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APPROPRIATE TECHNOLOGY FOR THE MANUFACTURE OF DRUGS AND PHARMACEUTICALS

APPROPRIATE TECHNOLOGY IN DRUG AND PHARMACEUTICAL INDUSTRIES ,
Background Paper

APPROPRIATE TECHNOLOGY IN DRUG AND PHARMACEUTICAL INDUSTRIES

by

Indian Drugs and Pharmaceuticals Limited,
New Delhi

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CONTENTS

SUMMARY

An attempt has been made in this paper to serve particularly the different aspects of the drugs and pharmaceuticals industry with particular reference to the drug needs in developing countries. There is no doubt that many developing countries have a long way to go in cultivating sophisticated technology in this field. However, the competence of various developing countries in adopting the production in the field of drugs and pharmaceuticals varies which is due not only to the different stages of educational development in general and of technological competence in particular, but also due to capital-intensive requirement of these industries. Such modifications need fairly accurate standards and where human life is concerned, this compromise is not possible. All the developing countries are in the process of reorganising their health needs and today even the more developed among the developing countries are not prepared to provide medical needs to more than 20% of their population. Obviously, therefore, the drugs and pharmaceutical industry in these countries envisages to have greater justification in this regard.

It is fairly necessary that each of the developing countries defines its scope of production and phases out the work to be undertaken in this direction with ability to expand this for future development. In fact, in conditions, such as bacterial, parasitic, helminthic infections, the spectrum of their drug needs is materially different as that of the developed countries. A reference to this has been made in some detail in this paper.

The developing countries are now in the process of drawing up lists of essential drugs that may fit in for their requirements, and that may take care of a large percentage of their health needs. Obviously, these countries did need to make concerted efforts in the production of these essential drugs. Some of the essential drugs that are available conform, in general, to the basic drug lists published by the World Health Organisation recently.

Whereas bulk drugs production is technology-and-capital-intensive, the formulation industry is historically less expensive. It is fairly easier for the developing countries to import bulk drugs to begin with and formulate them in their own countries. The technological content of bulk drugs also varies from drug to drug over a wide range and the developing countries would naturally have to begin with the production of such bulk drugs as may require simpler technologies so that they may create capability to scale up the same, and the more complicated technologies can be taken at a later stage.

It has been tried to impress that in spite of varying sizes of the different developing countries and their physical capabilities and needs, it may be more economic to organise such regional production units as may

1. PREFACE

THE term "technology" refers to the process of transformation of inputs into outputs. Modern technology tends to be capital intensive and maximises output per unit of time and labour. Such a technology is suited to countries where labour is scarce but capital is abundant. Some developing countries have, conscious or unconscious of the consequences of using such technologies adopted them in the early stages of planned economic development. The objective was to maximise output. But, it has turned out that as a long run measure it is not satisfactory. Developing countries generally have a large under-employed man-power, lack capital and have very uneven distribution of income. So, when capital intensive technologies are used, only a few are employed. Also, financial constraints limit the number of projects that can be taken up. The effect of these things is that income does not spread out and so the population does not have the purchasing power. So the outputs (which are attempted to be maximized do not /have any demand and leads to gross under utilisation of capacity. Also, even when the GNP grows, the poor stay poor and this leads to a lot of undersirable socio-economic problems. In short it is not advisible for developing countries to copy the developing world in choice of technology or in development strategy. The developed world maximises output per unit of labour (which is scarce) with the capital resources it has.

In the developing world it is the capital that is scarce so the objective should be to get the maximum output per unit of capital, cashing in on the labour resources they have. To put it more generally, every country should use the technology that takes both the strengths and weaknesses into account. Such a technology may be called the technology appropriate for that country or, for short, "Appropriate Technology".

Most of the developing countries do not have an established pharmaceutical industry even today. Obviously these countries would do well to keep the foregoing in mind when they start setting up one. Even those which have some what established Drug industry should try and adopt the kind of technology appropriate under the circumstances.

Let us not think of "Technology" as referring only to process know-how. We shall talk of it as "the mode of management of health care needs of the country". Technology, in this sense will refer to mode of manufacturing, marketing and financing.

This paper discusses the kind of technology would be appropriate to Drug Industry in Developing Countries.

2. INTRODUCTION

Health is one of the basic needs of all living beings. From the ages of alchemists and crude surgeons, medical science has developed and is to-day one of the pillars of modern civilization. Ever since it was discovered that certain chemicals administered in a certain fashion can lesson or completely cure diseases, a specialised sector of chemical industry has come to exist. This sector, which has already attained the status of an industry is the drugs and pharmaceutical industry.

Since the human body is very sensitive to foreign particles, the chemical used and the amount thereof and the form in which it is taken have to be very carefully determined, it has very strict specifications. Since the remedies have to have some bio-logical action, most drugs have complex structures and stero-specific action. Hence the complexity of industry itself.

Industrialisation and allopathy came rather late to what have come to be known as developing countries. Hence the drugs and pharmaceutical industry also lagged behind (in these countries) that in the developed world. Nevertheless, the D&P industry in developing countries has made commendable progress.

This paper is meant to be a basis for discussion at this UNIDO conference on Appropriate Technology for developing countries. This conference would take stock of the status of the D&P industry in the developing world, and, since the technology being used in the developed world is not necessarily

the most suited for every coun ry, suggest what kind of technology would be most ap ropriate for a developing country.

The word "Technology", in this paper has a broader sense and covers all aspects of business.

It is presented in ten sections. This presents the status of the industry in the developing world. It discusses vari us aspects of this industry briefly. It presents the trends in this industry today, and identifies the shortfalls of this industry in developing countries. A brief write-up on the processes used for different broad categories of drugs forms part of the paper. This part will enable better appreciation of the appropriate technology suggested for the developing countries. The question of distribution of drugs has also been touched upon. The constraints patent protections given to drugs or processes impose on development of pharmaceutical industry has also been discussed. The policy back up the govts. of the develop countries should provide to this industry have been elaborated. Finally, suggestions on the ap ropriate technology which could be employed by the developing countries have also been made.

3. Section I

3.1 World trends in health management and human welfare

With the progress of human knowledge and development of technological skills, the basic principles of health management have undergone rapid changes in the twentieth century.

Barely a century ago, health care was synonymous with apothecaries, alchemists and surgeons of doubtful knowledge. The ancient civilizations had their traditional systems of health care operative over generations. However, with the continuous discovery of new medicines, greater insights into the working of the human body and advent of electronic equipment, modern health care practices are constantly being improved for the benefit of humanity.

In the first half of the twentieth century, the major emphasis of health care was on prevention and cure of diseases and body disorders. The discovery of a large number of anti-microrganism drugs has certainly benefited mankind in the control and cure of diseases caused by microprganisms infecting the human body. This has primarily resulted in increased life expectancy for all those who have access to modern health care facilities. The developed countries have reached a stage wherein almost the entire population is supported by appropriate health care systems consisting of trained doctors, well equipped hospitals and ready availability of appropriate drugs. Developing countries have yet to reach this stage. A few developing countries have low cost traditional systems of medicine that are able to cover some of the disorders and diseases. However most of these traditional systems fail to counter infections caused by microorganisms in the human body as effectively as some of the modern remedies.

With a sufficient hold over microorganism caused diseases, newer discoveries were in the direction of regulation of malfunctions in the operation of the human body, for instance, anti-diabetic drugs. Another hallmark was the

advent of the oral contraceptive to control human reproduction.

With constant newer improvements in the direction of better control over microorganism caused diseases and body malfunctions the advent of psythotropic medicines began in the early 1960 and have reached a fairly reasonable stage of advancement as compared to their forerunners-pain killers.

The advent of vaccinations and immunizations as a preventive against diseases is a boon to the generations of the 20th century. Right at the infancy stage vaccinations against major killer diseases are administered, thus directly increasing the life expectancy. However, the field of development of preventives against all the common diseases is still open. This is an area where future developments in medicine are likely to be seen. A list of some predicted developments in medicines as foreseen by certain futurologists is given in Annexure I.

The table below gives the percentage of consumption of antibiotics to the total drug consumption for certain developed countries :

	% (1974)
USA	12.7
Japan	22.6
Germany	8.8
France	8.4
Italy	11.2
Spain	27.2
U K	14.7

(Source : SCRIP Magazine)

As against the above, the figure for India is between 20-30%. A survey of expenditure on drugs by Govt. Hospitals in India reveals that upto 50% of the total expenditure on drugs is spent on antibiotics and anit-infective drugs.

In most developing countries, the thrust of health care is primarily on the treatment of infections caused by micro-organisms, while in the developed countries, the emphasis is more towards other categories of drugs relating to less moderate affictions on the human race, for instance cardiovasculars, psychotropics, etc. Developing countries have yet to reach a stage whereby micro-organism infections are well under treatment and they would afford the necessary priority to be given to other avenues in health care.

3.2 Health care areas in developing countries and the role of drugs & pharmaceuticals in Health care.

According to information available from participating developing countries in a UNIDO consultation meeting on the pharmaceutical industry held at Lucknow in April-May 1976 the following disease conditions appear to be the most prevailent in these countries (including India). Though the list is not exhaustive, it is indicative of the specific areas of health care requiring attention in developing countries.

1. Tuberculosis
2. Gastroenteritis
3. Diahorrea and dysentry
4. Anemia and malnutrition
5. Other helminth infections
6. Respiratory infections
7. Ascariasis

8. Filariasis and Malaria
9. Typhoid and paratyphoid
10. Yaws
11. Conjunctivitis and trachoma
12. Schistosomiasis
13. Cancer
14. Venereal diseases
15. Viral infections
16. Cardiovascular diseases
17. Diabetes
18. Nervous system disorders
19. Tetanus
20. Scabies
21. Congevital disorders
22. Poliomyelitis
23. Measles
24. Whooping cough

The health care system in any country has to be related to the prevailing disease pattern and the particular socio-economic considerations, which, to some extent, will vary from country to country.

While the structure of support services like medical personnel, health centres and hospital and the requisite staff and equipment should relate to the quantum and the pattern of prevailing disease areas as indentified above, the drugs &pharmaceutical industry should be geared to perform the function of delivering the appropriate drugs to the ailing masses.

One of the first steps is to identify the priority or essential drugs that are re-quired for meeting most of the prevailing diseases. For instance, from the pattern of diseases for most developing countries as shown above, it is possible to draw out a complimentary list of drugs required cure the same.

It is necessary to draw up the list of essential drugs in cooperation with the industry, public health services and the medical profession. The best drugs needed for a particular treatment may not necessarily be cheap and in many cases the choice of the drug may have to be directed by the economic situtation of the country. For example, while the best drug for the treatment of leprosy today is Rifampicin, the cost of the drug would prohibitive for a developing country - over Rs. 2,500 per year patient. The older drug Dapsone would cost only Rs. 10-15. Similarly, for the treatment of isoniazid and thiacetazone or PAS and the much more expensive isoniazid plus streptomycin, and the choice for treatment is obvious.

While identifying essential drugs, it has to be borne in mind that reasonably good drugs for most of major disease conditions are available and many of the newely introduced drugs have either no additional advantage or at the most only a marginal one over existing drugs. In fact, if one surveys the recent additions, one would find that every year haraly one or two really better drugs emerge, others have been introduced for considerations other than their efficacy, such as their patentiability, greater profit margin. Therefore, while drawing up a list of essential drugs their superiority over known drugs should be carefully assessed, along with factors such as cost, patent position and the availability of the technology. It is a well-known fact that multi-national corporations tend to introduce new products with only marginal differences merely because the patent of older drugs with similar activity has expired and they would like to drugs for which they have a monopoly.

A list of essential drugs identified recently by a committee appointed by the Government of India is given as an illustration. (Annexure II). A number of variations of drugs included in this list have been introduced recently but with practically no major advantage over the listed drugs. If, therefore, India could produce these drugs in sufficient quantity, most of the requirement of the country would be met. With the addition of another 8-10 drugs to this list, some of the disease conditions which are prevalent is most of the developing countries would also be covered. There will be practically no problem with patents.

The World Health Organization also has recently drawn up a list of essential drugs relevant to disease patterns in developing countries (Annexure-III).

3.3 Gaps in demand for drugs & pharmaceuticals in developing countries.

With the technological levels of sophistication in the production of drugs and pharmaceuticals, most of the developing countries are trailing far behind in gearing up indegenous production to meet the demand. It may be pertinent to mention that while the majority of the world's population lives in the developing countries, the developed countries account for 88% of the world production and 85% of the world consumption of pharmaceuticals, which leaves only 15% of the world production for the developing countries. The developing countries account for the balance 12% of the world's production. The imports from developed countries to developing countries varies from country to country. For instance, India imported

Rs. 470 million worth pharmaceuticals in 1976-77 as against a total consumption of Rs. 7000 million, bringing the percentage of imports (by value) to total consumption to about 7%. This is because India has a well established pharmaceuticals Industry to meet its present requirements for the coverage of health services as established. Nevertheless, these health services are accessable by barely 20-25% of the population, while the vast majority of 75-80% do without drugs. Even the quality of health services coverage to the small proportion of the population in India is hardly comparable to that in any developed country.

Figures of approximate percentage of imports to total consumption of pharmaceuticals by value for certain developing countries is given below :

Country	Year	Approximate % imports to total consumption (by value)
Turkey	1974	0.8
Tanzania	1976	almost 100%
Zanzibar	1976	85% (by quantity)
Egypt	1975	16%
Philippines	1973	2%
Pakistan	1976	40%
Mexico	1974	6%
Liberia	1976	100%
Nigeria	1976	70%
Algeria	1975	67%

(Source : Country status papers presented at the UNIDO conference on pharmaceutical Technology at Lucknow in 1976)

While the above figures are indicative of order of magnitude of reliance on imports, it is quite evident that except for a few countries (like India, Mexico, Phillipines, Turkey, etc.) most of the developing countries rely substantially on imports to meet their requirements.

The gap in demand for pharmaceuticals in developing countries can be considered as two levels :

Level (1) Demand for pharmaceuticals governed by health care facilities in existance.

Level (2) Demand for pharmaceuticals for the entire population to control the major diseases.

