase containing penicillin is separated, then N-ethylpiperidine is added to the butyl acetate solution, the penicillin G-ethylpiperidine complex is precipitating in crystalline form. This product is filtered, washed and dried. The crude complex is dissolved in water, then the extraction by butyl acetate has to be repeated. When precipitating again by N-ethylpiperidine, a finer product is obtained.

For the preparation of penicillin G potassium, it is precipitated by addition of saturated a ueous solution of potassium carbonate to the butyl acetate solution. The semi-crude product is filtered, washed by acetone, ethyl alcohol and dried. The product is again dissolved in water, filtered and then precipitated by addition of warm acetone. After cooling, the crystals are filtered, washed by acetone and finally dried at 120°C. The pure penicillin G potassium is thus obtained.

Preparation of procaine-penicillin G and benzathine-penicillin G - The semi-crude penicillin-N-ethylpiperidine complex is dissolved in water and filtered. To the filtrate of penicillin solution, an a ueous solution of procaine hydrochloride is added. The precipitated procaine-penicillin G is filtered, washed and dried in vacuum. This manipulation should be made under strictly aseptic conditions. For the preparation of benzathine-penicillin G, the process is quite the same as described for the procaine-penicillin, except that dibenzyl-ethylenediamine is added to instead of procaine hydrochloride.

The sterile products are filled in vials or capsules or finished as tablets in the pharmaceutical processing department of the plant. The packing should also be performed under strictly aseptic conditions.

In the penicillin plant, a pilot plant is necessary for the plant evaluation study prior to every batch of fermentation, Adequate laboratory facilities should be installed for the quality control tests of antibiotics, and also for the research studies on the screening tests of new antibiotics from various soil samples colledted in Iran.

Procedure of procaine production

The p-nitrotoluene is oxidized by sodium dichromate to p-nitrobenzoic acid. The product is washed and dried. Dissolve p-nitrobenzoic acid in xylene, and then react with diethylaminoethanol in presence of dilute hydrochloric acid. The acid phase is separated, filtered and then a little ammonia is added. The acid solution is reduced by iron powder. The reduction mixture is filtered, acidified and filtered again. The procaine base is precipitated by adding ammonium hydroxide, filtered, washed, and dried in vacuum. Dissolve the base in alcohol, acidified with hydrochloric acid, decolorized and concentrated, the procaine hydrochloride is finally obtained by crystallization.

Table 9-1a - Raw Materials Required for the Manufacture of Penicillin

* Sucrose
  Lactose
  Corn steep liquor (solids)
  Sunflower oil
  Whey powder
  Phenylacetic acid
* Calcium carbonate
* Sodium hydroxide

Butyl acetate
* Sulfuric acid
N-ethylpiperidine
* Ammonium hydroxide
Acetone
Sodium sulfate
"Duopon 30"
Trisodium phosphate
* Alcohol, absolute
Potassium carbonate
* Acetic acid
Procaine hydrochloride
Dibenzylethylenediamine
"Tween 80"

Note: Materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 9-1b - Raw Materials Required for the Manufacture of Procaine Hydrochloride

p-Nitrotoluene
Sodium dichromate
Xylene
Diethylaminoethanol
* Hydrochloric acid
* Ammonium hydroxide
Iron powder (for reduction)
Active Charcoal
* Ethyl alcohol

Note: Materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 9-2 - Total Assets for Penicillin and Procaine Plant

Annual production:

(1) Penicillin and its derivatives, 20 million mega units (MMU); or 15,000 kg.

(2) Procaine hydrochloride, 10,000 kg.

Land (20,000 M^2)	Rs.	4,050,000	(US$ 54,000)
Buildings (75,000M^2)		18,750,000	($ 250,000)
Machineries & equipment* complete with technical know-how		105,000,000	($ 1,400,000)
Erection and start-up		12,000,000	($ 160,000)
Services		11,250,000	($ 150,000)
Working capital & others		43,950,000	($ 586,000)
Total	Rs.	195,000,000	(US$ 2,600,000)
Machineries & equipment for penicillin manufacturing:	Rs.	91,875,000	($ 1,225,000)
Machineries & equipment for procaine manufacturing:		5,250,000	($ 70,000)
Machineries & equipment for pharmaceutical processing unit:		4,500,000	($ 60,000)
Equipment and facilities for control laboratories and research laboratories:		3,375,000	($ 45,000)

Table 9-3a - Cost of Production for Penicillin G Potassium

Per 1000 million units (approx.627 Gm.)

Raw materials	₦. 810	(US$ 10.8)
Utilities (electricity, fuel, and water, etc.)	450	($ 6.0)
Machinery depreciation and maintenance	690	($ 9.2)
Labor, direct and indirect	285	($ 3.8)
Taxes and insurance	150	($ 2.0)
Overhead & miscellaneous	480	($ 6.4)
	₦. 2,865	(US$ 38.2)

Cost of production for penicillin preparations:

Penicillin G Potassium Injection (1 million U/vial): ₦.4.0/vial

Penicillin G Potassium Injection (500,000 U/vial): ₦.2.6/vial

Penicillin G Potassium Injection (400,000 U/vial): ₦.1.8/vial

Penicillin G Potassium Tablets (250,000 U/tab.): ₦.1.0/tab.

Table 9-3b - Cost of Production for Procaine-Penicillin G

Per 1000 M.U. (approx. 990 Gm)

Raw materials (penicillin procaine and others)	₦. 3,150	($ 42.0)
Labor and Overhead, etc.	450	($ 6.0)
	₦. 3,600	($ 48.0)

Cost of production for procaine-penicillin G preparations:

Procaine-penicillin G Injection (300,000 U/ml.,10ml/vial: ₦. 12 /vial.

Table 9-3c - Cost of Production for Benzathine-Penicillin G

Per 1000 MU (approx. 825 Gm.)

Raw materials (penicillin, dibenzylethylenediamine, & others)	₦. 3,975
Labor and overhead, etc.	425
	₦. 4,400 ($ 58.66)

Cost of production for Benzathine-Penicillin G Preparations:

Benzathine-penicillin G Injection (300,000 U/ml.,10 ml/vial): ₦. 15/vial

Benzathine-penicillin tablets (200,000 U): 1.05/tab.

Table 9-3d - Cost of Production for Procaine Hydrochloride

Raw materials	₦. 412.5 ($ 5.50)
Utilities (electricity, fuel, and water, etc.)	150.0 ($ 2.00)
Machinery depreciation & maintenance	90.0 ($ 1.20)
Labor, direct and indirect	105.0 ($ 1.40)
Taxes and insurance	60.0 ($ 0.80)
Overhead & miscellaneous	202.5 ($ 2.70)
	₦. 1,020.0 ($13.60)/kg.

Cost of production for procaine HCL injections, (2%, 2 ml.25'S box): ₦. 25/box

Table 9-4 - Estimated Profit from Penicillin and Procaine Plant

Annual production:

(I)	Penicillins, total amount, 19.756,000 million units		(15,000 kg.)
	Penicillin G Potassium (1595 U/mg)	11.000 MMU	6,896 kg.
	Procaine-Penicillin G (1009 U/mg)	5.280 MMU	5,234 kg.
	Benzathine-Penicillin (1211 U/mg)	3.476 MMU	2,870 kg.
		19.756 MMU	15,000 kg.

(a) 4.939 MMU (3,750 kg.) penicillins are supplied as basic drug to other domestic pharmaceutical plants for their processing;

(b) 14.817 MMU (11,250 kg.) penicillins are processed in forms of tablets, capsules, and injections, etc.

(II) Procaine Hydrochloride: 10,000 kg.

(a) 2,650 kg. are supplied for manufacturing procaine-penicillin G in the plant

(b) 7,350 kg. are provided in forms of powders, and injections, etc.

Total Sales[1]:

(Ia)	Penicillin G Potassium,	2.750 MMU (1,724 kg.) x ₦.3,375,000 ($45,000) = ₦. 9,281,250 ($ 123,750)
	Procaine-Penicillin G,	1.320 MMU (1,308.5kg.)x ₦.4,200,000 ($56,000) = ₦. 5,544,000 ($ 73,920)
	Benzathine-Penicillin,	0.869 MMU (717.5 kg.) x ₦.5,490,000 (73,200) = ₦. 4,770,810 (63,610)

(Ib) Penicillin G Potassium Tab.,
16,500,000 pcs. (250,000 U) x Rs.1.35 = Rs.22,275,000 ($297,000)

Penicillin G Potassium Injection,
4,125,000 vials (1,000,000U)x Rs.5.4 = Rs.22,275,000 ($297,000)

Procaine-Penicillin G Injection,
1,320,000 vials
(3,000,000 U/10 ml.vial) x Rs.16 = Rs.21,120,000 ($281,600)

Benzathine-Penicillin G Injection,
660,000 vials
(3,000,000 U/10 ml.vial) x Rs.20 = Rs.13,200,000 ($176,000)

Benzathine-Penicillin G Tab.,
3,135,000 pcs.(200,000 U) x Rs. 1.6 = Rs. 5,016,000 ($ 66,880)

Total (Ia, Ib) Rs. 103,482,060($1,379,760)

(IIa) Procaine Hydrochloride, 2,650 kg.
(used for manufacturing procaine - penicillin in the penicillin plant)
x Rs.1,275 = Rs. 3,378,750 ($ 45,050)

Procaine Hydrochloride, 4,350 kg.
(supplied to local manufacturers for their processing) x Rs.1,275 = Rs. 5,546,250 ($ 73,950)

(IIb) Procaine HCL Injection, 3,000,000 boxes
x Rs. 33 = Rs. 99,000,000 ($1,320,000)

Total (IIa, IIb) Rs.107,925,000 ($1,439,000)

Grand total(Ia,b,IIa,b) Rs.211,407,060 ($2,818,760)

Costs of Production [2]:

(Ia)	Penicillin G Potassium, 2.750 MMU x Rs.2,865,000 =	Rs. 7,878,750	($ 105,050)
	Procaine-Penicillin, 1.320 MMU x Rs.3,600,000 =	Rs. 4,752,000	($ 63,360)
	Benzathine-Penicillin, 0.869 MMU x Rs.4,400,000 =	Rs. 3,823,600	($ 50,985)
(Ib)	Penicillin Tab., 16,500,000 pcs. x Rs. 1.0 =	Rs. 16,500,000	($ 220,000)
	Penicillin G Potassium Injection, 4,125,000 vials x Rs. 4.0 =	Rs. 16,500,000	($ 220,000)
	Procaine-Penicillin Injection, 1,320,000 vials x Rs. 12 =	Rs. 15,840,000	($ 211,200)
	Benzathine-penicillin Injection, 660,000 vials x Rs. 15 =	Rs. 990,000	($ 13,200)
	Benzathine-Penicillin Tab., 3,135,000 pcs. x Rs. 1.2 =	Rs. 3,762,000	($ 50,160)
	Total (Ia, Ib)	Rs. 70,046,350	($ 933,955)
(IIa)	Procaine HCL, 7,000 (2,650 kg. and 4,350 kg.) x Rs.1,020 =	Rs. 7,140,000	($ 95,200)
(IIb)	Procaine HCL Injection, 3,000,000 boxes x Rs. 25 =	Rs. 75,000,000	($1,000,000)
	Total (IIa, IIb)	Rs. 82,140,000	($1,095,200)
	Grand total (Ia,b, IIa,b)	Rs. 152,186,350	($2,029,155)
	Estimated yearly gross profit [3]:	Rs. 59,220,710	($ 789,605)
	Estimated yearly net profit [4]:	Rs. 42,281,400	($ 563,752)

Note:

(1) (I) Penicillin G Potassium

Selling price of penicillin G Potassium in bulk: ₦.3,375/1000 MU

Estimated market price of penicillin tab.: ₦. 1.8

Wholesale price (75% of market price): ₦. 1.35

Estimated market price of Penicillin G Potassium Injection: ₦. 7.2

Wholesale price (75% of market price): ₦. 5.4

Procaine-penicillin

Selling price of procaine-penicillin in bulk: ₦.4,200/1000 MU

Estimated market price of procaine-penicillin Injection: ₦. 21/vial

Wholesale price (75% of market price): ₦. 16/vial

Benzathine-penicillin

Selling price of Benzathine-penicillin in bulk: ₦.5,490/1000 MU

Estimated market price of Benzathine-penicillin Injection: ₦. 26/vial

Wholesale price (75% of market price): ₦. 20/vial

Estimated market price of Benzathine-penicillin tables: ₦.2.1/tab.

Wholesale price (75% of market price): ₦.1.6/tab.

(II) Procaine Hydrochloride

Selling price of Procaine HCL in bulk: ₦.1,275 ($17.0)kg.

Estimated market price of Procaine HCL Inj.: ₦.44/box

Wholesale price (75% of market price): ₦.33/box

(2) Costs of Production

Cf. Tables 9-3a, 9-3b, 9-3c and 9-3d.