Achievement of Level (2) demand requires great efforts and substantial investment in health care facilities which most developing countries can scarcely afford. Thus, the difference between level (1) and level (2) is the demand for the "have not" the people who have to do without basic health care and medical treatment for common diseases. This difference is alarmingly large in developing countries, for instance, as pointed out earlier, the level (1) demand is India cocers barely 20-25% of the population.

H owever, even for level (1) demand, which caters to a small fragment of the population (the "haves"), most developing countries rely substantially on imports to meet the gap in demand since domestic production is scanty. Even those countries who produce some of their requirements mainly formulate imported bulk drugs - they are still far away from manufacturing the drugs themselves. However, for manufacturer of basic drugs, a developing country needs a sound industrial infrastructure and research facilities suppling raw materials,

technical skills, machinery, etc. and thus overall development of the pharmaceutical industry in any country is closely linked to the level of overall industrial development. However there is still a strong case for developing countries to formulate most of their requirements after importing the bulk drugs thus adding value (and simultaneously saving foreign exchange) and creating nuclei for further development of the industry at a later stage. The only developing countries manufacturing almost all their bulk drugs and intermediates and having complete facilities for research and development are India and Mexico, with barely a few other countries closely following.

What is more alarming is that almost all developing countries are quite far from being able to fulfil their level (2) demand. However, a single pronged strategy for covering the entire population with basic health care will not alone suffice - the need for all round development and raising the living conditions of the population above the poverty line is more important, since the population not covered by basic health care and medical facilities face shortage of the basic necessities - food, clothing and shelter - also.

3.4 International trade in drugs & pharmaceuticals

By the very nature of the commodity being high value low volume items, transportation cost offers no barriers in trade of pharmaceuticals. The developed countries trade their pharmaceutical products freely, since they are accorded the necessary importance being life saving in nature. As mentioned earlier, the developing countries import 3% of the

production of developed countries. Though these imports are a small fraction of what the developed countries produce, they amount to about 20% of the consumption of developing countries. Thus developing countries constitute a very small market for the developed countries.

3.5 The Indian experience in development of the pharmaceutical industry.

It is laid down in the constitution of India that "The State shall regard the level of nutrition and standard of living of its people and improvement of public health as among its primary duty".

During the period immediately preceeding Independence in 1947, health care and pharmaceutical industry development did not get adequate importance since the problems of consolidation of the nation were pressing.

However beginning from the onset of the First Five Year Plan in 1951, health has been given consierable priority in order to fulfil the objectives of the Directive principles of the state policy.

A beginning was made in the production of medicines by starting Cinchona plantations in the States of Bengal and Madras in the early 20th century (presently West Bengal and Tamil Nadu). Factories were set up in the vicinity for the extraction and purification of quinine. Under the guidance of visionary stalwarts like Acharya P.C. Ray, T.K. Gajjar and B.K. Amin, the indegenous pharmaceutical Industry began to take shape during the first world war period. Remarkable success was attained in the manufacture of sera and vaccines. During the second world war, the local industry made further progress by producing a number

of other products from locally available raw materials. Simultaneously, formulation activities were increasingly based on imported bulk drugs. The slow progress of the chemical industry in India also constrained the growth of the pharmaceutical industry.

In the early 1950 various foreign companies began to set up affiliates/sub-sidiaries in India. Some of them set up facilities for manufacture of bulk drugs while most of them were engaged in formulation activities based on imported bulk drugs. The entry of the multinationals has offered stiff and healthy competition to the local industry. The Govt. of India set up two large public sector units-Hindustan Antibiotics Ltd. in 1954 and Indian Drugs & Pharmaceuticals Ltd. in 1961 for the manufacture of bulk synthetic drugs/antibiotics and their formulations and surgical instruments.

Thus, through a course of rapid growth the pharmaceutical industry in India is well established today. It now produces a wide range of drugs including large number sophisticated antibiotics, vitamins, hormones and synthetic drugs and has developed a wide ranging capability and production in bulk drugs and formulations. From a total production of Rs. 100 million in 1948, the Indian Pharmaceutical Industry has produced Rs. 1500 million worth bulk drugs and Rs. 7000 million worth formulations in 1976-77. Imports of bulk drugs in this year were Rs. 470 million.

The break up of production of bulk drugs and formulations by various sectors of the industry in 1976-77 is as follows :

(Rs. million)

	Bulk	Formulations
Public sector	480	470
Foreign sector (Foreign equity exceeding 40%)	630	2920
Indian sector (including small scale sector)	390	3610
	1500	7000

There are over 2500 drug units in India of which 128 are in the organised sector including 45 companies with foreign equity exceeding 40%.

With the rapid growth in demand and attempts by India to give a wider coverage of basic health services, it is foreseen that the pharmaceutical industry in India is on the threshold for rapid growth. The Govt. of India are tentatively planning for a production level of Rs. 5,500 million worth of bulk drugs and Rs. 19,000 million worth of formulations in 1982-83. To achieve this target (which only increase the coverage to the population marginally), the pharmaceutical industry will have to increase to more than double its present size in barely five years.

Some Predicted Drug Developments of the Future

Nature of Development	Source of Production and Predicted Appoximate Date of Development
I. Greater emphasis on prevention and cure	
a) Anti-micro-organism	
New generation of antibacterials	1980 (Teeling-Smith)
Immunising against bacterial and viral diseases	1990 (Teeling Smith) 1980 (Gabor) 1978 (McGraw-Hill)
New, more effective antifungal agents	1988 (Bender)
Prevention or cure of autoimmune diseases	1988 (Bender)
Prevention or cure of dental caries	1993 (Bender)
b) Regulation of malfuditions in body chemistry	
Prevention or cure of hypertension	1982 (Bender, 1980 (Teeling-Smith)
Prevention or cure of skeletal muscle spasm	1988 (Bender)
Prevention or cure of thrombosis	1983 (Bender)
Prevention or cure of obesity	1988 (Bender] 1977 (Mc Graw Hill) 2000 (Kahn-Wiener)
Prevention or cure of asthma	1987 (Bender) 1980 (Teeling Smith)
Cure of depression	1988 (Bender)
Cancer cures	1990 (Gabor)
Immunisation against radiation	1986 (Mc Graw-Hill)

contd.

Control of neurological disorders	1990 (Teeling - Smith)
Control of most allergic conditions	1980 (Teeling - Smith)
Cure Mental illness	1980 (Mc Graw-Hill)
Prevention or cure of oedema	1982 (Bender)

II. Control on reproduction

Male contraceptive	1983 (Bender) 1975 (Teeling - Smith)
Cheap convenient, reliable contraceptive	2000 (Kahn-Wiener) 1975 (Teeling - Smith)

III. Increased manipulation of mental processes

Drugs to improve learning	1980 (Gabor), 1978 (Mc Graw - Hill 1990 (Teeling-Smith)
Prevention or cure of drug dependence or addiction	1988 (Bender)
Drugs to permanently raise intelligence	2020 (Garbor), 1990 (Mc Graw - Hill)
Controlled relaxation and sleep	1980 (Mc Graw - Hill) 2000 (Kahn - Wiener)
Control of senility	1985 (Mc Graw - Hill)
Improving analytical ability	1985 (Mc Graw - Hill)
Control of aging process	1990 (Mc Graw - Hill) 1990 (Teeling - Smith)
General Control of Psychobiological states	2000 (Kahn - Wiener)
Prolong chilhood and (shorten) adolescence	2000 or earlier (Evans-Kline)
Reduce need for sleep	"
Safe short-acting intoxicants	"
Regulate sexual responses	"
Mediate nutrition, metabolism and physical growth	"
Increase or decrease reactivity	"

contd.

Prolong or shorten memory	200 or earlier (Evans-Kline)
Provoke or relieve guilt	"
Foster or terininate mothering behavior	"
Shorten or extend experienced time	"
Create conditions of "Jamais Vu" or "Deja Vu"	"
Deeper awarencess of beauty and sense of awe	"

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LIST OF ESSENTIAL DRUGS

Tablets and Capsules (Granules included)

1. Cap. Chloramphenicol 250 mg.
2. Cap. Tetracycline Hydrochloride 250 mg.
3. Tab. Iodochlorhydroxy Quinoline 0.5 gm.
4. Tab. Nitrofurantoin
5. Tab. Chlorpheniramine
6. Tab. Ferrous Sulphate
7. Tab. Folic Acid
8. Tab. Digoxine
9. Tab. Aspirin
10. Tab. Phenobarbitone
11. Tab. Chlorpromazine
12. Tab. Hexa Vitamin (N.F.I.)
13. Tab. Prednisolone
14. Tab. Vitamin B. Complex
15. Tab. Vitamin C
16. Tab. Sulphadimidine
17. Tab. Metronidazole
18. Tab. Hydrochlorothiazide
19. Tab. Reserpine
20. Tab. Glyceryltrinitrate
21. Tab. Analgin
22. Tab. Antacid (B.N.F.)
23. Tab. Piperazine (Syrup Piperazine)
24. Tab. Tetrachlorethylene
25. Tab. Tolbutamide
26. Tab. Thiacetazone & Isoniazid (each tablet to contain Thiacotetazone 37.5 mg BPC & Isoniazid 75 mg IP)
27. PAS granules
28. Tab. I.N.H.
29. Tab. Dapsone (50 mg)
30. Tab. Chloroquine Sulphate 0.2 gm (or Tab. Chloroquine Phosphate 0.25 gm IP)
31. Tab. Primaquine Diphosphate (2.5 gm. of Primaquine Base)
32. Tab. Diethylcarbamazine Citrate (50 mg)
33. Tab. Anti-asthematic (containing ephedrine Hcl. 50 mg. Theophylline 65 mg and Phenobarbitone 30 mg)
34. Tablets containing alkaloids of Ergot equivalent to 0.4 mg of total alkaloids orgotoxin.
35. Capsules of Vitamin A 6000 units and Calciferol 100 Units.
36. Tab. Vitamin A
37. Tab. Vitamin D
38. Tab. Milk of Magnesia
39. Oral Contraceptive (approved by Family Planning Department)

Injections

1. Injection Penicillin
2. Inj. Streptomycin
3. Inj. Emetine Hydrochloride
4. Inj. Atropine
5. Inj. Adrenaline
6. Inj. Nor-Adrenaline
7. Inj. Dextrose Saline
8. Inj. Furosemide
9. Inj. Morphine Sulphate
10. Inj. Pethidine
11. Inj. Paraldehyde
12. Inj. Predinisolone
13. Inj. Anti-Tetanus Serum
14. Inj. Methyl Ergometrin
15. Inj. Chlorpheniramine Meleate
16. Inj. Fortified Benzyl Penicillin PP(Procaine Benzyl) Penicillin 3,00,000 units. Benzyl Penicillin 1,00,000 Units).
17. Inj. Aminophylline/0.5 gm/2ml.
18. Inj. Oxytocin (Oxytocin 5 i.u./ml)
19. Inj. Chlorpromazine
20. Antivenom Serum (Polyvalent)
21. Rehydration fluid (for treatment of cholera cases)
22. Glucose Ampoule containing dextross 25%)
23. Distilled Water (25cc ampoule)
24. Inj. Phenobarbitone Sodium (200 mg/ml)
25. Inj. Mepheteramine
26. Diphtheria-Pertussis-Tetanus Vaccine
27. Inj. Totanus toxoid
28. Inj. Diphtheria Toxoid
29. Inj. Anti-Diphtheria Serum
30. Oral Polio Vaccine
31. Inj. Insulin Plain (40 units per ml)
32. Inj. Sodium Pentathol
33. Inj. Succinyl Choline
34. Inj. Xylocaine.

Miscellaneous (Syrup, Ointments, mixtures, eye drops, ear drops etc.)

1. Sulphacetamide Eyer Drops
2. Homatropine Eye Drops
3. Esserine Sulfate eye drops
4. Benzyl B-enzoate Emulsion
5. Acid Carbolic
6. Lysol
7. Tr. Iodine
8. Syrup Piperazine
9. Ext. Belladonna (Combination of Phenobarb & Belladonna)
10. Chloramphenical suspension (125 mg/ml)
11. Syrup Paracetamol (125 mg in 5 ml)

12. Tetracycline Hydrochloride Ointment 1% in sterile ointment base
13. Gripe Mixture for infants (5 ml contains Dill oil BPC 0.005 ml; sodium bicarbonate I.P.O. 0.005 gm dehydrated alcohol I.P.O. 0248 ml(Syrup & Preservative).
14. Syrup Noscapine
15. Whitefields Ointment Benzoic acid 6 g; salicylic acid 32g; alcohol 70% upto 100g)
16. Nitrofurazone ointment (0.2% in non-grasy ointment base)
17. Petroleum jelly
18. Potassium Permanganate 5g packets
19. Diethyl Ether (Anaesthetic)
20. Cetrimide Lotion
21. Iodine Solution (Claudium Solution) for sterilizing raw catgut, loops and loop introducers (Iodinel 1g, Pot. Iodide 1.5 g, Distilled Water to produce 100 ml)
22. Plaster of Paris Bandages.
23. Adhesive Plaster
24. Ethyl Chloride (100 ml spray)
25. Boric Acid-Alcohol-Glycerol drops (Boric Acid 1.5% Glycerol 3.3% in alcohol 95%, 10 ml)
26. Bleaching Powder
27. Phenyle
28. Epsom Salt
29. Krushen's Salt (Each gram contains Sod. Sulphate Exsic 20 mg., Sod. chloride 10 mg., Pot. chloride 10 mg, Potassium Sulphate 55 mg., Citric Acid 45 mg., magnesium sulphate excis.)
30. Ointment containing Resublimed Iodine 4%, Mehyl Salicylate 5%.
31. Ointment containing: Oil Eucalyptus 8%, Oil clove 1%, Camphor 5%, Menthol 3%, Thymol 2%, Methyl Salicylate 5%.

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WHO's recommended Essential Drug list

I : Availability at Primary Health Centres

II : Availability of Secondary Level having more sophisticated diagnostic facilities.