(3) Estimated yearly gross profit = total sales - total costs of production

(4) Estimated net profit = 20% of total sales.

Table 9-5 - Pay-out Time for Penicillin and Procaine Plant

Estimated net profit per year	Rs. 42,281,400	($ 563,752)
Depreciation per year	14,532,000	($ 193,760)
	Rs. 56,813,400	($ 757,512)

Pay-out time for the plant: 3 years and 5 months.

(Total assets/net profit and depreciation: $ 2,600,000/$ 757,512)

2. MANUFACTURE OF TETRACYCLINE AND CHLORTETRACYCLINE

The tetracycline antibiotics including chlortetracycline, oxytetracycline and tetracycline are few antibiotics which are suitable for small scale manufacture. They are "broad-spectrum" antibiotics and are used in therapy in a considerable amount. Chlortetracycline, which was firstly introduced in the therapy under the trade name of "Aureomycin" and exytetracycline under the trade name of "Terramycin" are but two of a group of antibiotics biosynthesized by very closely related species of Streptomyces. Tetracycline is produced through catalytic reduction and dehalogenation of chlortetracycline, and may also be obtained directly by the submerged culture of Streptomyces viridifaciens. Tetracycline antibiotics are contri-

buted in the dosage forms of gelatin capsules and injections. They are widely used as the "broad-spectrum" antibiotics for human infectious diseases. They are also contributing substantially to the security and the success of the present-day agriculturists through their therapeutic properties to animal diseases, and also through their activity as growth stimulants for animals. For veterinary uses pure crystalline antibiotics are required, but for growth-stimulating supplements in animal feeding (antibiotic-supplemented diet), rigid standards are not required, and in fact, crude extract or even the dried microbial masses from fermentation liquids used for industrial production of tetracyclines may be preferred. Thus, the production of tetracyclines for veterinary uses, and of antibiotic-supplemented feeding may contribute to lower the production cost of tetracycline.

The annual consumption of tetracycline antibiotics is estimated to be 10,000 kg. in Iran, and 25,000-30,000 kg. in the three RCD countries. The manufacture scale of 10,000 kg. fits well for an economical production. According to the adequate demand of these antibiotics, it is worth to set up a plant with an annual production capacity of 10,000-15,000 kg. of tetracycline and chlortetracycline in Iran. The total assets (capital expenditure) of the sanctioned plant will be Rs. 90,000,000 (US $ 1,200,000) (Table 10-2). The tetracycline plant should consist of (a) a biosynthetic department for manufacturing antibiotics, tetracycline hydrochloride and chlortetracycline hydrochloride, and (b) a pharmaceutical processing department for manufacturing various pharmaceutical preparations, such as T/C capsules, injections and ointments, etc. The sanctioned plant

will have a space area of 16,800 square meters, and 6,000 square meters of buildings.

In the tetracycline plant, a pilot plant is necessary for the plant evaluation study prior to every batch of fermentation. Adequate laboratory facilities should be installed for the quality control tests of antibiotics and also at the same time, for the research studies (screening tests) on new antibiotics.

The annual production capacity of the plant is estimated to be 10,000 kg. of tetracycline HCL and chlortetracycline HCL, of which 3,000 kg. of sterile antibiotic powder might be sold to other domestic pharmaceutical plants for their processing, and 7,000 kg. of antibiotics might be supplied in the forms of capsules and injections. The full working capacity of the plant could be risen up to 50% more than the usual productivity and it would lead to a production of 15,000 kg. of the antibiotics per year. The yearly total sales are estimated to be Rials 95,820,000 (US $ 1,277,600) (Table 10-4). The value of yearly output will be approximately the same to the value of input. The cost production of tetracyclines is estimated to be Rials 3,150 (US $ 42,00) per kg., which is not high and competitive with the world price. A gross profit is estimated to be Rls. 48,850,000 (US $ 651,330) per year. If we count 20% of total sales as the net profit, an amount of Rls. 19,164,000 (US $ 255,520) of net profit per year may be expected from this project. It will yield a pay-out for the plant in 3 years and 2 months (Table 10-5).

Procedure of tetracyclines production

Good mutant strains of Streptomyces aureofaciens should

be selected for industrial biosynthesis of chlortetracycline by its superior yields in submerged fermentation. Oxytetracycline, biosenthesized by Streptomyces virusus, is also produced industrially by submerged cultures. Procedures for extracting chlortetracycline from the harvested culture liquid are developed around the differential solubilities of the free bases and their salts in differential solvents and their partition coefficients between aqueous and organic solvent phases at different pH values. Chlortetracycline, which occurs in the fermented liquid in the form of lightly soluble complexes, is liberated by acidification to a pH lower than 4, then extracted by organic solvent in the presence of a surface active agent that act as carrier. The extract is then concentrated under pressure. To the concentrate is added hydrochloric acid resulting in the immediate precipitation of chlortetracycline hydrochloride in amorphous form. The crude chlortetracycline is separated by filtraction and slurried with cellosolve (2 ethoxyethanol). The amorphous product then crystallizes, yielding purified chlotetracycline hydrochloride.

Table 10-1 - Raw Materials Required for the Manufacture of Chlortetracycline/Tetracycline

- * Sucrose
  Corn steep liquor
- * Cottonseed meal
- * Starch
  Ammonium chloride
  Ammonium sulfate
- * Calcium carbonate
  Manganese Sulfate
- * Lard oil
  Methylisobutylketone (MIBK)

Diatomaceous earth
"Arquard 16-33" (quaternary ammonium compound)
Oxalic acid
* Caustic soda
* Ammonia water
* Sulfuric acid
* Hydrochloric acid
Cellosolve (2-ethoxyethanol)
Butyl alcohol
Triethylamine
Palladium catalyst (for catalytic reduction)
Hydrogen gas (for catalytic reduction), etc.

Note: Raw materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 10-2 - Total Assets for Tetracycline and Chlortetracycline Plant

Annual production capacity: 10,000 kg. tetracycline and chlortetracycline

Land (16,850 M^2)	Rls. 2,275,000	($ 45,000)
Buildings (6,000 M^2)	15,000,000	($ 200,000)
Machineries & equipment	45,000,000	($ 600,000)
Erection and Start-up	7,500,000	($ 100,000)
Services	3,375,000	($ 45,000)
Working capital & others	15,750,000	($ 210,000)
Total	Rls. 90,000,000	($1,200,000)

Table 10-3a - Cost of Production for Tetracycline/chlor-tetracycline

Raw materials	Rs. 945.0	($ 12.60)
Utilities (water, electricity, fuel, etc.)	315.0	($ 4.20)
Machinery depreciation and maintenance	900.0	($ 12.00)
Labor, direct and indirect	315.0	($ 4.20)
Taxes and insurance	187.5	($ 2.50)
Overhead & miscellaneous	487.5	($ 6.50)
Total	Rs. 3,150.0	($ 42.00) per kg.

Table 10-3b - Cost of Production for 100 Tetracycline/chlor-tetracycline capsules (250 mg.)

Tetracycline/chlortetracycline HCL	Rs. 84
Packing charges	35
Overhead	25
Total	Rs. 134 (Rs. 1.34 per cap.)

Table 10-4 - Estimated Profit from Tetracycline Plant

Annual production: Total amounts of tetracycline/chlortetracycline HCL, 10,000 kg.

(I) 3,000 kg. tetracycline/chlortetracycline HCL are sold to other domestic pharmaceutic plants for their processing.

(II) 7,000 kg. tetracycline/chlortetracycline are processed in form of 28,000,000 capsules (250 mg.);

Other preparations as, eye solutions, injections (Sodium glycinate buffered, 500 mg./vial), syrups, ointments, and ophthalmic ointments are not counted.

Total Sales:		
(I) 3,000 kg. T/C x ฿.3,940 ($52.54)(1) =	฿. 11,820,000	($ 157,600)
(II) 28,000,000 T/C cap. x ฿.3.0[1]	84,000,000	($1,120,000)
	฿. 95,820,000	($1,277,600)
Cost of Production:		
(I) 3,000 kg. T/C x ฿.3,150 ($42.00)(2) =	฿. 9,450,000	($ 126,000)
(II) 28,000,000 T/C cap. x ฿.1.34[2]	37,520,000	($ 500,270)
	฿. 46,970,000	($ 626,270)
Estimated yearly gross profit[3]:		
(I) For T/C powder	฿. 2,370,000	($ 31,600)
(II) For T/C capsules	฿. 46,480,000	($ 619,730)
	฿. 48,850,000	($ 651,330)

Estimated yearly net profit:(4) ₨. 19,164,000 ($ 255,520)

Note: (1) Estimated wholesale price of T/C: ₨.3,940 ($52.24) per kg;

Estimated market price of T/C cap.: ₨. 4.00 per cap;

Wholesale price (75% of market price): ₨. 3.00 per cap;

(2) Cost of production for T/C powder: ₨.3,150 per kg;

Cost of production for T/C capsules: ₨.1.34 per cap.

(3) Gross profit = total sales - total costs of production.

(4) 20% of total sales as net profit.

Table 10-5 - Pay-out Time for Tetracycline/Chlortetracycline Plant

Estimated net profit per year	₨. 19,164,000	($ 255,520)
Depreciation per year	₨. 9,000,000	($ 120,000)
	₨. 28,164,000	($ 375,520)

Pay-out time for the plant: 3 years & 2 months

(total assets/net profit and depreciation:)

$ 1,200,000/$ 375,520

3. MANUFACTURE OF STREPTOMYCINS AND VITAMIN B_{12}

Streptomycin is the antibiotic biosynthesized by different species of Actinomycetes, belonging principally to the genus Streptomyces or related genera. Streptomycin is used in the forms of its acid salts. The reduced form of streptomycin, known as dihydrostreptomycin is administered largely in the form of the sulfate. Perhaps the greatest virtue of streptomycin and dihydrostreptomycin as chemotherapeutic agents in their effectiveness in the clinical management of tuberculosis as well as various gram-negative pathogens.

Cyanocobalamin, cobalamin or vitamin B_{12} is an effective antianemia remedy in modern therapy. Preparations containing B_{12} and intrinsic factor concentrate (or stomach powder) are now available for oral use. In pernicious anemia, the vitamin is usually administered parenterally. Vitamin B_{12} was first isolated from liver, and was later found to occur in minute quantities in the fermentation liquor of different Strains of Streptomyces. By using a strain of Streptomyces griseus in the fermentation process, it produces both the antibiotic, streptomycin and the vitamin B_{12}. The production of vitamin B_{12} may be looked as a by-product of streptomycin manufacture. It contributes to lower the production cost of streptomycin to certain extent.

The annual consumption of streptomycin is estimated to be 10,000 kg. in Iran. The total demands are about 45,000 - 50,000 kg. in the RCD countries. A streptomycin/vitamin B_{12} combined plant may be considered to build up in Iran with an annual production of 10,000 kg. of streptomycin and dihydrostreptomycin as well as 8 kg. of crystalline citamin B_{12}. Otherwise, a plant with a production capacity of 50,000 kg. of

streptomycins and 35 kg. of vitamin B_{12} for meeting the demands of the three RCD countries may be considered to set up in any one of the RCD countries (total assets of the plant is estimated to be US $ 2,400,000).

At a production capacity of 10,000 kg. of streptomycins per year, it is still not large enough for an economical production. Thus, the cost of production for streptomycin should reach Rls. 3,600 (US $ 48.0) per kg. (Table 11-3a). The selling price of 1 Gm. streptomycin vial in Iran is Rls. 8.0 (US $ 0.106), and the cost of production is estimated to be Rls.4.8 (US $ 0.064). If the annual production increase to 15,000 kg. or more, the cost of production might be reduced 20% below the previous price.

The total assets (capital expenditure) of the sanctioned plant is estimated to be Rls. 105,000,000 (US $ 1,400,000) (Table 11-2). For streptomycin and Vitamin B_{12}, there will be 30-37.5% of the products being supplied as basic drugs to other domestic pharmaceutical plants for their processing, and the rest will be provided in suitable dosage forms, such as sterile powder for injection, and parenteral solution, etc. The total sales for both streptomycins and Vitamin B_{12} are estimated to be Rials 129,970,000 (US $ 1,732,940) (Table 11-4). The value of yearly output will be greater than that of input. The gross profit per year is estimated to be Rls. 26,326,250 (US $ 351,020). If we count 15% of total sales as the net profit, it will have an amount of Rls. 19,495,500 (US $ 259,940) of net profit from this combined plant per year. It will yield a pay-out for the plant in 3 years and 8 months (Table 11-5).