Analgesic, antipyrestic, anti-inflammatory, uricosuric Agents.	
acetylsalicyclic acid	I
paracetamol	I
phenylbutazone	II
indomethacin	II
allopurinol	II
Anti-infectious agents	
aminoglycosides	
gentamicin or	II
kanamycin	II
penicillins:	
benzylpenicillin (Penicillin G)	I
benzylpenicillin in oil	I
benzathine benzylpenicillin	I
procaine benzylpenicillin	I
ampicillin	II
Chloramphenicol	I
erythromycin	II
Tetracycline :	
tetracycline or	I
doxycycline	II
Sulfonamides :	
Sulfamethoxypyridazine	I
trimethoprim - sulfamethoxazole	II
Sulfalene	I
Sulfadoxine	I
Antituberculous agents	
isoniazide	I
streptomycin	I
rifampicin	II
ethambutol	II
para-aminosalicyclic acid	I
thioacetazone	I
Antifungal agents	
nystatin	II
griseofulvin	I

Anthelmintics	
mebendazole	I
piperazine	I
pyramtelpamoate	I
Onchocerciasis and filariasis	
diethylcarbamazine	I
suramin	I
Malaria	
Chloroquine	I
pyrimethamine	I
primaquine	I
quinine	II
Leprosy	
dapsone	I
Amoebiasis	
emetine	I
metronidazole	I
clioquinol	I
Blood and blood disorders	
Hemostasis	
aminocaproic acid	II
heparin	II
protamine	II
phytomenadione (vitamin K)	I
Anaemia :	
iron preparation (ferrous sulfate)	I
folic acid	I
Cardiovascular system	
Antiangianl :	
glyceryl trinitrate (nitroglycerin)	I
Antiarrhythmic :	
lidocaine	II
procainamide	II
phenytoin	II
Antihypertensives/diuretics :	
methyldopa	II
reserpine	II
hydrochlorothiazide	I
furosemide	I
B-blockers :	
propranolol	II

CARDIAC GLYCOSIDES :	
digoxin	I
digitoxin	I
Central nervous system	
Anticonvulsants	
carbamazepin	II
diazepam	I
phenobarbital	I
phenytoin	I
ethosuximide	II
Antidepressants and neuroleptics :	
Tricyclic antidepressants (amitriptyline)	II
Phenothiazines (chlorpromazine)	I
Butyrophenones (haloperidol)	II
Antiparkinsonian agents :	
levodopa+decarboxylase inhibitors	II
Hormones and hormone-like substances	
Carticosteroids	
hydrocortisone	II
prednisolone	I
Obstetrics and gynaecology :	
oestrogen/progestogen and progestogen - preparations for contraceptive use	
oxytocin	II
ergometrine	I
Others :	
one short-acting isulin	II
one intermediate isulin	I
one oral antidiabetic preparation of the sulfonylurea type (tolbutamide)	II
levothyroxin	II
Respiratory system	
aminophylline	I
epherine (oral low dose)	I
sulbutamol	II
orciprenaline	II
epinephrine	I
codeine	I
Schistosomiasis	
niridazole	

Eye

Topical :
Anti-infectious :
chloramphenicol I
sulfonamides (sulfacetamide) I
tetracycline I
One of the many preparations for L
anti-inflammatory (corticosteroid)
and anaesthetics :
homatropine I
pilocarpine I

Systemic

acetazolamide II

Narcotic analgesics, drugs related to anaesthesia, other "emergency" drugs

morphine I
naloxone II
atropine I
charcoal, activated I
sodium thiosulfate I
antivenin I
tubocurarine II
suxamethonium I
thiopental II
nitrous oxide II
ethyl ether I
lidocaine (see also : antiarrhythmic) I
isoprenaline II

Vaccines

tetanus toxoids
diphteria-pertussis -tetanus vaccine
diphtheria-tetanus vaccine
rabies vaccine
BCG vaccine (Level to be determined)
measles vaccine
poliovirus vaccine
smallpox vaccine

Source : SCRIP NO. [illegible] dated 11th June, 1977.

4. SECTION II

OUTLOOK ON D&P INDUSTRY IN DEVELOPING COUNTRIES

4.1 i) TRENDS IN THE D&P INDUSTRY IN DEVELOPING COUNTRIES.

Developing countries, in their efforts to improve the living standards of their people direct their attention to the need for providing adequate quantity of quality drugs to their people. By such a service, the health of the population will be sustained at an adequate level. A number of developing countries have launched public sector health programmes towards this end.

The population pressures in most countries in the developing world are increasing and this also necessitates the development of drugs and pharmaceutical industry. With the rapid development of industry and introduction of alien cultural patterns, sometimes new diseases which were not experienced before are also making their appearance. Some of the disease-carrying insetts, have become resistant to the chemicals that have been in use and there is thus need for development of new chemicals. It is stated that Malaria, which, at one time was thought to have been eradicated, has made a re-appearance and the mosquitos have developed new strains which are resistant to DDT. Similarly influenza in various forms has been making its appearance periodically necessitating new strategies of attack.

In the light of growing population, their growing expectations in living standards and determination of the governments in the developing countries to increase living standards in their countries, there is great need for them to devote more and more attention to the development of

pharmaceutical industry to make available to the local populations adequate quantities of quality drugs at reasonable prices.

The discovery, development, manufacture and marketing of drugs is a very costly process. These costs have been increasing steadily. The cost is due to the fact that a large number of prospective compounds have to be screened before a single drug could be identified as having true commercial potential.

The drug requires large amount of experimentation, trials on the laboratory scale, runs at the pilot plant level, tests on animals, trials on human beings, satisfying the procedures laid down by the drug, and educating the market in the use of the new drug. All this takes a lot of effort and money. This also takes considerable amount of time. Before a drug is discovered in a laboratory and successfully introduced in a market, considerable time elapses. The drug also has to compete against drugs already existing in the market for serving the same purpose. Penicillin was accidentally discovered by Dr. Alexander Fleming in 1928. But it was only just before the World War II in July, 1939 that Ernst Chain and Howard Florey began their first experimental work on Penicillin. In case of sulpha drugs the time lag between the discovery of their antibacterial activity / commercialisation was a little shorter. The first sulpha drug Prontosil was discovered by Domack in1933 and was put in to the market in 1935. It took another 5 years for the different derivatives and sulpha drugs to come to the market. Although with modern tools and facilities available, the period could be shortened still it is quite a long and

costly process to introduce any new drug into the market. there is also fast obsolescence in the drug market.

One of the constraints of development process in the developing countries is the lack of adequate monetary resources. A number of these countries are now interested in increasing the basic health standards of their populations. They have no adequate resources for discovering new drugs. However, there is a desire on their part to become more and more self-reliant and also develop drugs and pharmaceuticals which will meet their needs.

4.2 MANUFACTURING CAPABILITIES

Some twenty-five years ago, very little of modern drugs were being consumed in developing countries. Many of these countries became free and the governments of these countries became aware of the need to provide health services to their people. The modern methods of cure began to be accepted and encouraged. Indian Govt. mentioned its commitment to provide health services to people in the constitution itself. Before and soon after independence, these countries were primarily importing formulations. Later bulk drugs were imported and the formulations were produced indigenously. Production of bulk drugs commenced after quite some time because the basic infrastructure and educational facilities (to provide competent technical people to handle complex processes) had to be established first of all.

India, which consumed Rs. 10 crore worth of modern drugs in 1948 to day consumes drugs, worth about Rs. 750 crores. It produces Rs. 700 crores worth of formulations

and Rs. 150 crores worth of bulk drugs. To day India produces a very wide range of bulk drugs ranging from antibiotics, Citamins and analgesics to antihypertensives and harmones. In India, Public Sector and Private Sector are both active in the field. In the private sector, multinational pharmaceutical companies dominate the scene. Two major bulk drug producing organisations were set up in India in the fifties, as a seliberate measure to put the country on a path to self sufficiency in health supplies. The strategy was to use imported technology initially and then assimilate it and improve upon it; the development of new processes for known effective drugs was to be taken up at the second stage.

Now, after two decades of setting up of these organisation, India can feel proud of its achievement. The country has not only attained confidence to produce drugs with complex processes but it has also been able to effect process improvements and even to develop economical processes for many known drugs.

The quantum of various bulk drugs produced in India in 1977-78 is given on pages 32 and 33 of this chapter.

Though the foregoing refers to India, it is true of many developing countries. Both consumption and production of modern medicines have considerably increased in every country.

But, even now, there is considerable time lag between the time at which a drug is introduced in the western countries and the time at which it is produced in the developing world.

this is because R&D is very costly and developing countries can not be themselves develop processes which are economical enough, within a short time. It is not usual to find a drug which is obsolete in the developed world being introduced by manufacturers in developing countries as a new and more effective drug. There is need to reduce this time lag.

ANNEXURE I
TO Section II

Production of some major Drugs

	Accounting Unit	Production during 1977 - 78
A) ANTI-BIOTICS		
1. Penicillin	MMU	300
2. Ampicillin & other semi-synthetic Penicillins	Tonnes	7.5
3. Streptomycin	Tonnes	256
4. Tetracycline/Oxytetracycline	Tonnes	225
5. Chloramphenicol and esters	Tonnes	200
6. Erythromycin and esters	Tonnes	22
B) ANTI-DYSENTERY DRUGS		
1. Halogenated oxyquinolines	Tonnes	250
2. Metronidazole	Tonnes	31
3. Diloxamide Furoate	Tonnes	6.5
C) ANTI-DIABETICS		
1. Insulin	I.U.	1050
2. Chlorpropamide	Tonnes	15
3. Ethambutol	Tonnes	30
D) ANTI-LEPROSY DRUG		
1. DDS and derivatives	Tonnes	18
E) ANTI-PYRETICS/ANALGESICS		
1. Aspirin	Tonnes	1150
2. Phenacetin	Tonnes	200
3. Paracetamol	Tonnes	250
4. Analgin	Tonnes	500
5. Amidopyrin	Tonnes	55 (Consumption)
F) ANTI T.B. DRUGS		
1. I.N.H.	Tonnes	125
2. PAS & Sales	Tonnes	650
3. Thiacetazone	Tonnes	30
G) ANAESTHETICS		
1. Procaine	Tonnes	100
2. Xylocaine	Tonnes	10 (Consumption)

	Accounting Unit	Production during 1977 - 78
H) ANTIMALARIALS		
1. Chloroquine	Tonnes	19.50
2. Amodiaquin	Tonnes	16.70
I) ANTINFLAMMATORY	[illegible]	45
1. Phenylbutazone	Tonnes	(Consumption)
2. Oxyphenbutazone	Tonnes	40 (Consumption)
J) SULPHA DRUGS		
1. Sulphadiazine	Tonnes	100
2. Sulphadimidine	Tonnes	500
3. Phthalylmphathiazole	Tonnes	55
4. Sulphaguanidine	Tonnes	200
5. Sulphaphenazole	Tonnes	115
6. Sulphacetamide Sodium	Tonnes	75
7. Sulfamoxol	Tonnes	82
8. Sulphasomidine	Tonnes	200
L) VITAMINS		
1. Vitamin A	MMU	65
2. Vitamin B12 (Cyano & hydroxycofalmine)	Kgs.	190
3. Vitamin C	Tonnes	600
4. Vitamin B1	Tonnes	36
5. Vitamin B2	Tonnes	7
6. Vitamin D2 and D3	Kgs.	100
7. Folic Acid	Tonnes	4.5

SECTION III

5. TECHNO-ECONOMIC PROFILES OF SELECTED PRODUCT GROUPS

Bulk Drugs which are used for preparing formulations the final form in which a patient takes the drugs - can be classified into antibiotics and synthetic drugs. The former are living organisms capable of combating disease imparting pathogens, whereas the letter are complex chemicals capable of curing diseases due to their influence on parts of the human anatomy or the materials in the cardio vascular system and alimentary canal. Because of the different in their nature, the methods of production of antibiotics and that of synthetic drugs also differ considerably. In the few sections that follow, the technologies generally used for the manufacture of antibiotics and Synthetic Drugs are described. Also, the mode of manufacture of formulations has also been detailed.

5.1 **Antibiotics :**

Antibiotics, essentially special chemotherapeutic agents, are produced by special kinds of miroonganisms. These are chemical substances used for the treatment of infectious diseases or diseases caused by the proliferation of malignant cells. Antibiotics can broadly be divided into two groups (i) antibacterial and (ii) antifungal. Examples of Antibacterial antibiotics are Penicillins, Streptomycin, tetracyclines etc. and of antifungal are Nystatin, Griseofulvin, Neomycin etc. Besides commercial antibiotics used for human thereapy there are several others, though toxic to man but may prove useful in the treatment of animal diseases or in combating insects, pests and plant diseases.

Antibiotics are produced commercially by bio-synthesis, cultivating the suitable microbes under suitable environment in appropriate medium. The production is normally by a fermentation technique and then purified by chemical processes.

The strain of micro-organism used in the Industrial Fermentation for production of an antibiotic has to go through a rigorous exercise before it is used in industrial Fermentation. It is well known that the productivity of an antibiotic during fermentation by a microbe is an interaction of its genetic potentiality and the environment within and outside the microbial cells, Augmentation of yield by altering genetic potentiality of a strain is a well known technique and results of the experiments with such micro-organisms in the area of mutation, microbial genetics and genetic control of secondary metabolites have given valuable information for application to industrial strains. What was 100 of units of penicillin per mili litre in the fermentor in late 1940 is now 30-40,000 units per ml. of broth in 1970's. Thus increased yield in the fermentors has led to the reduction in production cost. It could be seen that strain improvement is an important activity in

in the field of antibiotics which has bright future for further development.

The production on industrial scale is carried out in large vessels called fermentors. The process adopted is sub-merged aerobic fermentation under suitable conditions.

The culture of appropriate strain is grown first in the inoculators containing sterilized medium. Seed mycalium of the 1st generation cultivated in the inoculator is then transferred to the 2nd generation in seed vessels. In some cases like tetracyclines the seed is grown directly shipping inoculator stage. The seed multiplies within a period of 30-50 hrs. Fermentor containing sterlized medium is then seeded with the mycelium culture grown in the seed vessel. Fermentation is continued for over a week or even longer. In the course of fermentation the parameters like PH, temperature, dissolved oxygen, carbon source and nutrients like nitrogen and phosphorus are continuously monitored and optimum conditions are maintained. Besides this, supply of sterile air and continuous agitation are essential pre requisites for achieving desired results.

In the process of antibiotics fermentation, proper sterilisation of vessels, medium and all other inputs like air and intermediate feeds has to be ensured. The sterilization of the vessels and medium is carried out by thermal process using supper heated steam whereas sterilization of air is done by passing compressed deter-modified air through suitable filters.

The fermented broth at the end of fermentation cycle is harvested for recovery of antibiotics. The broth is treated suitably and the two phases i.e. liquid phase and mycelial cells are separated. The antibiotics is recovered from the native solution or mycelium as the case may be.

The process of recovery in case of antibiotic in native solution involves techniques like solvent extraction preciptation, absorption on ion-exchange resins etc. After isolation it is further purified using suitable methods. Similarly recovery of antibiotic from mycelium is done by means of methods like solid-liquid extraction and then purified. The final product is obtained by drying the purified concentrated antibiotic solution under suitable temperature and vacuum. The conditions of recovery and purification are so adjusted that the quality of the product conforms to pharmacopeial requirements. In this process recovery efficiencies are of paramount importance which affect the cost of production.

In the field of antibiotics great strides are being made to enhance the yield of various microbial strains by controlling important parameters and it is also well known that higher the yield more is the sensitivity of fermentation process to variation of such parameters. As such, a lot of emphasis is being laid today in introducing automation in the fermentation process both for research and commercial production. Among various parameters following are considered to play important role in achieving the right type of environment in the fermentor.

a) pH

b) Temperature

c) Dissolved Oxygen

d) Carbon dioxide generated during fermentation
Carbohydrate, nutrients, precursor etc.

e) Foam

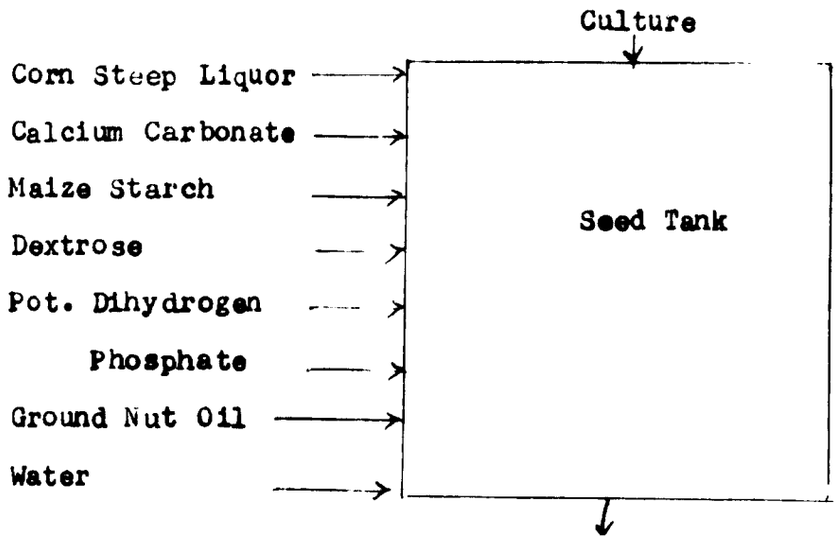
These parameters have been successfully controlled by automatic devices in several of the antibiotics producing industries specially in foreign countries. In this regard use of on-line computers to record the parameters, store the information and use them to signal or activate the rectifying systems is likely to be of greater application in future.

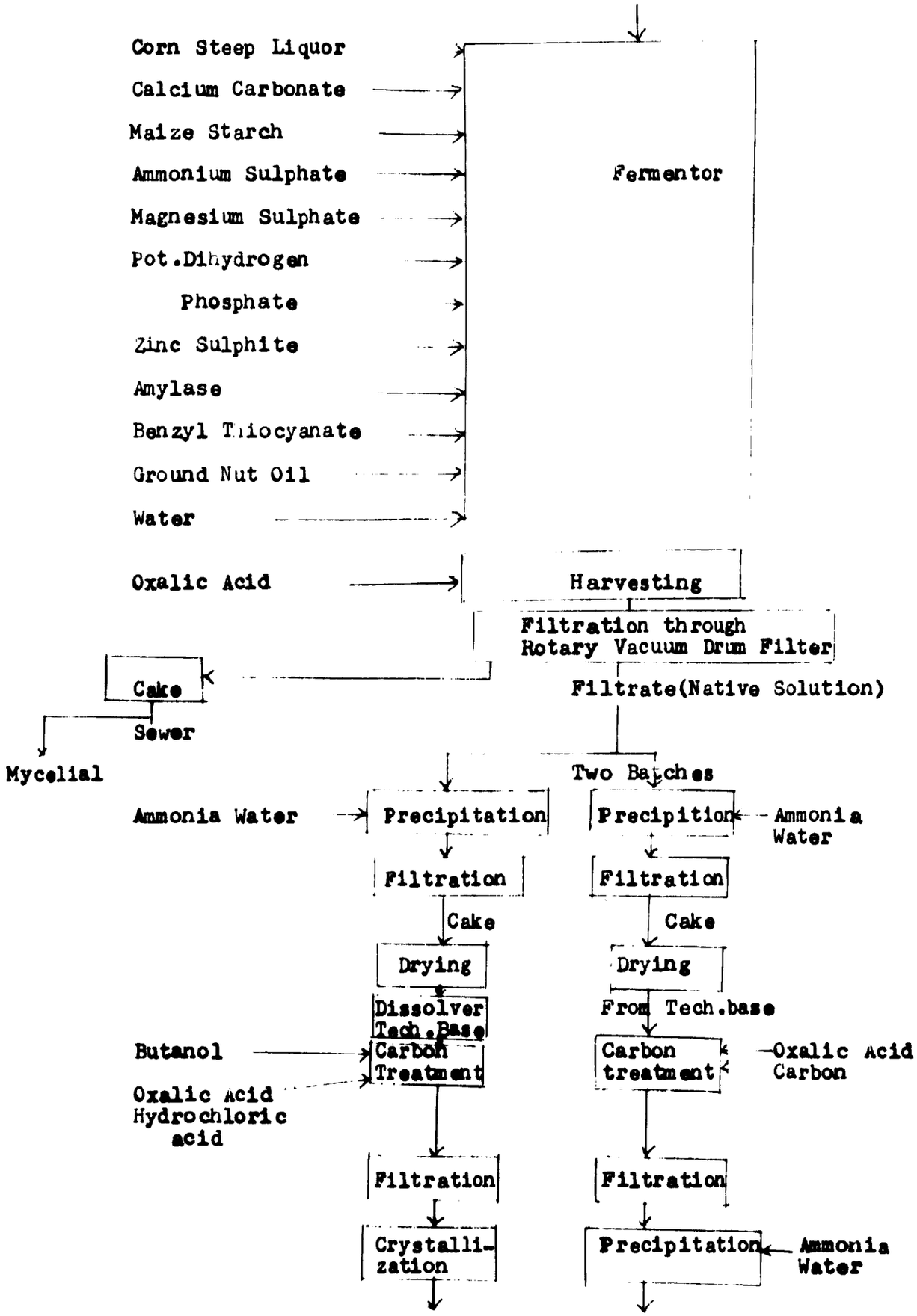
A typical case of tetracycline production as a model is given as under :

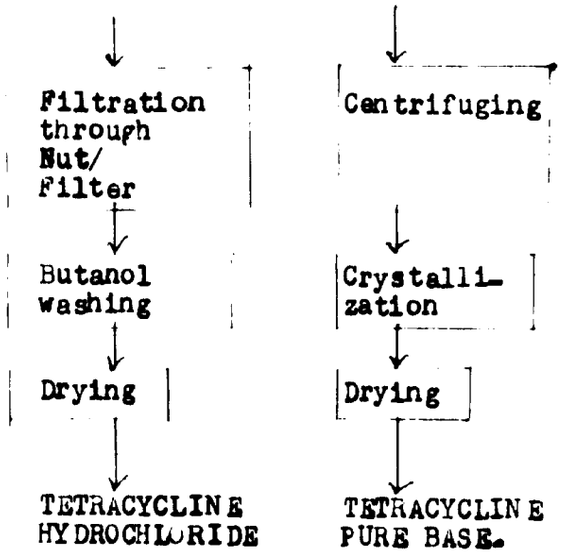
PROCESS DESCRIPTION :

A mutant of Streptomyces aurofaciens is used to produce Tetracycline. The culture is transferred from flask to seed tank having sterilized media. The time for seed cultivation in seed tank is 32-34 hours. The medium for fermentor is prepared and sterilized and inoculated with the mycelial culture from seed tank. The content of tetracycline by the end of fermentation is about 12,000/ml. The fermented broth is transferred to the vessel where it is treated with oxalic acid and is cooled down. The treated broth is filtered through Rotary Vacuum Drum Filter or filter presses. The filtrate (called Native Solution) is collected and antibiotics is precipitated with ammonia water, and is then filtered through Plate & Frame filter. The cake so obtained is dried and treated with Butanol, Oxalic acid, Carbon and Hydrochloric acid. It is then filtered, crystallised and centrifuged and washed with butanol. The Tetracycline Hydrochloride is dried in Vacuum Rotary Driers.

The flow sheet for the process is given as under :




Corn Steep Liquor
Calcium Carbonate
Maize Starch
Ammonium Sulphate
Magnesium Sulphate
Pot.Dihydrogen Phosphate
Zinc Sulphite
Amylase
Benzyl Thiocyanate
Ground Nut Oil
Water
Fermentor
Oxalic Acid
Harvesting
Filtration through Rotary Vacuum Drum Filter
Cake
Sewer
Mycelial
Filtrate(Native Solution)
Two Batches
Ammonia Water
Precipitation
Precipition
Ammonia Water
Filtration
Filtration
Cake
Cake
Drying
Drying
Dissolver Tech.Base
From Tech.base
Butanol
Carbon Treatment
Carbon treatment
Oxalic Acid Carbon
Oxalic Acid Hydrochloric acid
Filtration
Filtration
Crystalli-zation
Precipitation
Ammonia Water


Filtration through Nut/ Filter
Butanol washing
Drying
TETRACYCLINE HYDROCHLORIDE
Centrifuging
Crystalli- zation
Drying
TETRACYCLINE PURE BASE.

4.2 SYNTHETIC DRUGS :

The production of Synthetic Drugs from the basic stages depends mainly on the status of the chemical industry in the country. Where the chemical industry is itself inadequately developed, it is virtually impossible for the pharmaceutical industry to commence production from the basic stages. The development of chemical industry affects the pharmaceutical industry in many ways. Firstly it provides the raw materials which are major cost item in the total cost of production. Secondly, the synthetic drugs production involves various chemical reactions/unit processes. The country should have mastered these unit processes if it is to be able to handle synthetic drugs production effectively. Further, availability of the equipment for the various unit processes involved in production of synthetic drugs would be better if the chemical industry itself has advanced considerably.

The production of synthetic drugs calls for a very high degree of quality control on account of the end use of these materials- consumption by human beings.

The synthetic drugs are generally produced by batch process. In a batch process a series of unit operations are carried out on a certain optimum quantity of input. The continuous process of production which are generally applied for the manufacture of chemicals cannot be applied because of strict specifications of the drug. Some of the unit operations involve in the production of synthetic drugs are:

i) Sulfonation/chlorosulfonation
ii) Nitration
iii) Halogination
iv) Cyanidation
v) Hydrogenation
vi) Various condensation reactions involving the use highly inflammable, explosive, corrosive and toxic chemicals.

Usually, before the raw materials are charged into the reaction vessels, they are tested for their purity. Impure chemicals are not used as their use may lead to low yields/impure end product.

As can be conceived, there is no set series of chemical reactions/unit processes which can be used for the preparation of all drugs. The process varies considerably from drug to drug. To illustrate the complexity involved in the synthesis of biological active drugs, the process generally used for the manufacture of sulphamethoxazole has been described below:

The steps involved are:

1. Preparation of ethyl acetopyrurate from diethyloxalate and acetone by claisen condensation.
2. Conversion of ethylacetopyrurate to 3-carbamoyal -5-methyl isoxazole by condensation with hydroxylamine.
3. Production of 3-amino-5-methyl isoxazole from 3-carbamoyl derivative by reaction with sodium hypochlorite.(Hofmann reaction)
4. Production of N-acetyl sulphamethoxazole by condensation of 3-amino-5-methyl isoxazole with acetyl sulfanilyl chloride.
5. Production of sulphamethoxazole (tech.) from N-acetyl sulphamethoxazole by hydrolysis with alkali.
6. Production of Pharmacopeoal grade sulphamethoxazole.

The raw materials needed for the production of Sulphamethoxazole are:

1. Diethyloxalate
2. Sodium metal
3. Hydroxylamine hydrochloride
4. Acetyl Sulphanilyl chloride
5. Sodium hydrosulfite
6. Sulphuric Acid
7. Hydrochloric Acid
8. Sodium hydroxide
9. Ammonia water
10. Chlorine gas
11. Pyridine
12. Activated Carbon
13. Acetone
14. Benzene
15. Dichloroethane
16. Ethyl alcohol 95%
17. Ethylacohol absolute

The list of equipment needed for the production of 5 tonnes per annum of Sulphamethoxazole is detailed in Annexure I of this chapter.

Various utilities needed for the manufacture of this drug are steam 3 kg/cm2, water 32^0, 18^0, brine - 5^0 -15^0, process water, inert gas and electricity.

In bulk drugs production, manufacturers have to be careful if they want to reduce the cost of production. The possible areas are raw materials consumption, recovery of solvents and catalysts. Maintanance of process parameters is very essential to get the desired yields.

ANNEXURE-I

LIST OF EQUIPMENT WITH SPECIFICATIONS
(For the Production of Sulphamethoxazole 5 T/A).

Sl. No.	Description.	Material of Constn.	Capacity in Litres.	Qty. in Nos.
1.	2.	3.	4.	5.
1.	Reactor, jacketted, bottom outlet, anchor type agitator with explosion proof motor, 1.6 K.W. on lugs.	CI.GL.	250	1
2.	Vertical Measuring Tank, bottom outlet, level indicator with shut off device, on lugs.	S.St.	100	1
3.	Vertical Measuring Tank, bottom outlet, built in klinger gauge on lugs.	M.S.Lead lined.	250	1
4.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.7 K.W., on lugs.	S.St.	630	1
5.	Rectangular Nutsch filter.	M.S. Tile lined.	A.F. 2 1.5 L.	1
6.	Vertical Receiving Tank, bottom outlet, blow over pipe, built in klinger gauge.	S.St.	630	1
7.	Vertical receiving Tank, level indicator with shut off device, blow over pipe, bottom outlet on legs.	S.St.	400	1
8.	Reactor jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.7 K.W., on legs.	S.St.	630	1
9.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.7 K.W., on legs.	S.St.	400	1

Contd.