Procedure of production

When a strain of Streptomyces griseus which produces both Streptomycin and Vitamin B_{12} is used to ferment an aqueous nutrient medium, the Streptomycin and Vitamin B_{12} thus formed may be separated one from another by subsequent operations. The nutrient culture used for fermentation contains glucose, sodium citrate, inorganic salts and other organic compounds. Soybean meal and peptone are used as a source of nitrogen. Distillers' solubles (available as a by-product of molasses - ethyl alcohol fermentation), or corn steep liquor and calcium carbonate are also employed, the later to control PH value; lard oil and other fats may replace glucose and starch.

For industrial production of streptomycin and Vitamin B_{12}, the submerged fermentations are carried out in the large fermentation tanks, and particular attention should be paid in preparation of "seed" or "inoculum", in providing aeration and proper nutrients and in maintaining sterility, proper pH value, etc. It must continuously select active strains from cultures of parent strain of Streptomyces griseus because there is considerable variability in the capacity of different subcultures to produce the antibiotic. The histamine-like substance which is usually accompanied with streptomycin as impurities should be removed by passing adsorptive chromatographic columns.

Streptomycin may be isolated from the fermented liquid by adsorption on ion-exchange resin. An acid-alcohol mixture brings the streptomycin into solution. Concentrate the neutralised solution, and crude streptomycin is precipitated out from

solution by addition of ether and acetone. Further purification and subsequent crystallization involve additional steps. The dihydrostreptomycin is prepared through catalytical reduction of streptomycin.

The effuent broth, from which the Streptomycin has been guantitatively removed by passage of the fermented broth through the first series of ion-exchange resin columns, is then treated with active charcoal. The adsorbate is then eluted with an aqueous solution of pyridine, and the eluate evaporated. The residue is extracted with methyl alcohol, and the alcoholic extract is then passed through the columns containing activated alumina. The columns are eluted with fresh methanol, and those fractions of the eluate are concentrated together. The concentrated solution is then mixed with acetone whereupon crude Vitamin B_{12} precipitated and is removed by filtration. This material is purified by reprecipitation from ethanol solution by the addition of acetone and the product further purified by crystallization from aqueous acetone to produce crystalline Vitamin B_{12}.

In the streptomycin/vitamin B_{12} plant, a pilot plant is necessary for the plant evaluation study prior to every batch of fermentation. Adequate laboratory facilities should be installed for the quality control tests of antibiotics and vitamin and also at the same time, for the research studies (screening tests) on new antibiotics.

Table 11-1 - Raw Materials Required for the Manufacture of Streptomycin and Vitamin B_{12}

- * Glucose
- * Soybean meal
- * Distillers' solubles (by-product of molasses-alcohol fermentation)
- * Sodium chloride (or sodium citrate)
- Cobalt nitrate
- * Calcium carbonate
- * Sodium hydroxide
- Phosphoric acid
- Carboxylic acid ion-exchange resin (copolymer of acrylic or methacrylic acid and divinylbenzene resin; or "Amberite IRC-50")
- * Hydrochloric acid
- Ethylenediamine tetraacetic acid (EDTA)
- Weak acid cationic exchange resin
- Activated alumina for chromatography
- Anionic exchange resin
- * Sulfuric acid
- Sodium carbonate
- Platinum oxide
- Activated charcoal for chromatography
- Pyridine
- Methyl alcohol
- Acetone

Note: Materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 11-2 - Total Assets for Streptomycin/Vitamin B_{12} Plant

Annual production: 10,000 kg. streptomycin and dihydrostreptomycin 8,000 Gm. Crystalline Vitamin B_{12}

Land (18,000 M^2)	Rs.	3,637,500	(US$	48,500)
Buildings (6,500 M^2)		16,237,500	($	216,500)
Machineries & equipment		52,500,000	($	700,000)
Erection and Start-up		7,500,000	($	100,000)
Services		5,625,000	($	75,000)
Working capital & others		19,500,000	($	260,000)
	Rs.	105,000,000	($	1,400,000)

Table 11-3a - Cost of Production for Streptomycin and Dihydrostreptomycin

per kilogram

Raw materials	Rs.	1,350	(US $	18.0)
Utilities (water, electricity, & fuel, etc.)		360	($	4.8)
Machinery depreciation and maintenance		825	($	11.0)
Labor, direct & indirect		360	($	4.8)
Taxes and insurance		150	($	2.0)
Overhead & miscellaneous		555	($	7.4)
	Rs.	3,600	(US $	48.0) per kg.

Table 11-3b - Cost of Production for 100 Streptomycin/Dihydro streptomycin Injections (1 Gm./vial)

Streptomycin sulfate or/and dihydrostreptomycin sulfate (sterile powder)	Rs. 360
Packing charges	240
	Rs. 600/100 vials
	Rs. 6.0 per vial

Table 11-3c - Cost of Production for Vitamin B12 per kilogram

Raw materials	Rs. 123,750 (US$ 1,650)
Utilities (water, electricity, & fuel, etc.	26,250 ($ 350)
Machinery depreciation & maintenance	82,500 ($ 1,100)
Labor, direct and indirect	11,250 ($ 150)
Taxes and insurance	7,500 ($ 100)
Overhead & others	30,000 ($ 400)
	Rs. 281,250 ($ 3,750)/kg.
	Rs. 281 ($ 3.75)/Gm.

Table 11-3d - Cost of Production for 100 Vitamin B_{12} Injections

(100 mcg. per ml.; 10 ml./vial)

Vitamin B_{12}, Mannitol & others	Rs. 150
Packing charges	150
Overhead and others	700
	Rs. 1,000/100 vials
	Rs. 10/vial

Table 11-4 - Estimated Profit from Streptomycin and Vitamin B_{12} Plant

Annual Production:

(I) 10,000 kg. of streptomycin (S) and dihydrostreptomycin (DS)

(a) 3,000 kg. of S and DS are supplied as basic drugs to other domestic pharmaceutical plants for their processing;

(b) 7,000 kg. of S and DS are supplied in the forms of sterile powder, 1Gm./vial: 7,000,000 vials.

(II) 8,000 Gm. of crystalline Vitamin B_{12}

(a) 3,000 Gm. of Vitamin B_{12} are supplied as basic drug to other domestic pharmaceutical plants for their processing;

(b) 5,000 Gm. of Vitamin B_{12} are supplied in the forms of injections, 100 mcg. per ml., 10 ml.vial: 5,000,000 vials.

Total Sales:

(i) (a)	3,000 kg. S and DS powder x ₦.4,140 ($55.2)(1a)	= ₦. 12,420,000	($ 165,600)
(b)	7,000,000 S and DS vials x ₦. 7.0 (1a)	= ₦. 49,000,000	($ 653,340)
(II) (a)	3,000 Gm. Vitamin B_{12} x ₦.350 ($ 4.66) (1b)	= ₦. 1,050,000	($ 14,000)
(b)	5,000,000 Vitamin B_{12} Vials x ₦.13.5 (1b)	= ₦ 67,500,000	($ 900,000)
	Total	₦.129,970,000	($ 1,732,940)

Costs of Production:

(I) (a)	3,000 kg. S and DS powder x Rs.3,600 ($48.0) (2a)	= Rs. 10,800,000	($ 144,000)
(b)	7,000,000 S and DS vials x Rs. 6.0 (2a)	= Rs. 42,000,000	($ 560,000)
(II) (a)	3,000 Gm. Vitamin B_{12} x Rs.281.25 ($3.75)(2a)	= Rs. 843,750	($ 11,250)
(b)	5,000,000 Vitamin B_{12} vials x Rs. 10 (2b)	= Rs. 50,000,000	($ 666,670)
	Total	Rs.103,643,750	($1,381,920)
Estimated yearly gross profit(3):		Rs. 26,326,250	($ 351,020)
Estimated yearly net profit(4):		Rs. 19,495,500	($ 259,940)

Note:(1a) Sale price of S and DS powder per kg.: Rs.4,140 ($55.2)
Estimated market price of S and DS vial: Rs. 8.0
Wholesale price of vial: Rs. 7.0

(1b) Sale price of Vitamin B_{12} per Gm.: Rs. 350 ($ 4.66)
Estimated market price of Vitamin B_{12} injection: Rs. 18/vial
Wholesale price of vial: Rs.13.5/vial

(2a) Cost od production of S and DS powder per kg.: Rs.3,600 ($48.0)
Cost od production of S and DS vials : Rs. 6.0/vial

(2b) Cost of production of Vitamin B_{12} per Gm: Rs.281.25 (3.75)
Cost of production of Vitamin B_{12} vials : Rs.10/vial

(3) Estimated yearly gross profit = total sales - total cost of production

(4) 15% of total sales counted as net profit.

Table 11-5 - Pay-Out Time for Streptomycin/Vitamin B_{12} Plant

Estimated net profit per year	Rs. 19,495,500	(259,940)
Depreciation per year	Rs. 8,910,000	(118,800)
Total	Rs. 28,405,500	(378,740)

Pay-out time for the plant: 3 years and 8 months
(Total assets/net profit & depreciation:
$ 1,400,000/$ 378,740)

4. MANUFACTURE OF YEAST AND ITS PREPARATIONS

The dried yeast, also known as medical yeast is used in therapy for its rich source of vitamin and high content of protein. It is advisable to supply yeast as "meat substitute" to those convalescent patients, aged people, school children, youngsters and even soldiers who need the dietary supplements for building up their health. Yeast is also used in accompanying with rice bran, wheat bran and fish meal etc. in the animal feedings. A certain amount of yeast (active yeast) is used in the baking industry and for home baking. It is good to suggest that a yeast plant may be set up with annual production of 5,000 tons of dried yeast, of which 1,000 tons are supplied in the form of yeast powder, and the rest are supplied in the forms of tablets, yeast extract, and vitamin B complex capsules, etc.

Yeast is produced by the fermentation of Saccharomyces cerevisiae or other suitable species. On a dry basis, it assays around 50% of crude protein and 42% of carbohydrates. Yeast is extremely rich source of B- vitamins. Enriched yeast can be produced by adjusting the vitamin content with addition of pure synthetic vitamins. In the manufacturing of yeast, molasses is the main nutrient. In Iran, as a by-product of sugar industry, there is a production of large amount of molasses, which is mostly not well utilised and rejected. The manufacture of yeast is a best way to use molasses.

The total assets of yeast plant will be Rls. 90,000,000 (US $ 1,200,000) (Table 12-2), and the total sales per year is estimated to be Rls. 117,750,000 ($ 1,570,000) (Table 12-4). The value of output will be greater than the value of input. The gross profit is estimated to be Rls. 28,500,000 ($ 380,000). If we count 20% of total sales as the net profit, it will have an amount of Rls. 23,550,000 ($ 314,000) of net profit per year. It will yield a pay-out for the plant in about three years (Table 12-5).

Procedue of Yeast Production

The manufacture of yeast is in many ways analogous to a farming operation in tanks, except that sunlight is not required. During the fermentation prooess, nitrogen (generally as ammonia or ammonium salts), phosphorus (usually as ammonium phosphate or calcium superphosphate), organic nitrogen materials, water and small amounts of other growth factors are added to the culture medium to make it nutritionally complete. The quantity and sources of raw materials for preparing the

culture medium are kept quite flexible. The various sources of carbohydrate and nitrogen may be used singly or in combination. In the United States, the cane sugar molasses, beet sugar molasses and corn liquor are used simultaneously for the production of yeast. The beet molasses contains besides sucrose and invert sugars, a small amount of glutamate and betaine, and the later may be served as a nitrogen material in the medium, When the fermentation is completed, there will be no more betaine existing in the culture liquid. Thus it gives no harm to the final product, when the beet molasses is used.

The reproduction is started by planting the single cells of a selected strain of yeast in a test tube containing sterile medium. After several days of growth at 25°C, the contents are transferred through a number of successively large sterile flasks and tanks involving increasing amounts of a growth medium.

In the final stages, the molasses wort is fed incrementally and the entire mash is aerated vigorously to suppress alcohol fermentation. The optimum temperature is 30°C and the optimum pH is about 5.0. The yeast reproduce under these conditions by budding and the number of yeast cells may double every two to three hours. When the desired amount of growth has been achieved, the yeast is separated from the spent medium & washed by processing centrifugal separators. The resulting yeast suspension is then concentrated to 30% solids by means of filter presses. Active dry yeast (baking yeast) or inactive yeast (medical yeast) may be prepared from this product by further dehydration under controlled condition.

Table 12-1 - Raw Materials Required for the Manufacture of Yeast and its Preparations

* Molasses (cane sugar molasses, beet sugar molasses)
* Corn sugar liquor
* Grain extracts (derived from wheat, corn, barley, rice, malt sprouts, rice bran or combinations of these)
* Ammonia water (or ammonium sulfate)

Calcium superphosphate

Ammonium phosphate

Lactic acid

Magnesium stearate

Sodium benzoate

* Gum acacia

Lactose

Starch, corn

Thiamine hydrochloride

Riboflavin

Nicotinamide

Note: Materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 12-2 - Total Assets for Yeast Plant

Annual production capacity :	5,000 tons yeast		
Land (16,850 M^2)	Rs.	3,375,000	($ 45,000)
Buildings (6,000 M^2)		15,000,000	($ 200,000)
Machinery & equipment*		48,750,000	($ 650,000)
Erection & Start-up		4,125,000	($ 55,000)
Working capital & others		18,750,000	($ 250,000)
Total		90,000,000	($ 1,200,000)
* Machinery for yeast manufacture:		40,500,000	($ 540,000)
Machinery for yeast preparations processing:		6,000,000	($ 80,000)
Equipment for control laboratory:		2,250,000	($ 30,000)

Table 12-3 - Cost of Production for Yeast

Raw materials per ton of yeast	Rs.	6,000	($ 80)
Utilities (water, electricity, fuel, etc.)		1,500	($ 20)
Machinery depreciation and maintenance		1,500	($ 20)
Labor, direct & indirect		1,500	($ 20)
Overhead & miscellaneous		4,500	($ 60)
	Rs.	15,000	($200)/ton

Table 12-4 - Estimated Profit from Yeast Plant

Annual production: 5,000 tons yeast powder supplied in various forms:

a)	Yeast powder	1,000 tons;
b)	Yeast tablets (0.5 Gm.)	
c)	Yeast extract (water soluble extract od yeast)	
d)	Vitamin B complex capsules (approx. 0.5 Gm. yeast ext. enriched with thiamine, riboflavin & nicinamide)	
	Yeast contents in (b) (c) & (d), equivalent to	4,000 tons yeast

Total sales: (a)	Yeast powder 1,000 tons x ₦.18,750 ($ 250)	= ₦.18,750,000	($ 250,000)
(b)	Yeast tablets		
(c)	Yeast extract		
(d)	Vitamin B complex capsules		
	Yeast contents in (b) (c) & (d), 4,000 tons x ₦.24,750(330)[1]	₦.99,000,000	($1,320,000)
		₦.117,750,000	($1,570,000)

Costs of Production:

(a)	Yeast powder 1,000 tons x ₦.15,000 ($200) =	₦.15,000,000	($ 200,000)
(b)	Yeast tablets		
(c)	Yeast extract		
(d)	Vitamin B complex capsules		
	Yeast contents in (b) (c) & (d), 4,000 tons x ₦.18,562.5($247.5)[2] =	₦. 74,250,000	($ 990,000)
	Total	₦. 89,250,000	($1,190,000)

Estimated gross profit:(3)	₦. 28,500,000	($ 380,000)
Estimated net profit:(4)	₦. 23,550,000	($ 314,000)

Note: (1) Average sale price of yeast tablets, yeast extract and vitamin B complex capsules, counted in yeast powder by ton;

(2) Average cost of production of yeast tablets, yeast extract and Vitamin B complex capsules, counted in yeast powder, by ton (75% of sale price);

(3) Total sales - total costs of production = yearly gross profit;

(4) 20% of total sales as net profit.

Table 12-5 - Pay-Out Time for Yeast Plant

Estimated net profit per year	₦.23,550,000	($ 314,000)
Depreciation per year	7,500,000	($ 100,000)
Total	₦. 31,050,000	($ 414,000)

Pay-out time for the plant: 2 years & 11 months

(Total assets/net profit and depreciation: $1,200,000/$ 414,000)

5. MANUFACTURE OF CHLORAMPHENICOL

Chloramphenicol, now is the official name of the antibiotic, was first introduced in the therapy as "Chloromycetin". Chloramphenicol, next to penicillin and streptomycin in therapy, is used as a chemotherapeutic agent for typhus, typhoid, paratyphoid, reckettsial and enteric infections. The antibiotic was at first produced industrially by using Streptomyces venezulae for submerged fermentation. But now it is produced on an industrial scale by the organic synthetic method at a moderate price. The annual consumption of chloramphenicol is estimated to be 6,000 kg. in Iran and 30,000 kg. in the three RCD countries. In Turkey, no ohloramphenicol production has been started until now. In Pakistan, there is the plant with annual production of 6,000 kg. of chloramphenicol and 5,000 kg. of chloramphenicol esters and the sanctioned additional capaoity will provide the scope for doubling it. In Iran, according to medical necessity, the chloramphenicol plant with annual production of 6,000 kg. of chloramphenicol and its esters may be setting up at the present time. The production capacity might extend up to 8,000 kg. when the demand become larger. If there is certain amount of chloramphenicol out of local consumption, it might export it to Turkey.

The total assets (capital expenditure) of the sanctioned chloramphenicol plant is estimated to be Rs. 37,500,000 (US $ 500,000) (Table 13-2). The plant should consist of (a) a chemical synthetic division for manufacturing the basic drug, chloramphenicol and its esters, and (b) a pharmaceutical processing division for manufacturing various pharmaceutical preparations, such as chloramphenicol capsules, ointments, and

injections, etc. If a chloramphenicol manufacturing unit is set up in an existing pharmaceutical plant, a total assets of Rs. 30,000,000 ($ 400,000) would be enough for only establishing the chemical synthetic division.

The annual production capacity of the plant is estimated to be 6,000 kg. of chloramphenicol and its esters, of which 2,000 kg. supplied to other domestic manufacturers for their processing and 4,000 kg. provided in the forms of capsules and injections. The total sales will be Rs. 48,910,000 ($ 652,140) per year (Table 13-4). A yearly gross profit is estimated to be Rs. 12,625,000 ($ 168,340). If we count 20% of total sales as the net profit, it will have an amount of Rs. 9,782,000 ($ 130,428) of net profit per year (Table 13-4). And, it will yield a pay-out for the plant in 3 years and 3 months (Table 13-5).

Procedure of Chloramphenicol production

Chloramphenicol, which is chemically D-threc-1-p-nitrophenyl-2-diohloracetamide-1,3-propanediol, may be prepared synthetically from the starting material either p-nitrobenzoic chloride or p-nitroacetophenone or otherwise from the intermediate products by reacting p-nitrophenyl-aminopropanediol (known as "active aminodiol") with methyl-dichloracetate in isopropyl alcohol. By starting from the latter, the manufacturing process may be carried out as follows: Neutralize methyldichloracetate by anhydrous potassium carbonate to pH 5. Then take 3 parts of the solution to react with 4 parts of D-threo-1-p-nitrophenyl-2-amino-1,3-propanediol, $C_6H_4(NO_2)$ - CH(OH) - $CH(NH_2)$ - CH_2OH (L-base) in anhydrous isopropyl alcohol. Heat the reaction

solution while hot through filter press and cool to 20°C for crystallize. The product is collected by centrifuging and purified through recrystallization.

Chloramphenicol palmitate is prepared by treating chloramphenicol with palmitoyl chloride (CH_3-$(CH_2)_{14}$-COCl) in the presence of pyridine. The crude ester is obtained by pouring the reaction product into a large excess of dilute hydrochloric acid and filter. It is then purified by recrystallization.

Chloramphenicol sodium succinate is prepared by reacting chloramphenicol with an equimolar portion of succinic acid anhydride to yield chloramphenicol hydrogen succinate. The product after purification by recrystallization, is neutralized with sodium hydroxide to give the official ester salt.

Table 13-1 - Raw Materials Required for Manufacturing Chloramphenicol and Its Esters

"Active aminodiol", D-threo-1-p-nitrophenyl-2-amino-1,3-propanediol, ($C_6H_4(NO_2)$-CH(OH)NH_2)-CH_2OH)
Methyldichloroacetate
Isopropyl alcohol
Potassium carbonate
Active charcoal
* Ammonia water
* Ethyl alcohol
Benzene
Palmitoyl acid
* Hydrochloric acid
Pyridine
Potassium hydroxide

Acetone
Xylene
Succinic acid anhydride
* Sodium hydroxide

Note: Raw materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 13-2 - Total Assets for Chloramphenicol Plant/Unit

Annual production capacity: 6,000 kg.
(3,000 kg. chloramphenicol; 3,000 kg. chloramphenicol esters)

Land (9,400 M^2)	Rls. 1,875,000	($ 25,000)
Buildings (3,000 M^2)	7,500,000	($ 100,000)
Machinery & equipment	15,000,000	($ 200,000)
Erection and Start-up	1,875,000	($ 25,000)
Working capital & others	11,250,000	($ 150,000)
Total	Rls. 37,500,000	($ 500,000)

Table 13-3a - Cost of Production for Chloramphenicol

Raw materials	Rls. 750.0	($ 10.00)
Utilities (water, electricity, fuel, etc.)	187.5	($ 2.50)
Machinery depreciation and maintenance	252.0	($ 3.40)
Labor, direct & indirect	187.5	($ 2.50)
Taxes and insurance	150.0	($ 2.00)
Overhead & Miscellaneous	345.0	($ 4.60)
Total	Rls. 1,875.0	($ 25.00) per kg.

Table 13-3b - Cost of Production for Chloramphenicol Palmitate and Chloramphenicol Sodium Succinate

Raw materials (chloramphenicol and others)	₦. 1,800.0	($ 24.0)
Utilities (electricity, fuel and water, etc.)	112.5	($ 1.5)
Machinery depreciation & maintenance	37.5	($ 0.5)
Labor, direct and indirect	75.0	($ 1.0)
Taxes and insurance	75.0	($ 1.0)
Overhead & miscellaneous	150.0	($ 2.0)
Total	₦. 2,250.0	($ 30.0)

Cost of production for chloramphenicol preparations:

Chloramphenicol capsule (250 mg.): ₦. 1.4/cap.

Chloramphenicol Sodium Succinate Injection: ₦.30/vial (Sterile powder 1 Gm./vial)

Table 13-4 - Estimated Profit from Chloramphenicol Plant/Unit

Annual production: 6,000 kg. Chloramphenicol and its esters

(I) 2,000 kg. chloramphenicol and its esters are supplied to other domestic manufacturers for their processing:

(a) 1,000 kg. chloramphenicol;

(b) 1,000 kg. chloramphenicol palmitate and chloramphenicol sodium succinate.

(II) 4,000 kg. chloramphenicol and its esters are provided in the forms of:

(a) 14,400,000 chloramphenicol capsules (250 mg.)

(b) 400,000 chloramphenicol sodium succinate Injections, (freeze-drying sterile powder 1 gm/vial)

Total Sales[1]:

(I) (a)	1,000 kg. chloramphenicol x ₦.2,550 =	₦. 2,550,000	($ 34,000)
(b)	1,000 kg. chloramphenicol esters x ₦. 3,000 =	3,000,000	($ 40,000)
(II) (a)	14,400,000 chloramphenicol cap. x ₦. 1.9 =	27,360,000	($ 364,800)
(b)	400,000 vials of chloramphenicol sodium succinate Inj. x ₦. 40 =	16,000,000	($ 213,340)
	Total	₦. 48,910,000	($ 652,140)

Cost of production[2]:

(I) (a)	1,000 kg. chloramphenicol x ₦. 1,875 =	₦. 1,875,000	($ 25,000)
(b)	1,000 kg. chloramphenicol esters x ₦.2,250 =	2,250,000	($ 30,000)
(II) (a)	14,400,000 chloramphenicol cap. x ₦. 1.4 =	20,160,000	($ 268,800)
(b)	400,000 vials of chloramphenicol Sodium Succinate Inj. x ₦.30 =	12,000,000	($ 160,000)
	Total	₦. 36,285,000	($ 483,800)

Estimated Yearly Gross Profit:(3) Rls. 12,625,000 ($ 168,340)

Estimated Yearly Net Profit(4): Rls. 9,782,000 ($ 130,428)

( ) Sale prices of chloramphenicol & its preparations:

Note: (Ia) Selling price of chloramphenicol: Rls.2,550 ($34)/kg.

(Ib) Selling price of chloramphenicol esters x Rls.3,000 ($40)/kg.

(IIa) Estimated market price of chloramphenicol cap.: Rls. 2.5/cap.

Wholesale price (75% market price) Rls. 1.9/cap.

(IIb) Estimated market price of chloramphenicol inj.*: Rls. 54/vial

(2) Cost of production of chloramphenicol and its preparations:

Cf. Table 13-3a, Table 13-3b.

(3) Estimated yearly gross profit = Total sales - total cost of production.

(4) Estimated net profit = 20% of total sales.

* In Iran, the market prices of drugs are unstable and not under control. The market price of chloramphenicol Sodium Succinate injection is rather higher than usual, costing Rls. 80 or more per vial (1 Gm.vial).