1.	2.	3.	4.	5.
10.	Vertical Shell & Tube heat exchanger 1,4 pass on lugs.	S.St.	$\frac{\pi ht}{4I^2}$ =	1
11.	Vertical Receiving Tank, bottom outlet, level indicator with shut off device, on legs.	M.S.	400	1
12.	Vertical Receiving Tank, bottom outlet, blow over pipe, level indicator with shut off device on legs.	S.St.	63	1
13.	Reactor jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor 1.5 K.W., on legs.	S.St.	630	1
14.	Vertical Measuring Tank, bottom outlet, level indicator with shut off device, on lugs.	M.S.	160	1
15.	Vertical Measuring Tank, bottom outlet, level indicator with shut off device, on lugs.	M.S.	100	1
16.	Reactor, jacketted, bottom outlet, anchor type agitator with explosion proof motor, 1.5 K.W. on legs.	S.St.	400	1
17.	Vertical Shell & Tube heat exchanger, 1,4 pass, on lugs.	S.St.	$\frac{\pi ht}{4I^2}$ =	1
18.	Vertical Receiving Tank, bottom outlet, blow over piep, built in klinger gauge, on legs.	S.St.	250	1
19.	Centrifuge with explosion proof motor.	S.St.	ϕ =600 mm	1
20.	Centrifuge Trap, blow over pipe, on legs.	S.St.	250	1
21.	Reactor, jacketted bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W., on lugs.	S.St.	250	1

Cont.

1.	2.	3.	4.	5.
22.	Vertical Measuring Tank, jacketted, bottom outlet indicator with shut off device, on lugs.	S.St.	250	1
23.	Vertical Measuring Tank, jacketted, bottom outlet, level indicator with shut off device, on lugs.	S.St.	100	1
24.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W. on lugs.	S.St.	250	1
25.	Vertical Shell & Tube heat exchanger, 1,4 pass on lugs.	S.St.	Aht.= 4 m²	1
26.	Vertical Receiving Tank, bottom outlet, blow over pipe, built in Klinger gauge, on legs.	M.S.	100	1
27.	Centrifuge with explosion proof motor.	S.St.	Ø=600 mm	1
28.	Centrifuge Trap, blow over pipe, on lugs	S.St.	100	1
29.	Vertical Receiving Tank, bottom outlet, blow over pipe, built in Klinger gauge on lugs.	S.St.	100	1
30.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W., on legs.	S.St.	250	1
31.	Vertical Measuring Tank, bottom outlet, built in Klinger gauge, on legs.	M.S.	100	1
32.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W. on legs.	S.St.	250	1
33.	Mobile leaf filter with jacket.	S.St.	60	1
34.	Vertical Shell & Tube heat exchanger, 1,4 pass on lugs.	S.St.	Aht.= 4 m².	1
35.	Vertical Receiving Tank, bottom outlet, blow over pipe, level indicator with shut off device on legs.	M.S.	100	1

Contd.

1.	2.	3.	4.	5.
36.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W. on legs.	S.St.	250	1
37.	Vertical Shell & Tube Heat exchanger,1,4 pass on lugs.	S.St.	Aht.= 4M².	1
38.	Vertical Receiving Tank, bottom outlet, blow over pipe, level indicator with shut off device on legs.	M.S.	630	1
39.	Rectangular Nutsch filter.	M.S. Tile lined.	A.F.= 1.5 M²	1
40.	Vertical Receiving Tank, blow over pipe on legs.	S.St.	250	1
41.	Reactor, jacketted, bottom, outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.1 K.W. on legs.	S.St.	250	1
42.	Vertical Shell & Tube heat exchanger,1,4 pass on lugs.	S.St.	Aht.= 4M²	1
43.	Mobile leaf filter with jacket.	S.St.	60	1
44.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.6 K.W. on lugs.	CI.GI.	250	1
45.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor 1.6 K.W., on lugs.	CI.GL.	250	1
46.	Heat exchanger, bell type.	CI.GI.	Aht.= 4M²	1
47.	Reactor, jacketted, bottom outlet, blow over pipe, anchor type agitator with explosion proof motor, 1.6 K.W. on lugs.	CI.GI.	250	1

Contd.

1.	2.	3.	4.	5.
48.	Centrifuge withexplosion proof motor.	S.St.	∅=600 mm	1
49.	Centrifuge Trap, blow over pipe on legs.	S.St.	250	1
50.	Mobile leaf filter with jacket.	S.St.	60	1
51.	Vacuum Tray dryer, with steam heating tubes.	S.St. Trays.	Aht.=$_2$ 1.3 M^2	1
52.	Vacuum Tray dryer, with steam heating tubes.	S.St. Trays.	Aht.=$_2$ 1.3 M^2	1

5.3 THE PROJECT PROFILE
(For a Drug Formulation Unit)

An attempt has been made in the following paragraphs to draw plan for setting up a progressive and viable drug formulation unit to cater the needs of a developing nation. Experience of Indian Pharmaceutical Industry has helped to draw the requirement of essential drugs which can be taken up for manufacture initially. But, who experts believe that a list of 130 to 140 drugs will suffice to cover the health needs at two levels: the primary level where patients have limited access to medicines at the health care centres and the secondary level where there are established medical facilities such as hospitals, laboratories etc.

This profile has been drawn out for an average sized pharmaceutical formulation industry which is manageable and economical in terms of production and the skill available. The profile gives an idea for the production of following dosage formulations in a year :

Tablets	...	1500 million nos.
Capsules	...	240 million nos.
Liquids	...	1800 Kilo-litres.
Injectables	...	300 Kilo-litres.
Infusions	...	12,00,000 bottles
Ointments	...	60 tonnes
Powder/Granules	...	60 tonnes

Production capacity of various departments of the Unit are worked out on the basis of the WHO's list of essential drugs and on working of two shifts (13 productive hours) a day for 300 days in a year. The unit will have a centrally airconditioned plant with a common utility services for various production activities Based on today's prices of plant and machiery, the recommended pharmaceutical formulation unit will involve a capital investment in plant and machineries to the tune of Rs 18 millions (US $2.15 millions) excluding the cost of land and building. The suggested unit would require floor space ademeasuring 11,000 sq. metres of land, would consume 700 KW of electric power and would give direct employment to 76 technicians, 240 skilled workers and 500 unskilled workers.

Details of equipments needed, personnel requirements in various manufacturing activities and processes involved have been given in the following pages.

Besides giving details of different manufacturing departments, full details of the Quality Control Department, Maintenance Department and also a Research & Development Section for development of formulations have also been provided.

PRODUCTION PROCESSES FOR DRUG FORMULATIONS

The manufacturing activities in formulation of drugs comprise of various departments such as Tablet Department, Capsule Department, Powder & Granules Section, Liquid Department, Parenterals and Ointment Department. For manufacture of transfusion fluid viz. normal saline, Dextrose, etc. a separate department may have to be provided.

The process for manufacturing each product varies from product to product as far as the manual details such as pH stabilisation, inert atmosphere in container, temperature, mode of sterilisation (whether autoclave sterilisation or by filteration) etc. It will not be feasible to give such manual details in manufacturing process of each product, but as far as the different dosage formulations are concerned, namely tablets, injectables, capsules etc., an attempt has been made to detail unit processes required in manufacture of different dosage forms.

All the raw materials (active therapeutic ingredients as will as excipients) are first tested by the Quality Control Department. On getting O.K. report from the Quality Control Department, the raw materials are supplied for production by the main store. Wherever cold storage is required, such items are stored in airconditioned storage. Secondly, there is an in-process quality control where the sampling during manufacturing process is done by the Quality Control Department and the sample is tested to see that the manufacturing process is going on properly. At the end of the manufacturing of the batch, a sample is again drawn from the bulk at the time of filling and finally, the finished product is tested by the Quality Control Department for the laid down standards for each product and if that is found O.K., the release order is given by the Quality Control Department for supplying to the finished products stores. Periodical testing is

also done regualrly on a few batches during the shelf life.

It may also be noted that for every batch, one has to rely on random sample checking as no unit to unit checking is possible and therefore, the observation of good manufactureing practice during the process is most essential.

TABLETS DEPARTMENT :

Annexure - A gives flow-chart for the process adopted for manufacture of Tablets.

The raw materials as per the formula of the product with other excipients as mentioned in the Master Card for each product batch size are weighed under the supervision of a qualified chemist. The batch is then further processed by mixing in a mixer. The granulating solution is added to prepare a moist mass which is passed through a granulator for wet granules. The wet granules are dried in a chermostatically controlled over at a reasonable temperature, so that the potency of the product is not affected.

The dried or semi-dried granules are again passed through a smaller mesh in granulator and then they are lubricated with lubricant and mixed with disintergrating material. A sample is tested from bulk granules before compressing the mass into tablets.

The dry granulation process is followed when the active ingredient is major part of the formulation and is affected by moisture. In this process the powder is directly slugged and reduced through desired mesh, lubricated and compressed into required tablets.

The lubricated granules are then pressed into tablets in a tabletting machine. During compression, samples are regularly drawn for hardness testing and for the distintergration testing, uniformity and friability.

At the end of the compression, samples are drawn by the Quality Control Department for carrying out the necessary test for each active ingredient.

Finally, the tablets are packed into respective containers which may be glass bottles, plastic containers or strips made of aluminium, celopoli, paper poli, etc. The labelling is completed after putting the batch number, manufacturing date and expiry date, if any.

If required, tablets may be film-coated, sugar - coated or enteric coated.

CAPSULE DEPARTMENT :

Annexure - B gives flow-chart for the process adopted for manufacture of Capsules.

As per the Master Card, the raw materials are weighed under supervision of a chemist and they are thoroughly mixed in a mixer. If small granules are required, granulating solution is put and the wet mass is passed through granulator. Wet granules are then dried at the required temperature in a thermostatically controlled drying ovem. The empty gelatin capsules are then taken into hopper of automatic capsule filling and closing machine and after adjusting the weight, the batch is filled in the machine. The filled capsules are regularly checked for weight variation, if any. If required, the machine would be adjusted to avoid any weight variation.

In the manufacturing process of capsules, the main requirements are the temperature and the controlled humidity. Hence, the manufacturing is carried out in an airconditioned area having controlled relative humidity around 50%.

Finally, samples are drawn by the Quality Control Department and after testing, the batch is released for the finished products stores. The filling of the capsules in the contrainer is also done in an airconditioned area and in a humidity controlled area, so that the capsules are not spoiled during the storage. The containers are finally labelled after printing the batch number, manufacturing date, and expiry date, if any. Capsules can be strip packed also.

LIQUID DEPARTMENT :

Annexure - C gives flow-chart for the process adopted for manufacture of liquid preparations.

The raw materials are weighed under the supervision of a chemist and the manufacturing process is carried out as per the Master Card.

pH, Viscosity and volume are to be adjusted and checked for getting stabilised product.

If the product is a suspension, it will be required to pass through c Colloid Mill or a Homogeniser.

After making the final volume of the batch, it is filtered through a filter press, if it is a clear solution.

The sample is drawn from the bulk by the Quality Control Department and also the final finished containers are sampled by the Quality Control Department for releasing the batch.

The product is filled into bottles or in jars and in case of Vitamin preparations, the air gap is flushed with inert gas to replace the air for stabilising the product. The containers are finally capped in a capping machine and then labelled by putting batch number, manufacturing date and expiry date, if any.

PARENTERAL DEPARTMENT - INJECTABLES & TRANSFUSION FLUIDS :

Annexure DI & DII show the flow-charts for the processes adopted in manufacture of Injectables and Transfusion Fluids respectively.

The solution making process and the filling sealing of the product in an ampoule or vial are carried out in a sterile area. This sterile area is airconditioned and is maintained under a positive pressure to prevent the outside air to contaminate the sterile area. The air which is taken through the airconditioned unit is also filtered through different filters and finally through bacteriological filter, so that the sterility of the area is strictly maintained. The duct carrying the air from the airconditioned unit is also fitted with bactericidal lamps. The bactericidal lamps are also fitted in sterile room and aseptic filling cabinets. The filling and sealing process is further carried out under laminar flow. Sterile area is regualrly checked for any contamination and to ensure sterility.

The raw materials are weighed under the supervision of a qualified chemist for making the solution with required solvent as per Master Card. After the solution is ready, if the product is temolabile, it is sterilised by filtering through bacteriological filters, say either G-4 or G-5 filters or preferably through millipore filters. The sample from the bulk container is drawn and sent to the Quality Control Department for testing the sterility of the product. Thermostable products are sterilised by autoclaving at the end.

Containers and closures such as ampoules or vials and transfusion bottles as the case may be, and rubber closures are first preliminarily washed and then they are finally washed with distilled water for a number of times. Ampoules, vials and transfusion bottles are also flused with filtered compressed air. These containers are then sterilised in hot-air oven at a high temperature in closed containers. The closures are sterilised by autoclaving. The bulk sterile solution is then filled into ampoule, vial or transfusion bottles, as the case may be, in a sterile area.

The ampoules are tested under vacuum for leak test.

The filled ampoules, vials and transfusion bottles are individually inspected for any particulate matter present.

Finally, samples are again drawn by the Quality Control Department and again tested for sterility and for active ingredients. On passing the test, the batch is then released by the Quality Control Department. The containers are finally labelled after putting the batch number, manufacturing date and expiry date, if any.

OINTMENT DEPARTMENT :

Annexure - E shows the flow-chart for the process adopted in manufacture of Ointments.

For ointment, fine particle size of the raw materials is one of the most important requirements.

As per the Master Card, the base for the ointment is separately prepared in a jacketed mixing tank. After preparing the base, the ingredients are added and during addition, constant stirring is maintained for proper mixing.

Finally, batch is then passed through a triple roller mill for the fineness of the product.