Table 13-5 - Pay-Out Time for Chloramphenicol Plant

Estimated net profit per year	Rls. 9,782,000 ($ 130,428)
Depreciation per year	1,800,000 ($ 24,000)
	Rls.11,582,000 ($ 154,428)

Pay-out time for the plant: 3 years & 3 months

(Total assets/net profit & depreciation:)

$ 500,000 / $ 154,428

6. MANUFACTURE OF P-AMINOSALICYLIC ACID

P-Aminosalicylic acid (PAS) is one of the chemotherapeutic agents for the treatment of tuberculosis. The annual consumption of aminosalicylic acid is estimated to be 15,000 kg. in Iran, and 80-100 tons in the three RCD countries. But it is not economical to establish a plant with a production capacity of less than 40,000 kg. per year. Since the PAS is a common classic drug used in the therapy, and the raw materials used for manufacturing are quite cheap in the industrialized countries, thus the world price of PAS is considerably low. It will be not very profitable for an establishment of a PAS plant in Iran.

By setting up a plant with the annual capacity of 40,000 kg. of PAS, it would not only meet the domestic demand of this drug in Iran, but there are also surplus amount for exporting to other RCD countries. The total assets of the plant is estimated to be Rs. 22,500,000 (US $ 300,000) (Table 14-2). The total sales is estimated to be Rs. 16,350,000 ($ 218,000) per year. The yearly gross profit will reach Rs. 4,475,000 (US $ 59,600). If we count 20% of total sales as the net profit, it will have Rs. 3,270,000 ($ 43,600) (Table 14-4). And, it will yield a pay-out for the plant in 4 years and 3 months (Table 14-5).

Procedure of Production

P-Aminosalicylic acid is prepared industrially with a good yield by reacting m-aminophenol with carboxylating agent in presence of water at 110°C in autoclave. The carboxylating agent may be sodium, potassium or ammonium carbonate or otherwise liquid carbon dioxide. Aminosalicylic acid may also be

prepared from the basic material, phenol and the later is converted into m-aminophenol by further nitration and reduction. During the nitration of phenol, the ortho, meta and para isomers of nitrophenols are formed in different proportions depending upon the condition of reaction. But only m-aminophenol can be used in the manufacture of p-aminosalicylic acid. Unless there is some way to utilize or sell out the ortho and para isomers of nitrophenol, it would be more economic to use directly m-aminophenol as the starting material. Although the m-aminophenol is not available in Iran, but it can be imported in a reasonable price without any difficulty.

Table 14-1 - Raw Materials Required for Manufacturing P-Aminosalicylic Acid

M-Aminophenol
Sodium carbonate
Active Charcoal
* Hydrochloric acid
Calcium hydroxide
* Ethyl alcohol, etc.

Note: Raw materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 14-2 - Total Assets for P-Aminosalicylic Acid Plant

Annual production: 40,000 kg. PAS

Land	Rls. 1,500,000	($ 20,000)
Buildings	5,625,000	($ 75,000)

Machinery & equipment	Rs. 11,250,000	($150,000)
Erection and start-up	1,875,000	($ 25,000)
Working capital & others	2,250,000	($ 30,000)
	Rs. 22,500,000	($300,000)

Table 14-3 - Cost of Production of PAS

Per Kg. of PAS

Raw materials	Rs. 145
Utilities (electricity, fuel, & water, etc.)	40
Machinery depreciation and maintenance	50
Labor, direct & indirect	30
Taxes and insurance	20
Overhead & miscellaneous	77.5
	Rs. 262.5 ($ 3.5)/kg.

Cost of production of PAS Tab. (0.5 Gm.): Rs. 200/1000 tab.

Table 14-4 - Estimated Profit from PAS Plant

Annual production: 30,000 kg. PAS are supplied to other domestic manufacturers for their processing and for exportation to other RCD countries.

10,000 kg. PAS are provided as tablets (0.5 Gm.): 20,000,000 tablets.

Total Sales[1]: 30,000 kg. PAS x ₦.345 ($4.6)	= ₦. 10,350,000	($138,000)
20,000,000 tab. x ₦. 0.3	= ₦. 6,000,000	($ 80,000)
	₦. 16,350,000	($218,000)
Costs of production[2]:		
30,000 kg. PAS x ₦.262.5 (3.5)	= ₦. 7,875,000	($105,000)
20,000,000 pcs. PAS tab. x ₦.0.2	= ₦. 4,000,000	($ 53,340)
	₦. 11,875,000	($158,340)
Estimated Yearly Gross Profit[3]:	₦. 4,475,000	($ 59,660)
Estimated Yearly net profit[4]:	₦. 3,270,000	($ 43,600)

Note: (1) Selling price of PAS powder: ₦.345 ($4.6) per kg.
Estimated market price of PAS tab.: ₦.0.4/tab.
Wholesale price (75% market price): ₦.0.3/tab.

(3) Estimated yearly gross profit = Total sales - total costs of production.

(4) Estimated yearly net profit = 20% of total sales.

Table 14-5 - **Pay-Out Time of PAS Plant**

Estimated net profit per year	₦. 3,270,000	($ 43,600)
Depreciation per year	₦. 1,968,250	($ 26,250)
	₦. 5,238,250	($ 69,850)

Pay-out time of the plant: 4 years and 3 months
(Total assets/net profit & depreciation:)
$300,000 / $ 69,850

7. MANUFACTURE OF SULFA DRUGS

Sulfa drugs are the widely used antimicrobial agents to against infectious diseases. In spite of the dominance of the antibiotics, the Sulfa drugs still retain an important place in the chemotherapy of infectious diseases. The antimicrobial spectrum of all sulfa drugs is essentially the same. However, on the basis of solubility and degree of absorption from the gastro-intestinal tract, the sulfa drugs can be divided into two broad classes, namely those employed for systemic chemotherapy and those intended only for intestinal chemotherapy. Sulfa drug of the first category includes sulfonanilamide, sulfadiazine, sulfamerazine, sulfamethazine, sulfamethoxine, sulfisoxazole, and sulfamethoxypyridazine, etc. Sulfadiazine is the single sulfa drug most widely employed at the present when the systemic antibacterial actions of these agents are desired. And, sulfamethoxypyridazine has an exceptionally long duration action for a sulfonamide.

On the other hand, certain insoluble sulfa drug congeners, such as succinylsulfathiazole (sulfasuxidine), and Sulfaguanidine, are poorly absorbed from the gastrointestinal tract, to be employed only as an intestinal chemotherapeutic agent.

The annual consumption of various sulfa drugs is estimated to be 60,000 kg. in Iran, and 220,000 kg. in the three RCD countries. At a production capacity of 60,000 kg. per year, it is not an economic scale of production. So, it is better to set up a sulfa drug plant in Iran, with an annual

production of 200,000 kg. of three kinds of representative sulfa drugs for meeting the demands of three RCD countries. In the sanctioned plant, other sulfa drugs may also be prepared by using general method of manufacturing. It will provide 50,000 kg. of sulfadiazine, sulfamethoxypyridazine and sulfaguanidine for domestic consumption, and the surplus plant will be exported to other RCD countries.

The total assets (capital expenditure) of the plant will be Rs. 71,250,000 (US $ 950,000) (Table 15-2). The total sales is expected to be Rs. 155,890,000 ($ 2,078,000) per year. A yearly gross profit is estimated to be Rs. 31,262,000 ($ 416,830). If we count 10% of total sales as the net profit, it will have an amount of Rs. 15,589,000 ($ 207,850) of net profit per year (Table 15-4). And, it will yield a pay-out of the plant in 3 years and 4 months, (Table 15-5).

Procedure of Production

P-Acetaminobenzenesulfonyl chloride, made by treating acetanilide with chlorosulfonic acid, is the basic intermediate of all the sulfonamides. This is treated with the desired amine in presence of a weak base such as pyridine, and the resulting acetyl compound is hydrolytically deacetylated by treating with acid.

Sulfadiazine is prepared by reacting p-acetaminobenzenesulfonyl chloride with 2-aminopyrimidine in the presence of pyridine, then spliting off the acetyl group by hydrolyzing with hydrochloride acid. Sulfamethoxypyridazine is prepared by using 3-amino-6-methoxypyridine for the condensation with the sulfonyl chloride.

For the preparation of sulfaguanidine, p-aminobenzene-sulfonyl chloride is reacted with guanidine nitrate, and then hydrolysed with hydrochloric acid.

Table 15-1 - Raw Materials Required for Manufacturing Sulfa Drugs

Acetanilide
Chlorosulfonic acid
2-Aminopyrimidine
3-Amino-6-methoxypyridazine
Guanidine nitrate
Pyridine
* Hydrochloric acid
Sodium carbonate
Active charcoal
* Ethyl alcohol

Note: Raw materials marked with asterisk (*) are available in Iran, the rest should be imported.

Table 15-2 - Total Asstes Sulfa Drugs Plant

Annual production: 200,000 kg. of sulfadiazine, Sulfa-methoxypyridazine and Sulfaguanidine

Land (11,240 M^2)	Rls. 2,250,000	(US$ 30,000)
Buildings (4,400 M^2)	11,025,000	($ 147,000)
Machinery & equipment	36,000,000	($ 480,000)
Erection and Start-up	3,750,000	($ 50,000)

Services	Rs. 1,875,000	($ 25,000)
Working capital & others	16,350,000	($ 218,000)
	Rs. 71,250,000	($ 950,000)

Table 15-3a - Cost of Production of Sulfadiazine

Per Kilogram

Raw Materials	Rs. 210
Utilities (electricity, fuel, & water, etc.)	70
Machinery depreciation & maintenance	38
Labor, direct & indirect	45
Taxes & insurance	22
Overhead	95
	Rs. 480 ($ 6.4)/kg.

Cost of production of sulfadiazine Tab. (0.5 Gm.): Rs.0.88/tab.

Table 15-3b - Cost of Production of Sulfamethoxypyridazine

Per Kilogram

Raw Materials	Rs. 275
Utilities (electricity, fuel, & water, etc.)	60
Machinery depreciation & maintenance	65
Labor, direct & indirect	56
Taxes & insurance	28
Overhead	116
	Rs. 600 ($ 8.0)/kg.

Cost of production of sulfamethoxypyridazine tab.: Rs.0.96/tab.

Table 15-3c - Cost of Production of Sulfaguanidine

Per Kilogram

Raw Materials	Rls. 60
Utilities (electricity, fuel, & water, etc.)	20
Machinery depreciation & maintenance	12
Labor, direct & indirect	18
Taxes & insurance	8
Overhead & others	26
	Rls. 144 ($ 1.92)/kg.

Cost of production of sulfaguanidine tab.: Rls. 0.66/tab.

Table 15-4 - Estimated Profit for Sulfa Drugs Plant

Annual production: 200,000 kg. Sulfa drugs

		For Iran	Exportation for Pakistan & Turkey	Total
(I)	Sulfadiazine (SD)	25,000 kg.	75,000 kg.	100,000 kg.
(II)	Sulfamethoxypyridazine (SMP)	10,000 kg.	30,000 kg.	40,000 kg.
(III)	Sulfaguanidine (SG)	15,000 kg.	45,000 kg.	60,000 kg.
		50,000 kg.	150,000 kg.	200,000 kg.

Total Sales(1):

(I)(a) SD powder 82,500 kg. (4,500 kg. are supplied to domestic manufacturers & 78,000 kg. for exportation) x Rls.600 ($ 8.00) = Rls.49,500,000 ($660,000)

(b) SD tablets (0.5 Gm.) 35,000,000'S x Rls. 1.1 = Rls.38,500,000 ($513,340)

(II)(a)	SMP powder 33,000 kg. (3,000 kg. are supplied to domestic manufacturers & 30,000 kg. for exportation) x ₦. 750 ($ 10.00)	= ₦. 24,750,000	($ 330,000)
(b)	SMP tablets (0.5 Gm.), 14,000,000'S x ₦. 1.2	= ₦. 16,800,000	($ 224,000)
(III)(a)	SG powder 49,500 kg. (4.5 kg. are supplied to domestic manufacturers & 45.0 kg. for exportation) x ₦. 180 ($ 2.4)	= ₦. 8,910,000	($ 116,600)
(b)	SG tablets (0.5 Gm.) 21,000,000'S x ₦. 0.83	= ₦. 17,430,000	($ 132,400)
		₦.155,890,000	($2,078,540)

Costs of production[2]:

(I)(a)	SD powder, 82,500 kg. x ₦. 480 ($ 6.4)	= ₦. 39,600,000	($ 528,000)
(b)	SD tablets, 35,000,000'S x ₦.0.88	= ₦. 30,000,000	($ 410,670)
(II)(a)	SMP powder, 33,000 kg. x ₦. 600 ($ 8.0)	= ₦. 19,800,000	($ 264,000)
(b)	SMP tablets, 14,000,000x₦.0.96	= ₦. 13,440,000	($ 179,200)
(III)(a)	SG powder, 49,500 kg. x ₦. 144 ($ 1.92)	= ₦. 7,128,000	($ 95,040)
(b)	SG tablets,21,000,000'Sx₦.0.66	= ₦. 13,860,000	($ 184,800)
		₦.124,628,000	($1,661,710)

Estimated yearly gross profit[3]: ₨. 31,262,000 ($ 416,830)

Estimated yearly net profit[4]: ₨. 15,589,000 ($ 207,850)

Note: (1)

(Ia) Selling price of SD powder: ₨. 600 ($ 8.0)

(Ib) Estimated market price of SD tab.(0.5 Gm): ₨.1.5
Wholesale price (75% market price): ₨.1.1

(IIa) Selling price of SMP powder: ₨. 750 ($10.0)

(IIb) Estimated market price of SMP tab.(0.5 Gm): ₨.1.6
Wholesale price (75% market price) : ₨.1.2

(IIIa) Selling price of SG powder: ₨. 180 ($ 2.4)

(IIIb) Estimated market price of SG tab.(0.5 Gm): ₨.1.1
Wholesale price (75% market price): ₨.0.83

(2) Costs of production of sulfa drugs and their preparations, Cf. Tables 15-3a, 15-3b, 15-3c.

(3) Estimated yearly gross profit = total sales = total costs of production.

(4) Estimated yearly net profit = 10% total sales.

Table 15-5 - Pay-Out Time of Sulfa Drugs Plant

Estimated yearly net profit per year	₨.15,589,000 ($207,850)
Depreciation per year	6.300,000 ($ 84,000)
	₨.21,889,000 ($291,850)
Pay-out time of the plant:	3 years and 3 months

(Total assets/net profit & depreciation:)
$ 950,000 / $ 291,850

8. MANUFACTURE OF ASCORBIC ACID (VITAMIN C)

Ascorbic acid or Vitamin C is necessary for the prevention and cure of the deficiency disease scurvy. Anemia is a common occurence in scurvy. Vitamin C is essential for the healing of bone fractures and wound healing and is also a factor in resisting infection. In modern therapy, Vitamin C preparations are widely used either as the curative or the preventive agent for those Vitamin C deficiency cases.

This Vitamin occurs naturally in many plants, vegetables and fruits. It was firstly obtained from the extraction of plant materials. But now it is produced on an industrial scale by the organic synthetic method. The synthetic process starts with glucose or D-Sorbitol and the latter is converted to ascorbic acid through six subsequent steps. Raw materials for the manufacturing ascorbic acid are mostly common in nature and easily obtained either from the local market or by importation from other countries.

Vitamin C is one of the widely used vitamins. The consumption amount of this vitamin is estimated to be 20,000 kg. per year in Iran, and 70,000 kg. in the three RCD countries. At a production capacity of 20,000 kg. of ascorbic acid per year, it is still not large enough for an economical production. Thus, it is better to set up an ascorbic acid plant with annual production of 70,000 kg. for meeting the demands of the three RCD countries, of which 20,000 kg. for the domestic consumption in Iran, and 50,000 kg. may be exported to Pakistan and Turkey.

The total assets of the plant is estimated to be Rls. 45,000,000 (US $ 600,000),(Table 16-2). The value of output (Rls. 63,000,000) will be much greater than the value of input. The yearly gross profit is estimated to be Rials 15,750,000 ($ 210,000). If we count 20% of total sales as the net profit, it will have Rls. 13,600,000 ($ 178,000) as the net profit per year (Table 16-4). And, it will yield a pay-out for the plant in 2 years and 7 months (Table 16-5).

Procedure of Production

One process in common use of the synthesis of ascorbic acid starts with D-glucose which is converted to D-Sorbitol by hydrogenation in presence of a Cu-Cr catalyst. The D-Sorbitol in aqueous solution is converted by the action of the micro-organism, Acetobacter suboxydans to L-sorbose, which is a ketose. The L-sorbose is then condensed with acetone by means of Sulfuric acid to form diacetone sorbose. The diacetone sorbose, after suitable purification, oxidized by potassium permanganate in aqueous alkaline solution and then hydrolysed with water at boiling temperature forming 2-keto-L-gulonic acid. This acid is esterified with methanol and an intermediate Sodio compound is formed with sodium methoxide. Hydrolysis with aqueous HCL in presence of nitrogen removes the methyl group and sodium and lactonises it yielding the final product, ascorbic acid.

Table 16-1 - Raw materials Required for Manufacturing Ascorbic Acid

D-Sorbitol

Acetobacter suboxydans, strain

- * Sucrose
  Lactose
- * Glucose
- * Ammonium sulfate
  Sodium citrate
  Sodium phosphate
- * Grain extracts
- * Calcium carbonate
  Acetone
- * Sulfuric acid
  Potassium permanganate
- * Sodium hydroxide
  Ethylenediamine-tetraacetate (EDTA)
- * Hydrochloric acid
  Nitrogen, liquified, etc.

Note: Raw materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 16-2 - Total Assets for Ascorbic Acid Plant

Annual production: 70,000 kg.

Land	Rls. 3,750,000	(US$ 50,000)
Buildings	7,500,000	($ 100,000)
Machineries & equipment	22,500,000	($ 300,000)
Erection & start-up	3,750,000	($ 50,000)
Services	1,500,000	($ 20,000)
Working capital and miscellaneous	6,000,000	($ 80,000)
	Rls. 45,000,000	($ 600,000)

Table 16-3 - Cost of Production of Ascorbic Acid

Raw materials	Rls. 187.5
Utilities (electricity, fuel, and water, etc.)	60.0
Machinery depreciation & maintenance	63.8
Labor, direct & indirect	48.7
Taxes and insurance	15.0
Overhead & others	75.0
	Rls. 450.0/kg.

Costs of production of ascorbic acid preparations:

Ascorbic Acid Tablets (100 mg.): Rls. 0.18/tab.

Ascorbic Acid Injection: Rls.24.0 /box
(100 mg/2 ml., 100 ampoules each box)

Table 16-4 - Estimated Profit from Ascorbic Acid Plant

Annual production: 70,000 kg. Ascorbic acid

5,000 kg. supplied to other domestic manufacturers for their processing;

15,000 kg. provided in the forms of preparation:
Tablets (100 mg.), 75,000,000 pcs;
Injections (100 mg./2 ml., 100 amp. each box):
375,000 boxes.

50,000 kg. for expertation to other members of the RCD countries, Pakistan and Turkey.

Total Sales:(1)

55,000 kg. Ascorbic acid x ₦.600 ($8.0)	= ₦. 33,000,000	($ 440,000)
75,000,000'S Tab. (100 mg.) x ₦. 0.24	= ₦. 18,000,000	($ 240,000)
375,000 boxes of Inj.(100 mg./2ml., 100 amp. each box) x ₦. 32	= ₦. 12,000,000	($ 160,000)
	₦. 63,000,000	($ 840,000)

Costs of Production:(2)

55,000 kg. Ascorbic acid x ₦.450 ($6.0)	= ₦. 24,750,000	($ 330,000)
75,000,000'S Tab. (100 mg.) x ₦. 0.18	= ₦. 13,500,000	($ 180,000)
375,000 boxes of injection x ₦. 24	= ₦. 9,000,000	($ 120,000)
	₦. 47,250,000	($ 630,000)

Estimated Yearly Gross Profit:(3) ₦. 15,750,000 ($ 210,000)

Estimated Yearly Net Profit:(4) ₦. 13,600,000 ($ 178,000)

Note:

(1) Selling price of ascorbic acid: ₦.600 ($8.0) per kg.

Estimated market price of Ascorbic acid Tab.: ₦.0.32/tab.
Wholesale price (75% market price): ₦.0.24/tab.

Estimated market price of Ascorbic acid Inj. ₦. 42/box
Wholesale price (75% market price): ₦. 32/box

(2) Costs of production:

Ascorbic acid in bulk:	₦. 450 ($ 6.0)
Ascorbic Tab.:	₦. 0.18/tab.
Ascorbic Acid Inj. : (cf. Table 16-3)	₦. 24/box

(3) Estimated yearly gross profit = total sales - total costs of production

(4) Estimated yearly net profit: 20% total sales

Table 16-5 - Pay-out Time for Ascorbic Acid Plant

Estimated net profit per year	฿.13,600,000	($ 178,000)
Depreciation per year	4,462,500	($ 59,500)
	฿.18,062,500	($ 237,500)

Pay-out time for the plant: 2 years and 7 months

(Total assets/net profit & depreciation:)
$ 600,000 / $ 237,000

9. MANUFACTURE OF CALCIFEROL (VITAMIN D_2)

Calciferol, or ergocalciferol is known as Vitamin D_2, and like other forms of Vitamin D, it exhibits both anti-rachitic and calcemic effects. In former days, the cod liver oil and other fish liver oils were used for their contents of Vitamin A and D. It offers the advantages of being relatively inexpensive, the disadvantage of the large volume dosage in comparison with concentrates, and other pure vitamin A and D preparations. Pure vitamin D_2 or D_3 (cholecalciferol, activated 7-dehydrocholesteral) is mostly recommended in modern therapy as the preventive and curing agents for vitamin D deficiency cases. Addition of vitamin D to appropriate foods has been an important factor in the prevention of any important degree of rickets in many countries. Vitamin D milk has been of particular importance of this respect, because of its use for infant feeding, during the stage of growth most susceptible to rachitic change.

The annual consumption of calciferol (vitamin D_2) is estimated to be 100 kg. in Iran and 500 kg. in the three RCD countries. It is suggested to set up a calciferol plant/unit with an annual production capacity of 100 kg. of crystalline calciferol, of which 50 kg. are supplied to other domestic manufacturers for their processing and also for enriched foodstuffs, and 50 kg. are provided in the forms of tablets, oily solutions and injections. The total assets of the sanctioned calciferol plant/unit will be only Rls. 6,000,000 (US $ 80,000), (Table 17-2). The value of output will be approximately four times greater than the value of input, because

the calciferol is a product of high price. The yearly gross profit is expected to be ₹. 6,322,500 ($ 84,310). If we count 20% of total sales as the net profit, it will have ₹. 4,738,000 ($ 63,176) of net profit per year (Table 17-4). The expected profit from this project is anyhow attractive. It will yield a pay-out of the plant/unit in only one year and 2 months (Table 17-5).

Procedure of Production

Vitamin D_2 may be obtained from natural sources such as fish liver oils or prepared synthetically. The plant sterol, ergosterol is the precursor of vitamin D_2. Ergosterol is activated to Vitamin D_2 by irradiation of its alcohol, ether or benzene solution in a concentration of 20% with ultra violet light at the wave length between 275-300 mu. for about ten hours. There is a large portion (around 60%) of ergosterol transformed to irradiated product, which should be separated from other inactive neighboring substances. It involves a series of chemical compounds in the operation, only one of which is active as vitamin. Upon prolonged irradiation, the vitamin D formed is destroyed, and a toxic substance, toxisterol is produced. The amount of toxisterol formed is dependent in part upon the solvent used. Thus it is important that the irradiation process be carefully controlled, both from standpoint of obtaining the high yield of vitamin D_2 and of preventing the formation of toxiferol. Vitamin D_2 may be separated from other impurities (inactive substances) and purified by passing its benzenic or ethereal solution through the chromatographic columns of activated alumina. The adsorbent is eluted with benzene and finally the pure vitamin D_2 is obtained by crystallization from benzenic solution.

Table 17-1 - Raw Materials Required for Manufacturing Vitamin D_2

Ergosterol
Ether, anhydrous
Benzene
Activated alumina for chromatography

Note: Raw materials should be imported from other countries.

Table 17-2 - Total Assets for Calciferol (Vitamin D_2) Plant/Unit

Annual production: 100 kg. (4 million mega units)
calciferol 0.25 mg. = 10,000 U

Land	฿. 375,000	(US$ 5,000)
Buildings	1,200,000	($ 16,000)
Machinery & equipment	2,850,000	($ 38,000)
Erection & start-up	450,000	($ 6,000)
Services	375,000	($ 5,000)
Working capital & others	750,000	($ 10,000)
	฿. 6,000,000	($ 80,000)

Table 17-3 - Cost of Production of Calciferol

Per kg.

Raw materials	₦. 15,000	($ 200)
Utilities (electricity, fuel, & water, etc.)	4,050	($ 54)
Machinery depreciation & maintenance	4,500	($ 60)
Labor, direct & indirect	3,300	($ 44)
Taxes & insurance	750	($ 10)
Overhead & other	6,150	($ 82)
	₦. 33,750	($ 450)/kg.

Cost of production of calciferol preparations: ₦.33.75 ($0.45)/Gm.

Calciferol Tab. (50,000 U): ₦. 1.0 each tab.