If the ointment is to be used for eye, all the above mentioned processes are carried out in a sterile area, exactly as narrated in parenteral department.

Ointment tubes are flushed with compressed air and in case of a sterile preparation, they are sterilised.

The filled ointment tubes are then sampled by the Quality

Control Department and tested for active ingredient, contents, sterility , etc. and on getting them O.K., the batch is released for finished products stores. At the time of filling the tube, batch number, manufacturing date and expiry date, if any, is pressed on the tubes right on the ointment filling machine.

POWDER & GRANULE SECTION :

Annexure - F shows the low chart for the process adopted in the manufacture of Powder & Granules.

Prepare granules of the dry syrup as per the Master Card. Specified weight of the granules are filled by automatic filling machine and capped. During the bottle filling, sampling is carried out for weight variation. The finished product is analysed before final packing. After testing, the batch is released for finished product stores. The bottles are finally labelled after printing batch number, manufacturing date and expiry date, if any.

.....

REQUIREMENT OF EQUIPMENTS IN VARIOUS DEPARTMENTS OF DRUG - FORMULATION UNIT.

1. **Tablet Department :**

Capacity — 1500 million tablets/years 6.25 million tablets/2 shifts/day.
Average Wt/table : 350 mg.
2.5 tonnes/day - 62,50,000 tablets.

Floor Area — 485 sq. metres.

Equipment :

Granulation :

1.	Platform balance - 1 tonne capacity	1
	Platform balance - 300 kg. capacity	1
	Two Pan Balance - 10 kg. capacity	1
	Chemical Balance - --	1
2.	Powder Sifter:	
	Comminuting Mill - Jackete(Cadmill)	1
	Comminuting Mill - Simple (Cadmill)	1
3.	Mixer :	
	Hobart type Mixer with Stirrer - 500 Litres capacity	1
	Extra bowls for above	3
	Hobart type Mixer with Stirrer-100 Lts.capacity	1
	Extra bowls for above	1
	Steam operated kettle S.S. - 500 Litres	1
	Steam operated kettle - 100 Litres	2
	Mortar and Pestle(5 kg. & 10 kg. capacity)	1 each
	Cabinet dryer-Thermostatically controlled-100°C (Steam operated 48 trays)	2
	Fluid Bed Dryer - 120 kg.	1
	Fluid Bed Dryer - 60 kg.	1
	Extra Vessels for above	3 each
	Drying room(50 sq.metres), thermostatically controlled, with 6 Trollies of 48 trays	1

Lubrication :	
Powder Shifter- 50 kg.	1
Cadmach Granulator	2
Hobart Mixer (500 litres)	1
Platform balance- 500 kg. capacity	1
Platform balance - 10 kg. capacity	1
Compression Section :	
Press Coat (900 series)	1
Rota Press- 45 station(8000 tablets/minute)	1
37 Station Rotary Tablet Machine(Cadmach) (2500 Tabs/minute)	2
27 station Cadmach Rotary Tablet Machine (1500 tablets/minute)	2
16 Station Cadmach Rotary Tablet Machine (500 Tabs/minute)	2
Single Stroke Compression Machine(90 tabs/minute)	1
Hardness Tester	4
Vernier Calipers	2
Disintegration time unit	2
Chemical Balance	1
Chilsonator (Roll dia-20 cm x 10 cm 250 kg/hr)	1
Tablet Dedusting Unit	4
Coating Section : 1.5 million Tablets/2 shifts/day.	
Coating Pan - 60"	1
Coating Pan-72"	1
Jacketed Kettle (20 lit)	2
Colloid Mill	1
Polishing Pan with Drive	1
Dryer :	
48 trays cabinet type	2
Two Pan Balance 80 kg.	1
Two Pan Balance 1 kg.	1
Chemical Balance	1

II. CAPSULE DEPARTMENT :

Capacity 240 million capsules/year

1 million capsules/2 shifts/day.

Average Wt/Capsule : 300 mg.

300 kgs/day.

Floor Area 255 Sq. metres.

EQUIPMENT :

Platform Balance - 300 kg.	1
Two Pan Balance - 10 kg.	1
One Pan Balance - 1 kg.	1
Mixer - Cadmach - 210 lt. capacity	2
Double Conc. Mixer - 100 lt. capacity	1
Mortar and Pestle - 5 kg. capacity	1
Chilsonator - 40 kg./hr.	1
Dryers specially designed	2
Vacuum Dryer - 40 trays	1
Automatic Capsule Filling Machine(ACF-Cadmach)- 500 Caps/minute	2
Extra accessories for filling other size capsules for above	
Semi-Automatic Capsule Filling Machine(300 capsules)	3
Extra accessories for other size caps.	
Empty Capsule Loader	2
Capsule Inspection Unit with belt - 2 (1 Penicillin and 1 others	
Capsule Printing Machine	2(1+1)
Chemical Balance	3
Humidity Recorders	6(Roomwise each)
Capsule Polishing Unit	2(1 Penicillin+ 1 others)

III. LIQUID DEPARTMENT :

Capacity	1800 Kilo-Litres/year	
	7500 litres/2 shifts/day	
	60 ml. and 120 ml. pkgs.	
	94,000 units/2 shifts/day.	
Floor Area	890 Sq. metres	

EQUIPMENT :

Weighing Balance	Platform type 500 kg. capacity	1
	Double Pan 10 kg. capacity	1
	Mono Pan Balance 1 kg.	1
Mixing Tanks S.S. with Stirrer	5000 lt. capacity	2
	1500 lt. capacity	2
	500 lt. capacity	2
Jacketed Tanks with Stirrer	2000 lt. capacity	1
	1000 lt. capacity	1
Planetary Mixer, Hobart Type 500 lit. capacity		2
Colloid Mill		2
pH Meter		1
Viscometer		1
Lob pump (Pharma Lab.) - 1500 lit/hr.		2
Filter Press-2000 lit/hr.		2
Eight heeds filling unit(48000 units/shifts)		1
Automatic Capping Unit		2
Automatic Labelling Unit		2
Automatic Carton Opening Machine		2
Conveyor belts with checking units		2(7 metres each)
Automatic Gravity Filling Machine for viscous liquid like Malt		1
Kettle S.S. - 500 litres		1

IV. OINTMENT DEPARTMENT :

Capacity	60,000 kg/year
	250 kg/2 shifts/day
Floor Area	200 Sq. metres.

EQUIPMENT :

Cleaning Sterilizer for tubes

Isopropyl Sterilizer for tubes	1
Powder Sterilizer U.V. Close Cabinet of 5 kg.capacity	1

Manufacturing :

Weighing Platform type Balance 200 kg. capacity	1
Weighing two Pan Balance 10 kg. capacity	1
Weighing Monopan Balance 1 kg. capacity	1
Chemical Balance	1 (Sterile & Non-Sterile)

PREPARATION :

Jacketed Mixing Tank with Stirrer 200 kg. capacity	2(1 Sterile + 1 Non-Sterile)
Triple Roller S.S. Roll	2 (" " ")
Ball Mill 50 kg. capacity	1
Edge Runner Mill 25 kg. capacity	1
Jacketed Colloid Mill	1
Hot Air Oven(for Ophthalmic preparation) 200°C 48 trays	1
Autoclave Double - Door	1

Filling and Crimping :

Automatic tube filling and crimping machine 4000 tubes per hour	1
Chemical Balance - Mono Pan	1

V. PARENTRAL DEPARTMENT - INJECTABLES AND TRANS-FUSION FLUIDS :

A. INJECTABLES :

Capacity	300 kilo litres/year
	1250 litres/2 shifts/day.
Floor Area	305 Sq. metres.

EQUIPMENT :

Washing :

Automatic Rotary Type High Speed Washing Machine for ampoules and vials	1
Demineralisation Plant 300 lit/hr	1
Distillation Plant - 500 lit/hr.	1
Rubber Stopper Washing Machine 100 kg/capacity	1

Sterilisation :

Double-Door Autoclave with thermo-recorder 2400 vials capacity (42"x48"x84")	1
Double Door Dry Heat Steriliser 20000 vials capacity (65"x33"x32")	2
Storage tank with constant temperature for distilled water 1000 litres	2

Manufacturing :

Weighing Balance Platform type 100 kg.capacity	1
Two Pan Balance 100 kg. capacity	1
Single Pan Balance 200 gms. capacity	1
S.S. Tank 200 Lit. capacity Jacketed with Stirrer	3
S.S. Tank 100 Lit. capacity Jacketted with Stirrer	3
S.S. Pressure Vessel 100 lt. capacity	2
S.S. pressure Vessel 50 lit. capacity	1
Membrane filtering unit column type	2
Membrane filtering Unit 193 mm.	2
Membrane filtering unit 141 mm.	2
Vacuum Pump with high capacity	1
Air Compressor	1

Filling and Sealing :

Automatic multi-head vials filling and rubber stoppering unit with sealing unit	1
Three head ampoules filling and sealing machine	2
Laminar Flow (6 feet)	3 units

Lead Test :

Vacuum Operated Vessel	1
Inspection Unit for physical checking	10

B. TRANSFUSION FLUIDS :

Transfusion fluids which are widely used in hospitals are one of the essential items where every developing country would like to have its own manufacturing facility. Working details for the manufacture of transfusion fluids with capacity of 2000 bottles per day are given here below :

Capacity	2000 bottles/day
Area	630 sq. metres

EQUIPMENT :

For Washing :

Automatic Rotary Washing Machine for bottles	1
Demineralisation Plant 300 lit/hr.	1
Distillation Plant 400 lit/hr.	1
Water Softening Plant 600 lit/hr.	1
Rubber Stopper Washing machine-25 kg. capacity	1
Double Door Autoclave with Thermo-recorder size 12'x10'x12'	1
Double Door Dry Heat Sterilizer Size : 12'x10'x12'	1
Storage Tank with constant temp. for destilled water - 1000 litre capacity	1

For Manufacturing :

Balance - 100 kg.	1
Balance - 10 kg.	1
Jacketed S.S. Tank with Stirrer-1200 litres	1
S.S. Tank - 200 litres	1
Filter Press Plate type-1000 litres/hr.	1
Sinter glass funnel-120 mm. funnel unit 6 SG4.	1

For Filling & Sealing :

Bottle Filling Machine	1

	Sealing Machine for transfusion bottles		1
VI.	POWDER & GRANULES SECTION :		
	Capacity	60 Tonnes/year	
		250 kg/2 shifts/day	
		or 12,500 bottles	
	Floor Area	165 Sq. metres	
	EQUIPMENT :		
	Mixer (210 litres capacity)		2 (1 Penicillin + 1 others)
	Dryer (48 trays)		2 (-do-)
	Augur type Automatic bottle Filling Machine		2 (-do-)
	Conveyor Belt		2 (-do-)
	Semi-Automatic Capping Machine		2
	Granulator		2 (-do-)
VII.	QUALITY CONTROL DEPARTMENT :		
	A. Chemical Analysis Division :		
	Mettler balances		3
	Melting Point apparatus		2
	Hot air Oven		3
	Vacuum Oven with vacuum pump		1
	Distilled water unit		1
	Muffle Furnace		1
	Oxygen flask with platinum basket		2
	Platinum dishs and crucibles		6
	Various tpes of Glassware		
	Waterbath (Electrical)		3
	Gas Plant		1
	Other miscellaneous equipments		
	B. Instrumental Analysis Division :		
	Gas Chromatograph		1
	I.R. Spectophotometer		1

	U.V. Spectophotometer	1
	Flourimeter	1
	pH Meter	2
	Refrectometer	1
	Paper Chromatographic equipment	1
	Thin Layer Chromatographic equipment	1
	Air permeability apparatus for surface area	1
	Polarimeter	1

VIII. RESEARCH & DEVELOPMENT DEPARTMENT (FORMULATION)

Area 150 sq. metres.

EQUIPMENT :

Tablet Compression Machine-Single Stroke	1
Rotary Tablet Machine-16 Station	1
Mixer	1
Granulator	1
Coating Pan	1
Oven Small size(range 40°C - 200°C)	1
Capsule Filling Machine(200 capsules)capacity	1
Balance - 5 kg. capacity	1
Chemical Balance Single Pan-200 Gms.capacity	1
Triple Roller Mill- small size	1
Colloid Mill - small size	1
Jacketed Vessel & Stirrer-5 lit. capacity	1
Ball Mill- kg. capacity	1
Tube Filling Machine-semi-automatic	1
Tube Crimping Machine-semi-automatic	1
Liquid Filling Machine(range 1 to 30 ml.)	1
Capping Machine for vials & bottles	1
Mini-bottle and Vial Washing Machine	1
Autoclave Small size	1
Ampoule Sealing Machine	1

	Incubator 30°, 45°, 60° each	3
	Refrigerator small size	1
	Humidity & Temperature Control Cabinet	1
	Library Books and Periodicals	

IX. CENTRAL PACKING DEPARTMENT :

Area 750 Sq. metres

EQUIPMENTS :

Strip Packing Machine(Six Tablets)	6
Conveyor Belts (5 Metre each)	12
Automatic Tablet Counting and Filling Machine	2
Automatic Capsule Counting and Filling Machine	1
Automatic Capping Machine	2
Tin Sealing Machine	1
Gumming Machine	2
Automatic Carton Opener	3
Automatic Label & Carton Printing Machine	2
Automatic Printing & Labelling Machine for Vials and Ampoules	3
Heat Sealer for Plastic bags	3

X. MAINTENANCE & COMMON UTILITY SERVICES DEPARTMENT :

Area 375 Sq. metres

EQUIPMENTS :

Lathe (165x600 mm) (Kirloskar)	1
Lathe (300x200 mm) -do-	1
Drilling Machine (2") (Praga)	2
Bench Grinder (150 mm) (Wolf)	1
Flexible Grinder- medium size(wolf)	1
Portable Drill Machine :	
Upto 13 mm. size (wolf)	1
Upto 38 mm. size (wolf)	1
Portable Blower- small size (wolf)	1

Electric Welding Machine 12 KVA 3 Phase Oil cooled (Advani)	1
Gas Welding Set (standard size)	1
Air Compressor-20 HP, 3 phase 60 CFM, 150 PSI (Ingersoll Rand)	1
Vacuum Pump - 10 HP, 3 Phase, 177.0 CFM, Ultimate vacuum-0.005 (J.B. Sawant Engg.)	1
Gas Plant- 8A Size Gas produced 41.5 c.m,etre per hr.(Ganson)	1
Boiler- tons capacity (Wanson or WIMA India)	1

Water Treatment Plant :

i) Demineralised water plant - 1000 lit. per hr.

ii) Water Softening Plant - 10000 lit. per shift.

iii) Distilled water plant - 500 lit. per hr.