Calciferol Inj. (500,000 U/ml., 10 ml.vial): ₦. 24/vial

Table 17-4 - Estimated Profit from Calciferol Plant/Unit

Annual production: 100 kg. crystalline calciferol

(a) 50 kg. are supplied to other domestic manufacturers for their processing;

(b) 10 kg. are provided as 8,000,000 tablets (50,000 U each tablet);

(c) 40 kg. are provided as 320,000 vial of injections (500,000 U/ml., 10 ml. vial)

Total Sales:(1)

(a)	50 kg. Calciferol x ₦.45,000 ($600)	= ₦. 2,250,000	($ 30,000)
(b)	8,000,000 tablets x ₦. 1,4	= ₦. 11,200,000	($ 149,340)
(c)	320,000 vials x ₦. 32	= ₦. 10,240,000	($ 136,540)
		₦. 23,690,000	($ 315,880)

Costs of production:(2)

(a)	50 kg. Calciferol x ₦.33,750 ($450)	= ₦. 1,687,500	($ 22,500)
(b)	8,000,000 tablets x ₦. 1.0	= ₦. 8,000,000	($ 106,670)
(c)	320,000 vials x ₦. 24	= ₦. 7,680,000	($ 102,400)
		₦. 17,367,500	($ 231,570)

Estimated yearly gross profit:(3)	₦. 6,322,500	($ 84,310)
Estimated yearly net profit:(4)	₦. 4,738,000	($ 63,176)

Note:(1)(a) Selling price of Calciferol: ₦. 45,000 ($600)/kg.

(b) Estimated market price of Calciferol tab.: ₦.1.8/tab.
Wholesale price (75% market price): ₦.1.4/tab.

(c) Estimated market price of Calciferol in.: ₦.42/vial
Wholesale price (75% market price): ₦.32/vial

(2) Costs of production of Calciferol and its preparations, Cf. Table 17-3.

(3) Estimated yearly gross profit = total sales - total costs of production.

(4) Estimated yearly net profit = 20% total sales.

Table 17-5 - Pay-Out Time of Calciferol Plant/Unit

Estimated net profit per year	Rs. 4,738,000	($ 63,176)
Depreciation per year	450,000	($ 6,000)
	Rs. 5,188,000	($ 69,176)

Pay-out of the plant: 1 year and 2 months

(Total assets/net profit & depreciation)
$ 80,000 / $ 69,176

10. MANUFACTURE OF DEXTROSE (D-GLUCOSE)

Glucose is a sugar usually available in commerce in two forms: liquid glucose is known as syrup glucose and crystallized D-glucose is known as dextrose. There is only pure, crystallized dextrose (D-glucose) being recommended for the pharmaceutical uses. In the therapy, dextrose is given in all conditions associated with insufficiency of carbohydrates. It provides a rapidly source of energy. Dextrose powder or with vitamins are provided for oral administration and dextrose injection is for the parenteral use. It is also used to supplement the sugar content of cow's milk or of milk powder in infant feeding.

According to information compiled by the Iranian Custom Office, the annual importation of glucose amounted to 3,862 tons in 1965, and 2,470 tons in 1966. By the term "glucose", it included both dextrose and liquid glucose. The annual consumption of dextrose is estimated to be 500-800 tons in Iran.

The productive capacity of the sanctioned dextrose plant will be 500 tons, of which 200 tons are supplied to other domestic manufacturers for their processing, and 300 tons are provided in powder form (with or without addition of vitamins) for oral administration. The total sales of dextrose plant is estimated to be Rls. 45,000,000 (US $ 600,000) (Table 18-2). The value of out-put is almost the same as the value of input. A gross profit is estimated to be Rls. 10,800,000 ($ 144,000). If we count 20% of total sales as the net profit, it will have a net profit of Rls. 9,160,000 ($ 122,134) per year (Table 18-4). It will yield a pay-out for the plant in 3 years and 5 months (Table 18-5).

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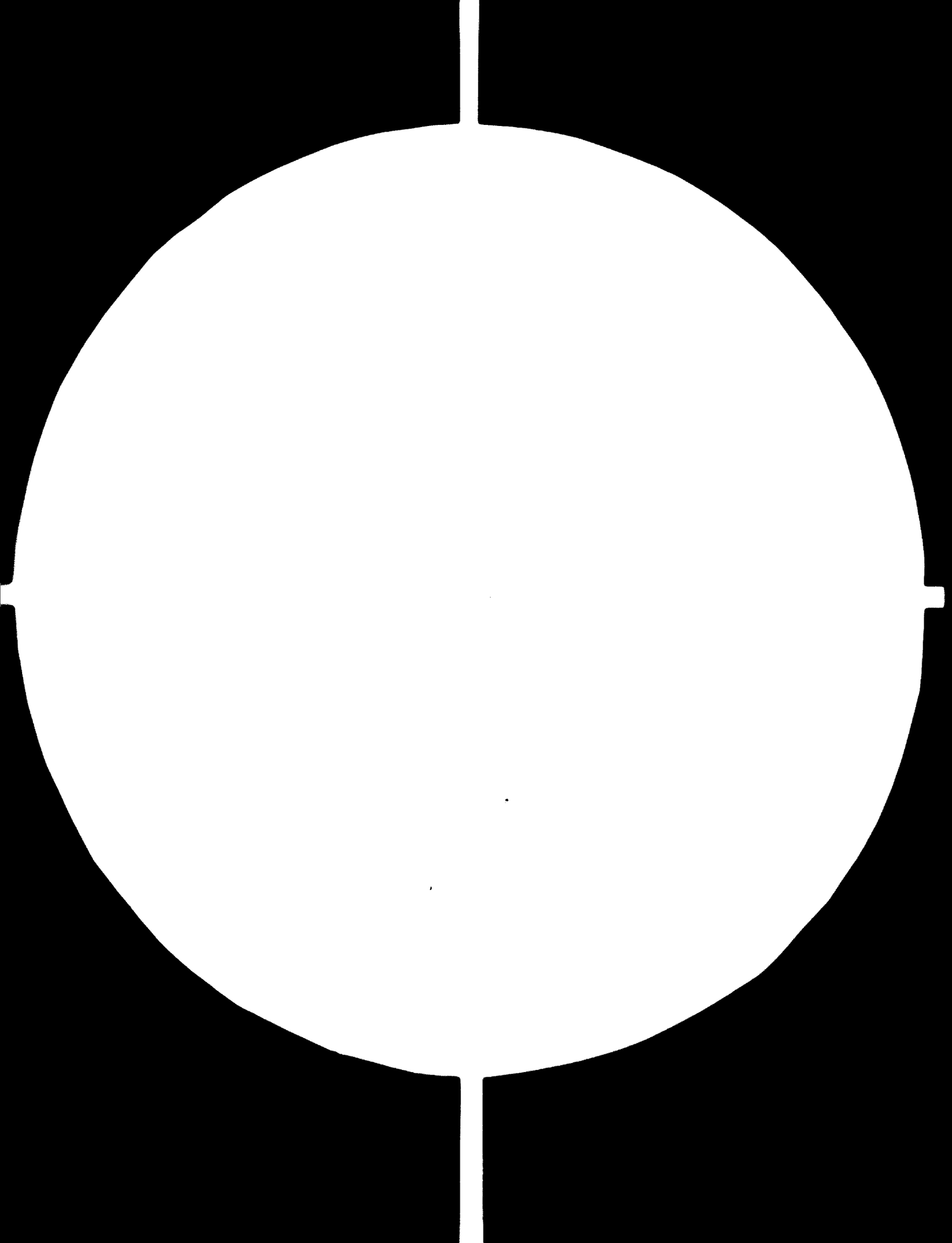

There is a liquid glucose plant, the Glucose and Starch Factory of Iran, which was built at Tehran in 1965, producing about 2,000 tons of liquid glucose per year. It is suggested that the liquid glucose plant, with additional equipment to its existing facilities of machinery and installation, could produce 500 tons more of pure, crystallized dextrose. For the expansion programme, the additional equipment and installation at a cost of Rs. 7,500,000 (US $ 100,000) will be required.

Procedure of dextrose production

The industrial scale of dextrose production starts with starch by hydrolysis. The starch is mixed with 10 times its weight of dilute sulfuric acid at 5%, the mixture is heated in an autoclave to about 105-110°C. The temperature is maintained at this point for about an hour more or until tests show the complete disappearance of starch. After acid hydrolysis, the material is neutralized with calcium carbonate, filtered, then decolorized with charcoal or bone-black.

For manufacturing pure dextrose, it is necessary to purify the dextrose solution from hydrolysing by passing ion-exchange resin columns prior to vacuum concentration. The concentrated dextrose solution is then introduced into crystallizer for crystallization. The crystal dextrose is separated from mother liquor after centrifuging, purified by recrystallization from alcohol (90%) twice, and finally dried in the steam-heated rotary tube-dryer.

In the manufacture of dextrose, it is necessary to operate in a closed system. All manipulations as separating, collecting and drying of dextrose crystals should be undertaken

in a separated working area of filtered air in order to prevent the product from any contamination by bacteria, molds and other micro-organisms.

Table 18-1 - Raw Materials Required for Manufacturing Dextrose

Starch, corn
* Sulfuric acid
* Calcium carbonate
Active charcoal, decoloring
Ion-exchange resins
* Ethyl alcohol

Note: Materials marked with asterisk (*) are available in Iran; the rest should be imported from other countries.

Table 18-2 - Total Assets for Dextrose Plant

Land (10,000 M^2)	Rls. 2,025,000	($ 27,000)
Buildings (37,500 M^2)	9,375,000	($ 125,000)
Machinery & equipment	22,500,000	($ 300,000)
Erection & start-up	3,750,000	($ 50,000)
Services	750,000	($ 10,000)
Working capital & others	6,600,000	($ 88,000)
Total	Rls. 45,000,000	($ 600,000)

Table 18-3 - Cost of Production of Dextrose

Raw materials	Rs. 34
Utilities (electricity, fuel, and water, etc.)	6
Machinery depreciation and maintenance	8
Labor, direct & indirect	4
Taxes and insurance	1.5
Overhead and others	5.5
	Rs. 60.0
Packing charges	10.0
	Rs. 70.0/kg.

Table 18-4 - Estimated Profit from Dextrose Plant

Annual production: 500,000 kg. dextrose

(a) 200,000 kg. supplied as basic drug. to other domestic manufacturers for their processing;

(b) 300,000 kg. provided in the form of dextrose powder (with or without vitamins) for oral use.

Total Sales:

(a) 200,000 kg. x Rs. 88[1a] = Rs. 17,600,000 ($ 234,670)

(b) 300,000 kg. x Rs. 94[1b] = Rs. 28,200,000 ($ 376,000)

Rs. 45,800,000 ($ 610,670)

Costs of production:

(a)	200,000 kg. x Rs.70[2]	= Rs. 14,000,000	($ 186,670)
(b)	300,000 kg. x Rs.70[2]	= Rs. 21,000,000	($ 280,000)
		Rs. 35,000,000	($ 466,670)

Estimated yearly gross profit[3]: = Rs. 10,800,000 ($ 144,000)

Estimated yearly net profit[4]: = Rs. 9,160,000 ($ 122,134)

Note: (1a) Selling price of dextrose powder: Rs. 88/kg.

(1b) Estimated market price of dextrose powder for oral use: Rs. 125/kg.

Wholesale price (75% market price): Rs.94/kg.

(2) Cost of production of dextrose (Table 18-3): Rs.70/kg.

(3) Estimated yearly gross profit = Total sales - total costs of production

(4) Estimated yearly net profit: 20% of total sales.

Table 18-5 - Pay-out Time for Dextrose Plant

Estimated net profit per year	Rs. 9,160,000	($ 122,134)
Depreciation per year	4,000,000	($ 53,334)
	Rs. 13,160,000	($ 175,468)

Pay-out time for the plant: 3 years and 5 months

(Total assets/net profit & depreciation:)

($ 600,000 / $ 175,468)

Among the above mentioned basic drug plants to be sanctioned in Iran, the priority of establishing plants is recommended according to the value of output and the profitableness of the plants as follows:

Priority order	Sanctioned Plants	Annual Production	Total Assets	Estimated Yearly output U.S.$	Estimated Yearly net profit US$	Pay-out time of plant, year-month
1	Tetracycline plant	10,000	1,200,000	1,277,600	255,520	3-2
2	Chloramphenicol plant	6,000	500,000	872,340	158,468	3
3	Penicillin & procaine plant	15,000 Ph. (20 MMU) 10,000 Pr.	2,600,000	2,818,760	563,752	3
4	Streptomycin & Vitamin B_{12}	10,000 Str. 8 V.B_{12}	1,400,000	1,735,740	260,360	3-8
5	Calciferol (Vit. D_2) plant	100	80,000	310,880	62,770	1-2
6	Yeast plant	5,000,000	1,200,000	1,560,000	312,000	3
7	Ascorbic acid (Vit. C.) plant	70,000	600,000	775,000	155,000	2-10
8	Sulfa drugs plant	200,000	950,000	2,078,540	207,850	3-3
9	P-Aminosalicylic acid plant	40,000	300,000	285,000	57,000	3
10	Dextrose plant	500,000	600,000	610,000	122,134	3-5

CHAPTER IV

CONCLUSIONS AND RECOMMENDATIONS

(1) The total importation of pharmaceuticals in Iran reached Rls. 3,598,956,000 (US$ 47,987,080) in 1966. The domestic pharmaceutical production ranged between 6.5 - 8.1% against the imported products, 91.9% - 93.5% in 1963 through 1965.

(2) It is recommended that the importation of unnecessary proprietary drugs should be restricted and reduced to a minimum amount without depriving the medical profession of essential life-saving drugs.

(3) The processing capacity for pharmaceuticals is slightly short in Iran at the present. Domestic pharmaceutical plants should be encouraged in producing more quality pharmaceuticals, and also bringing their production up to the full capacity. It is recommended that four or more larger scale pharmaceutical processing plants, with the capital cost of Rls. 187,500,000 (US$ 2,500,000) for each plant may be planned to set up for meeting the full demands. The total value of yearly output of those sanctioned plants is expected to be Rls.750,000,000-900,000,000 ($ 10,000,000 - 12,000,000).

(4) Temporary moratorium on the establishment of new small scale domestic plants and foreign pharmaceutical processing plants should be declared.

(5) At present, there is no basic drug manufacture in Iran. The manufacture of basic drugs should be encouraged under the Government's protective policy, or under Governmental management and financed by the Government. Since the world prices of some basic drugs such as, acetylsalicylic acid (aspirin), p-aminosalicylic acid, and sulfa drugs, etc. are considerably low and the costs of production for local manufacture are high, fairly heavy protection would permit the joint venture manufacture of basic drugs in the RCD countries.

(6) A modern drug control law should be enacted with provision for regulating the manufacture, distribution, and sale of drugs. Strict quality control inspection of all pharmaceutical products should be established. The regulation and control of the pharmaceutical industry should be effected from the very beginning. An uncontrolled and irresponsible pharmaceutical industry can do more harm than good to a country.

(7) The central drug control laboratory should be reinforced for carrying its big responsibility to examine and test different batches of imported and domestic manufactured pharmaceuticals.

(8) National pharmacopoeia is a collection of well recognized basic drugs and formulas with given standards, methods of preparation, test and assay, etc., usually served as a guide book for drugs in medicine and pharmacy. A national Iranian Pharmacopoeia Committee should be organized

under the auspices of Government in preparing and issuing the first edition of Iranian pharmacopoeia as soon as possible.

(9) The use of pharmacopoeial official drugs for prescription by the physicians should be encouraged. The use of official drugs is more safe and economic.

(10) It is suggested that the Iranian Government provide a fund for establishing a national pharmaceutical research institute, or otherwise asking the collaboration of pharmacy colleges for carrying out the pharmaceutical research works. The research project will cover: (a) basic pharmaceutical research; (b) domestic manufacturing of basic drugs; (c) new drug research; and (d) new pharmaceutical product development, etc.

(11) It is recommended that the Ministry of Economy could send the national counter-part of my programme to the U.S.A. by the United Nations Fellowship grant for a period of one year to study at first hand the regulatory operations including the pharmaceutical factory registration and inspection system, etc.

(12) Feasibility studies on the establishment of some basic drug plants in Iran have been made.

(a) Plants of antibiotics and other products by fermentation:

1. Penicillin and procaine plant, with annual production of 20 million mega units or 15,000 kg. of penicillins, will have its capital cost, Rls.195,000,000 (US Dollars 2,600,000). The value of yearly output is estimated to be Rls. 211,407,060 ($ 2,818,760), and yearly net profit, Rls. 42,281,400 ($ 563,752). It will yield a pay-out for the plant in 3 years and 5 months.

2. Tetracycline and chlortetracycline plant, with annual production of 10,000 kg. of tetracycline and chlortetracycline, will have its capital cost, Rls. 90,000,000 ($ 1,200,000). The value of net profit is estimated to be Rls. 19,164,000 ($ 255,520). It will yield a pay-out for the plant in 3 years and 2 months.

3. Streptomycin and Vitamin B_{12} plant, with annual production of 10,000 kg. of streptomycin and dihydrostreptomycin, as well as 8 kg. of vitamin B_{12}, will have a capital cost of Rls. 105,000,000 ($ 1,400,000). The value of yearly output is estimated to be Rials 130,180,000 ($ 1,735,740), and net profit, Rials 19,527,000 ($ 260,360). It will yield a pay-out for the project in 3 years and 8 months.

4. Yeast plant, with annual production of 5,000 tons yeast in the forms of powders and preparations, will have the capital cost, Rls. 90,000,000 ($ 1,200,000). This is a project for the three RCD countries. The value of output is estimated to be Rls. 117,000,000 ($ 1,560,000), and net profit, Rls.23,400,000 ($312,000). It will yield a pay-out for the plant in 3 years.

(b) Plants of Synthetic drugs:

5. Chloramphenicol plant, with annual production of 6,000 kg. chloramphenicol and its esters, will have the capital cost, ₨. 37,500,000 ($ 500,000). The value of yearly output is estimated to be ₨. 65,425,000 ($ 872,340) and yearly net profit, ₨. 11,885,000 ($ 158,468). The pay-out time for the plant is 3 years.

6. P-Aminosalicylic acid (PAS) plant, with annual production of 40,000 kg. of PAS, will have its capital cost ₨. 22,500,000 ($ 300,000). Besides the domestic consumption, there is the surplus amount for exporting. Estimated value of output will be ₨. 21,375,000 ($ 285,000), and net profit, ₨.4,275,000 ($ 57,000). It will yield a pay-out for the plant in 3 years.

7. Sulfa-drugs plant, with annual production capacity of 200,000 kg. of sulfadiazine, sulfamethoxypyridazine, and sulfaguanidine, will have its capital cost, ₨. 71,250,000 ($ 950,000). This is a project for the three RCD countries. Estimated yearly output will be ₨. 155,890,000 ($ 2,078,540) and net profit, ₨. 15,589,000 ($ 207,850). The pay-out time for the plant is 3 years and 3 months.

8. Ascorbic acid (Vitamin C) plant, with annual production of 70,000 kg. of ascorbic acid, will have the capital cost, ₨. 45,000,000 ($ 600,000). This

is a project for the three RCD countries. The value of yearly output is estimated to be Rls. 58,125,000 (Dollars 775,000), and net profit, Rls. 11,625,000 ($ 155,000). It will yield a pay-out for the plant in 2 years and ten months.

9. Calciferol (Vitamin D_2) plant, with annual production capacity of 100 kg., will have its capital cost, Rls. 6,000,000 ($ 80,000). Estimated value of output will be Rls. 23,690,000 ($ 310,880), and net profit, Rials 4,708,000 ($ 62,770). It will yield a pay-out for the plant in only one year and 2 months.

10. Dextrose (D-glucose) plant, with annual production of 500,000 kg. of crystalline dextrose, will have its capital cost, Rls. 45,900,000 ($ 600,000). The value of yearly output is estimated to be Rls.45,800,000 ($610,670) and net profit, Rls. 9,160,000 ($ 122,134). The pay-out time for the plant is 3 years and 5 months.

(c) Drugs of vegetable origin:

The top items of vegetable drug exportation cover liquorice (glycyrrhiza) roots, gum tragacanth and asafetida, etc. It is recommended that the liquorice roots for exportation are better processed into the forms of liquorice extracts and fluidextracts. It will be more profitable for the exportation of those liquorice products.

(d) Drugs of animal origin:

No plants of animal product manufacture can be established until the large-scale slaughter houses are available.

(e) Plants of biological products

The expansion project of biological products manufacturing for the Razi Institute may be undertaken into consideration. Otherwise, the new sera and vaccines plant may be set up in producing more biological products for human and veterinary uses.

A big item of imports under pharmaceuticals is baby food, chiefly milk powders. The imports amounted to Rs. 263,887,000 in 1966. It is suggested that the manufacture of baby food (milk powder enriched with sugar, vitamins and minerals) from locally produced milk and other accessories may be started at an early date.

(13) Among the above mentioned basic drug plants to be sanctioned in Iran, the priority of establishing plants is recommended according to the value of output and the profitableness of the plants as follows:

Priority order	Sanctioned Plants	Annual Production kg.	Total Assets US $	Estimated Yearly output U.S.$	Estimated Yearly net profit US$	Pay-out time of plant, year-month
1	Tetracycline plant	10,000	1,200,000	1,277,600	255,520	3-2
2	Chloramphenicol plant	6,000	500,000	872,340	158,468	3
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5	Calciferol (Vit. D_2) Plant	100	80,000	310,880	62,770	1-2
6	Yeast plant	5,000,000	1,200,000	1,560,000	312,000	3
7	Ascorbic acid (Vit. C) plant	70,000	600,000	775,000	155,000	2-10
8	Sulfa drugs plants	200,000	950,000	2,078,540	207,850	3-3
9	P-Aminosalicylic acid plant	40,000	300,000	285,000	57,000	3
10	Dextrose plant	500,000	600,000	610,000	122,134	3-5

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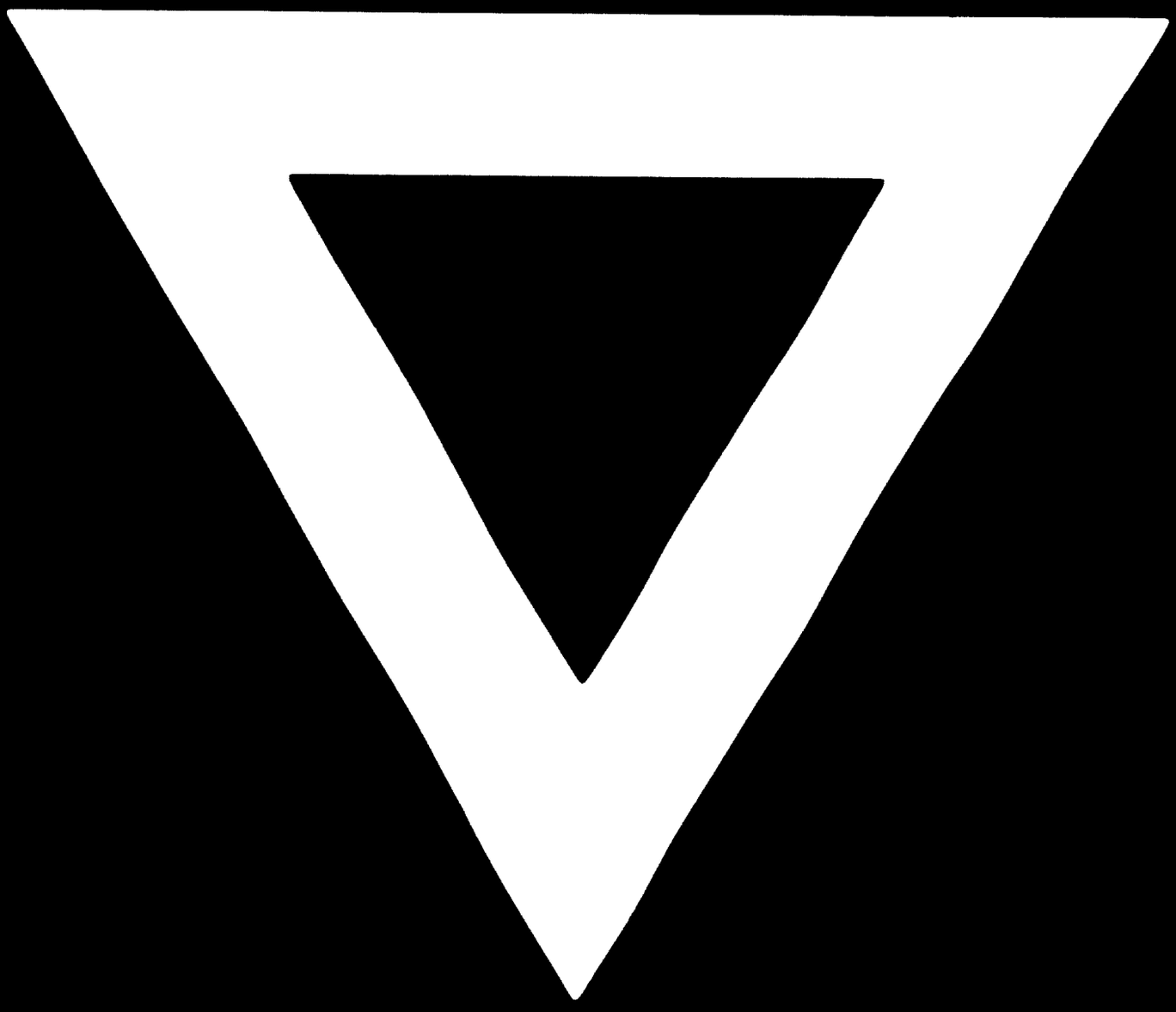

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