Air-conditioning Plants 80 tons capacity plants.

QUALITY CONTROL DEPARTMENT :

The Quality Control Laboratory should be staffed and equipped in such a way as to carry out effectively all the required tests on samples of raw materials as well as the finished products.

RAW MATERIALS :

The control of raw material has a special significance, as it constitutes the beginning of the long series of controls. The primary reason for exercising controls over raw materials is one of quality assurances.

Adequate and realistic specifications should be established for raw materials. Reliable and suitable methods of testing for these specifications should be developed. Specific procedure for receiving, inspecting and sampling consignments should be followed. Data obtained from testing raw materials should be recorded in the control record sheets. If the consignment is accepted, the approval release document is

made and despatched to stores after which the lot is removed from the quarantine. It is desirable to stick control release labels to indicate that the material is passed or 'Hold' label for rejected materials to every container. Rejected materials should not be moved from quarantine and should be returned to supplier with the minimum delay. The quality control department advises the stores department for the proper storage conditions. Quality Control Department also fixes the specification of packing components, such as ampoules, vials, bottles, closures, empty capsules, labels cartons etc.

INPROCESS CONTROLS :

Inprocess controls at various stages of production are of considerable importance. Rigid Control over sterilisation temperature, pressure differntial between the sterile and non-sterile side of the premises, bacterial count of the inlet air and the entire sterile area, especially the cubicles, analysis of mixed powders and granules, weight variation of tablets, capsules or volume in disages delivered to vials, temperature and humidity in coating and filling rooms and inspection of filled containers for the absence of particulate matter, quality of sealing, hardness and friability of tablets, pH and volume of liquid preparations-all contribute to a great extent in building the quality of the product.

Before and after the finished product is ready, Quality Control Chemist withdraws the sample and analysis. Specifications for the finished products at different stages are established by the Quality Control Department.

PHARMACOLOGICAL ANALYSIS :

In addition to chemical analysis, biological testing is included for raw materials as well as finished products. Biological tests include pyrogen testing, toxicity tests and depressor tests and bio-availability test in certain sensitive products.

Pyrogen test is carried out in rabbits for water for injection, antibiotics and injections of antibiotics. Toxicity tests are carried out on mice for antibiotics in raw from as well as finished products. Depressor test is carried out in cats for antibiotics in raw form and finished products.

RETAINED SAMPLES :

Adequate quantity of each and every batch of the fianished product is stored for a desired time in a retained sample room. The products with expiry dates are kept for e months beyond the expiry date and n on-expiry products for 3 years from the date of manufacture at prescribed temperature. A periodical observation of these samples is carried out and record of it is maintained.

Quality Control Department analysis raw materials, packaging materials, in process products, finished products, products from research and development departments and samples of periodical and stability studies and controls the manufacturing processes.

Load for analysis per day :

6.25 million tablets	6 batches
500 kg. powder for capsules and dry syrups	4 batches
3750 litres liquid	2 batches
250 kg. Ointment	2 batches
1250 litres Injections	5 batches
Total batches per day	19

i.e. 100 ingredients per day including raw materials and packing materials.

5.4 **Area of modifications possible :**

As far as the manufacturing activities are concerned, the following are the salient features which are amenable to change.

I. a) Scale of production
   b) Batch-wise/continuous production
   c) Packing (in the case of formulations)
   d) Size of equipment used

II. a) Stage from which drugs are produced
   b) Product-mix

Items II (a) & (b) are of a policy nature. The list of essential drugs is to be drawn up by every country, taking into account the prevailing disease patterns and economic situations. India has already drawn up a list of 117 drugs which are considered essential. The decisions of this nature help in pricing, licensing and import policies of the Govt. Left to themselves, the manufacturers will end up producing high value-low volume drugs and the needs of the population will go unmet; the investment will go into areas which are socially less desirable. The public sector, if any, must be assigned the responsibility of meeting the major portion of needs of essential drugs of the population.

Secondly, the stage from which drugs are to be produced is to be determined taking into account the availability of technical skills, availability of established chemical industry in the country etc. The D&P industry may choose to operate at any the following stages :

i) Import finished medicines and repack
ii) Import bulk and formulate
iii) Import penultimate intermediate, produce in bulk and formulate
iv) Import basic raw materials and produce bulk drugs from various stages
v) Produce bulk from indigenous raw materials.

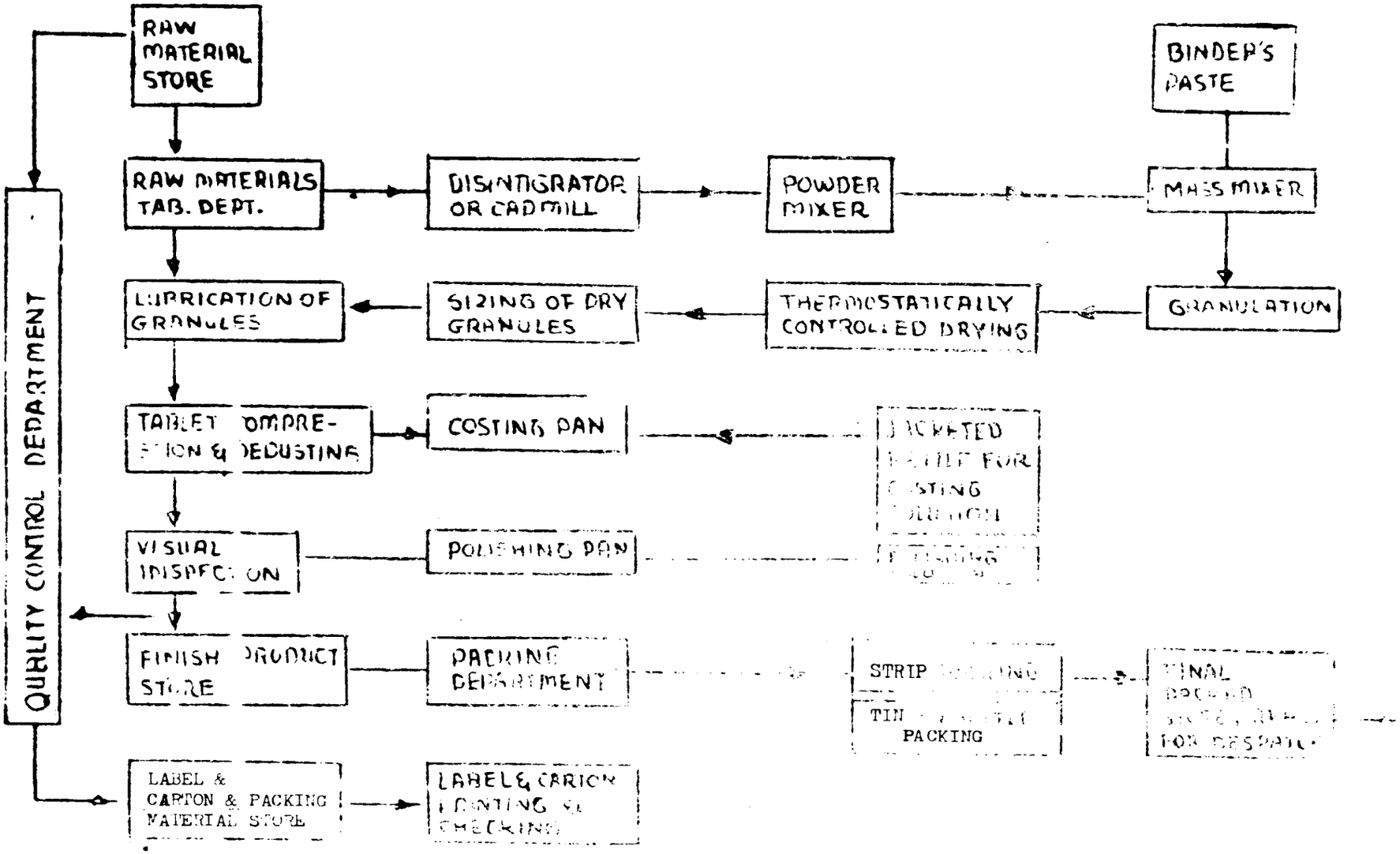
Obviously, as a country develops, it will move down this list. While it is quite desirable that a country be self sufficient in needs of drugs, the viability and sustainability lity of the proposal must be considered before any decision is taken in this regard. Also, these countries need not aim

at self sufficiency in all drugs. The country may be better-off producing those drugs for which skill, raw materials and demand exist and importing the other drugs. A feasible strategem in this regard is to start at the top of the above list to meet the current demand for drugs at the same time improving the infrastructure so that the degree of self reliance increased rapidly.

Regarding in the technical choices, the scale on which the production units are set up depends naturally on the demand. It is necessary to point out that the developing countries need not adopt the large scale manufacture technology which are proved to be least cost ones, even when demand constraints do not exist. This is because the resources available are different, and it may be desirable to have a few small units instead of a big one.

In the drug industry, generally much choice doesn't exist between batchwise and continuous production. Mostly, it would have to be batch wise because of the quality standards.

As regards packing, both the kind of packing and the technology for packing can be different . For example, there is no need to go in for very convenient but costly packing of tablets like blister packing. Such things make drugs avoidably costly. The quality standards can be met by packing tablets/ capsules in bulk in glass bottles. It is needless to say that packing and packaging are the areas where human labour can be used and that labour intensive methods must be chosen.



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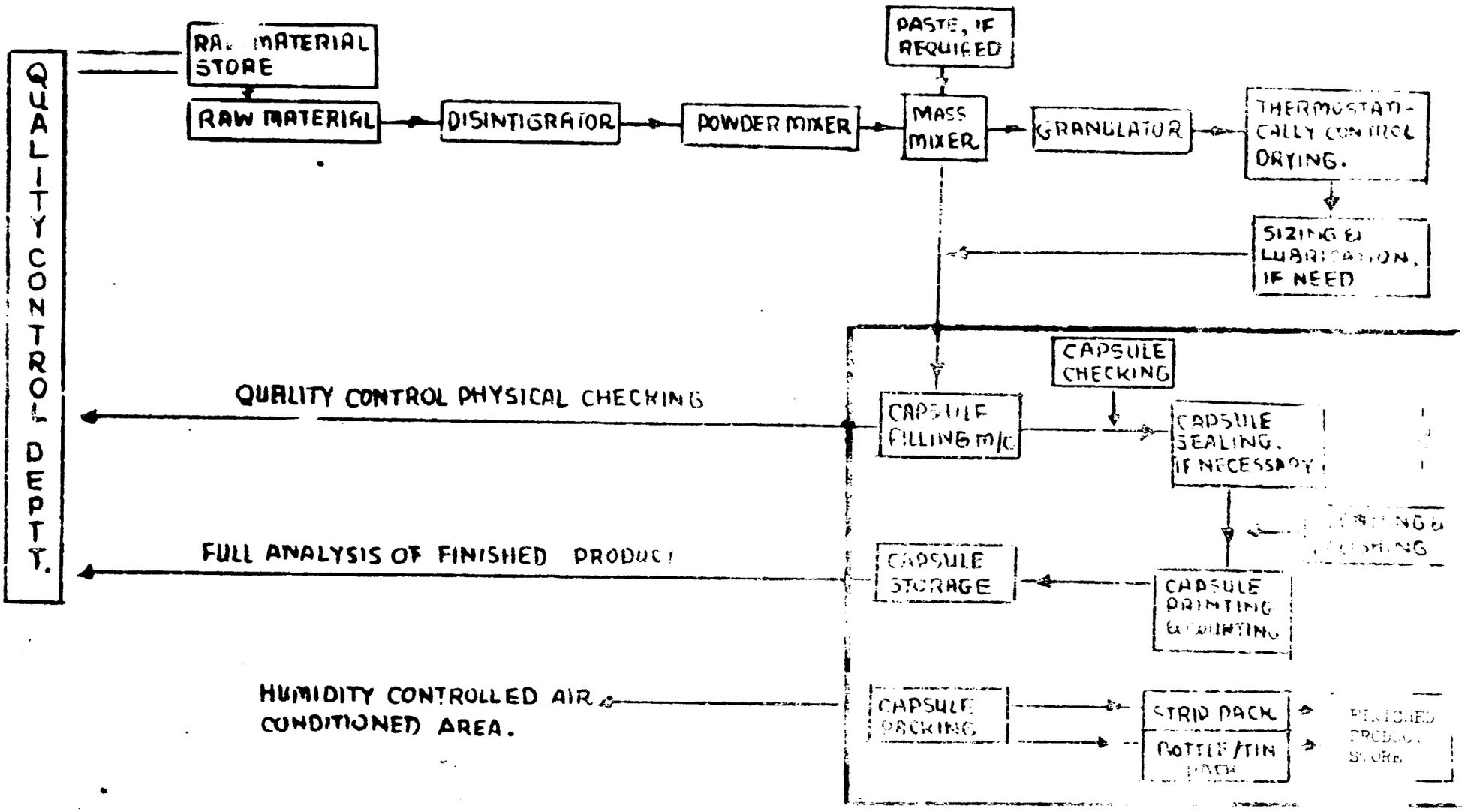

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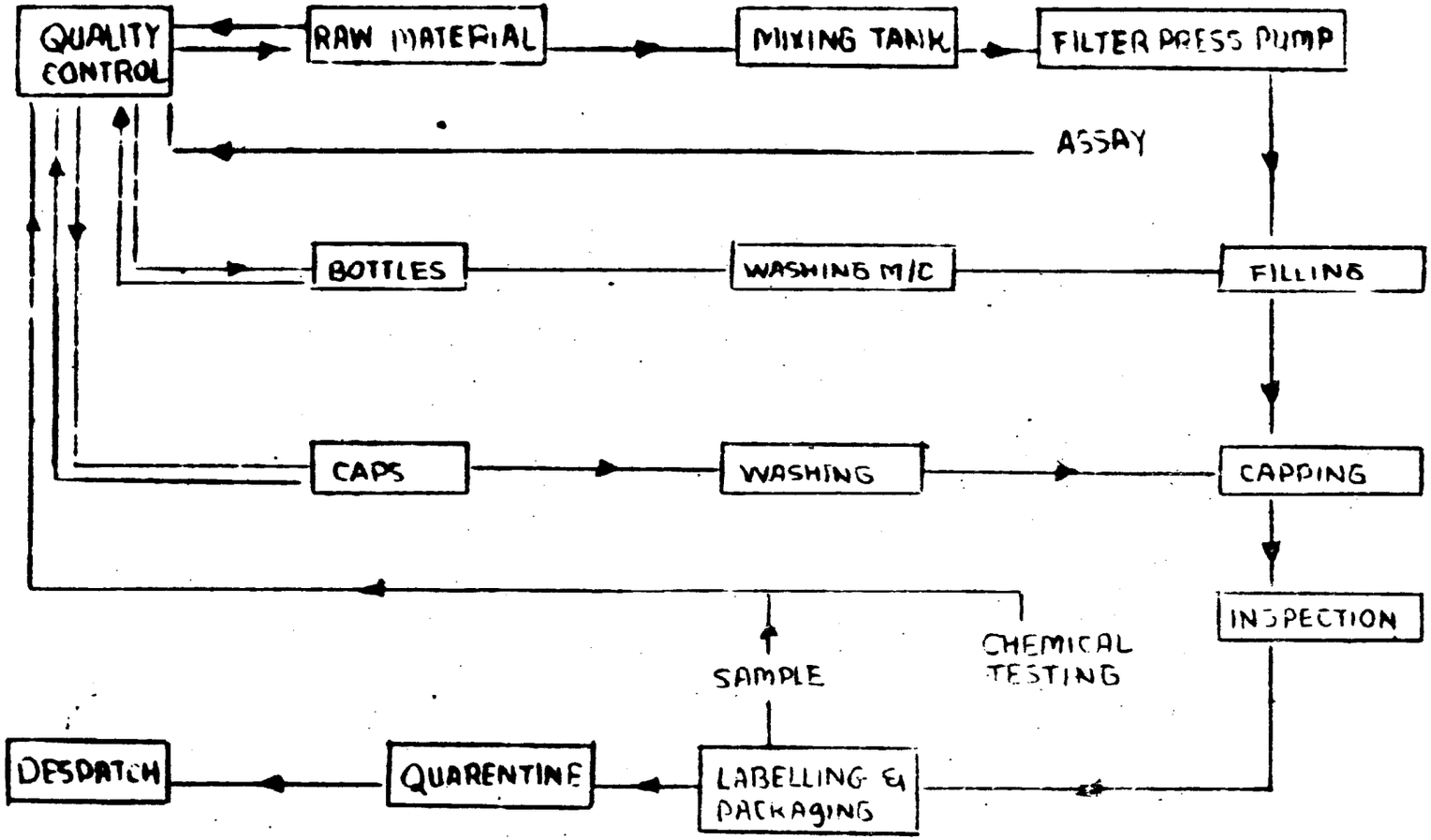

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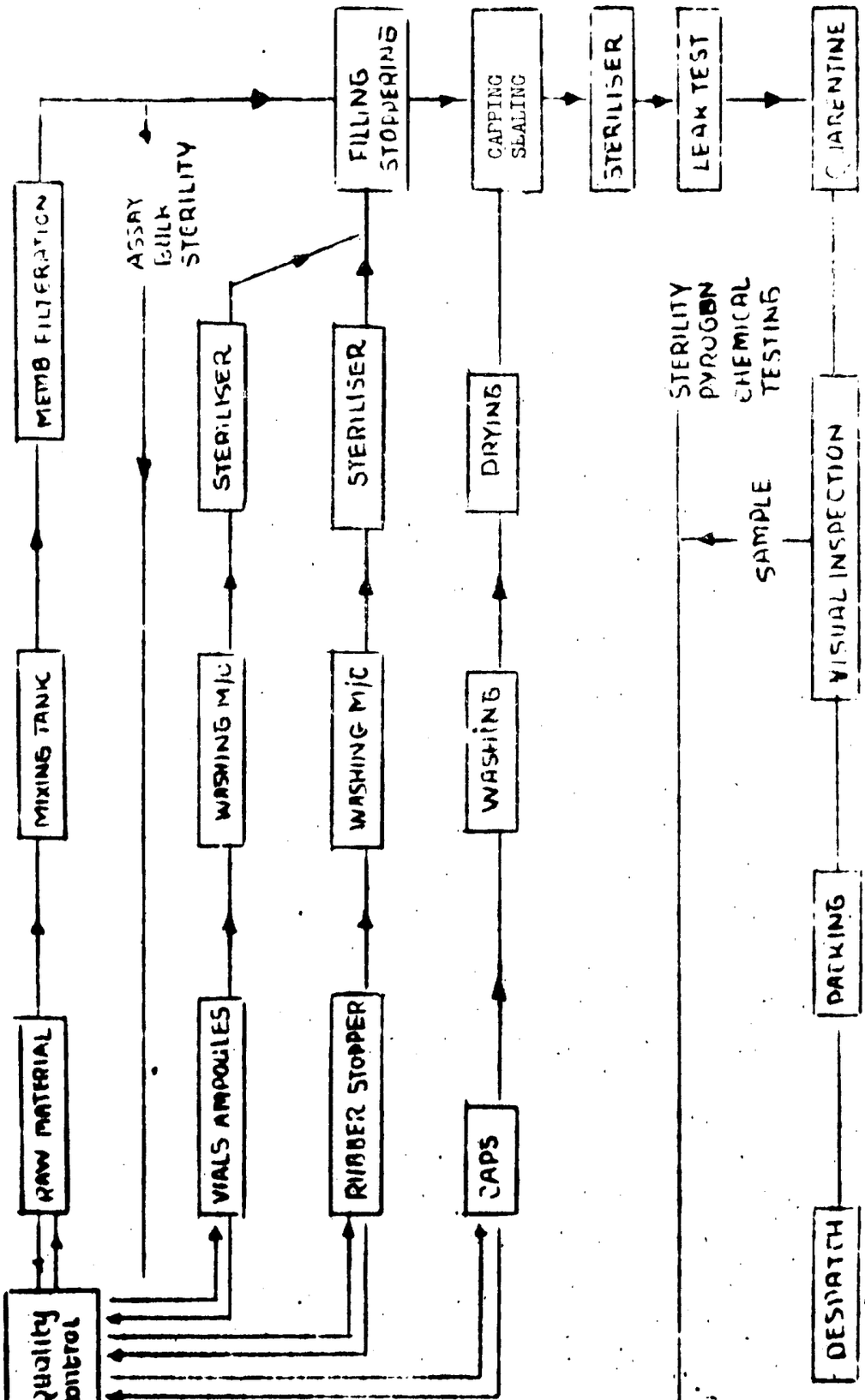

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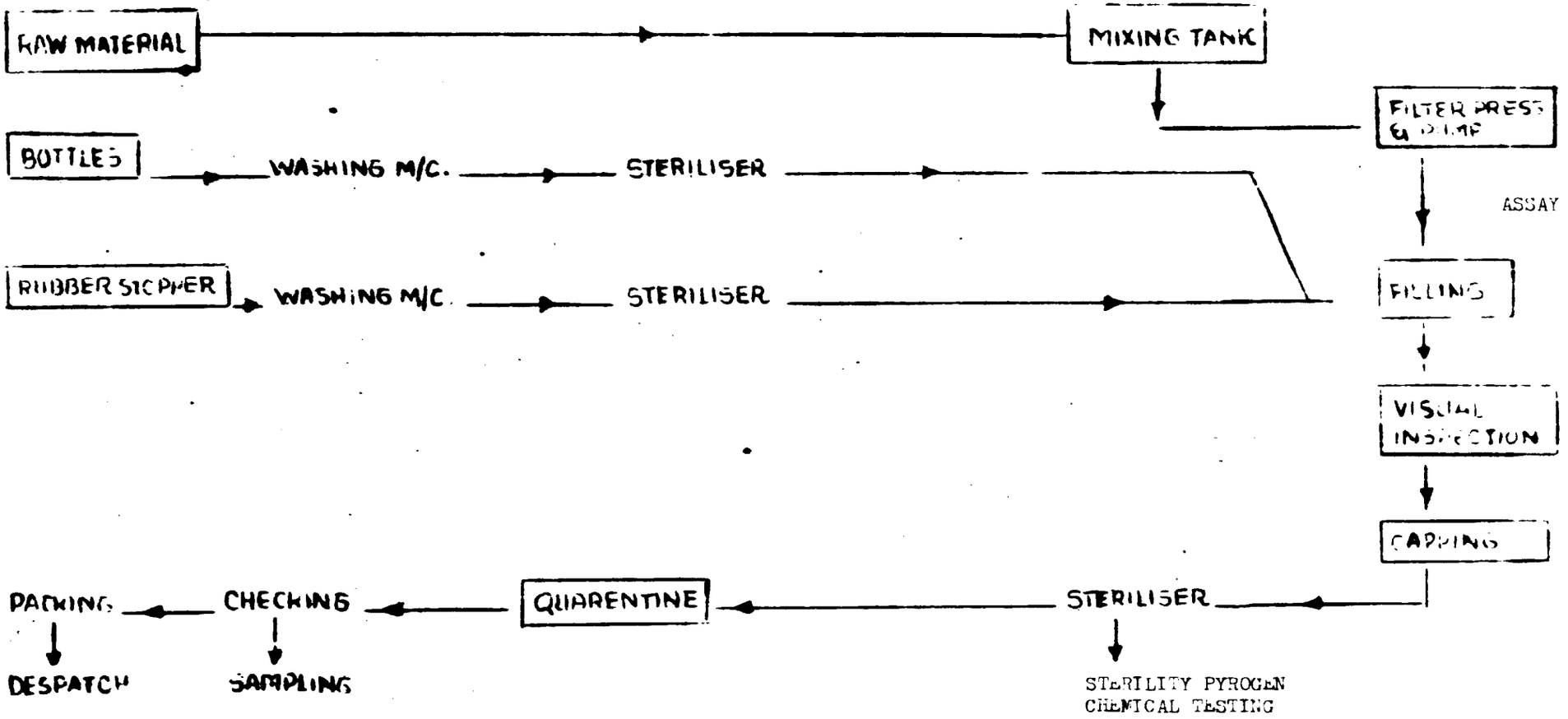
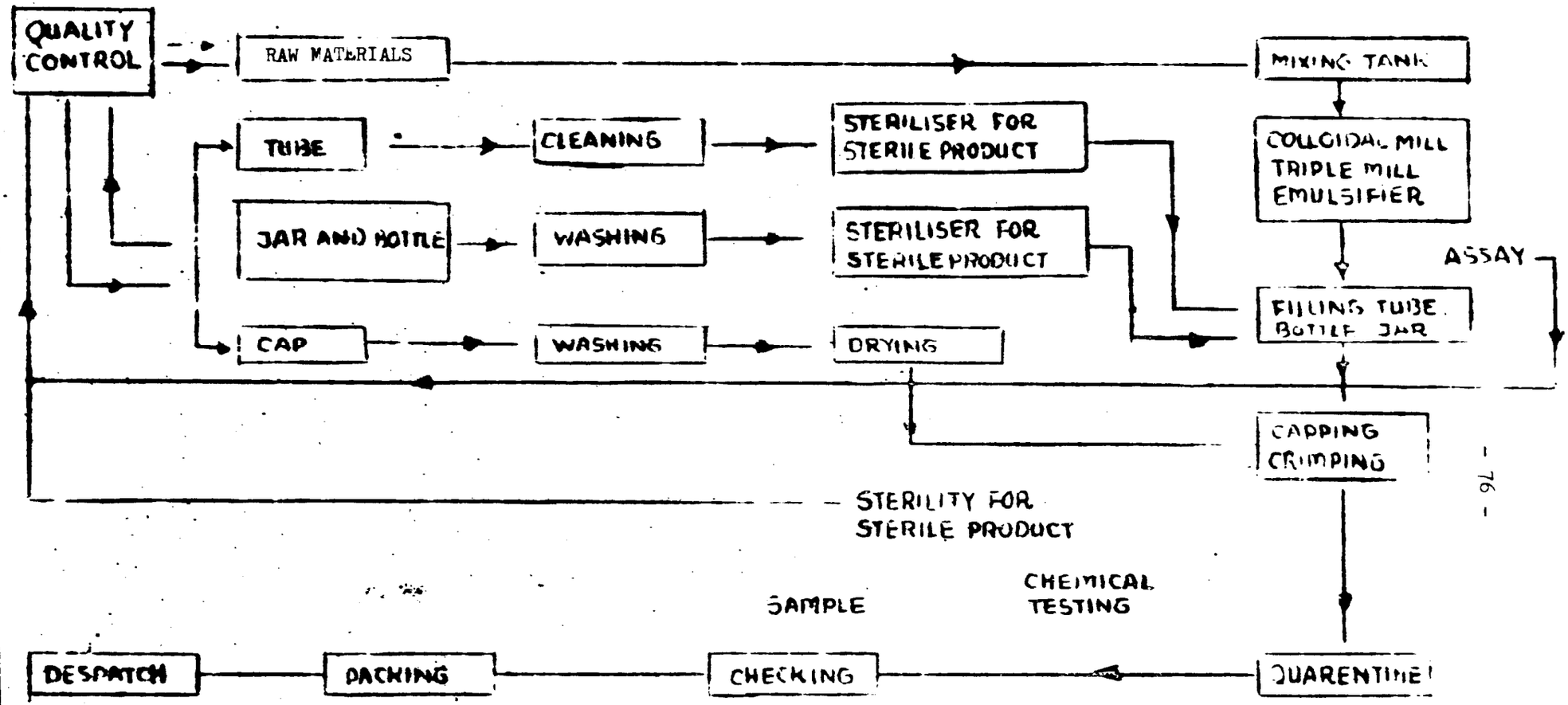


FLOWING SHEET FOR TRANSFUSION FLUIDS



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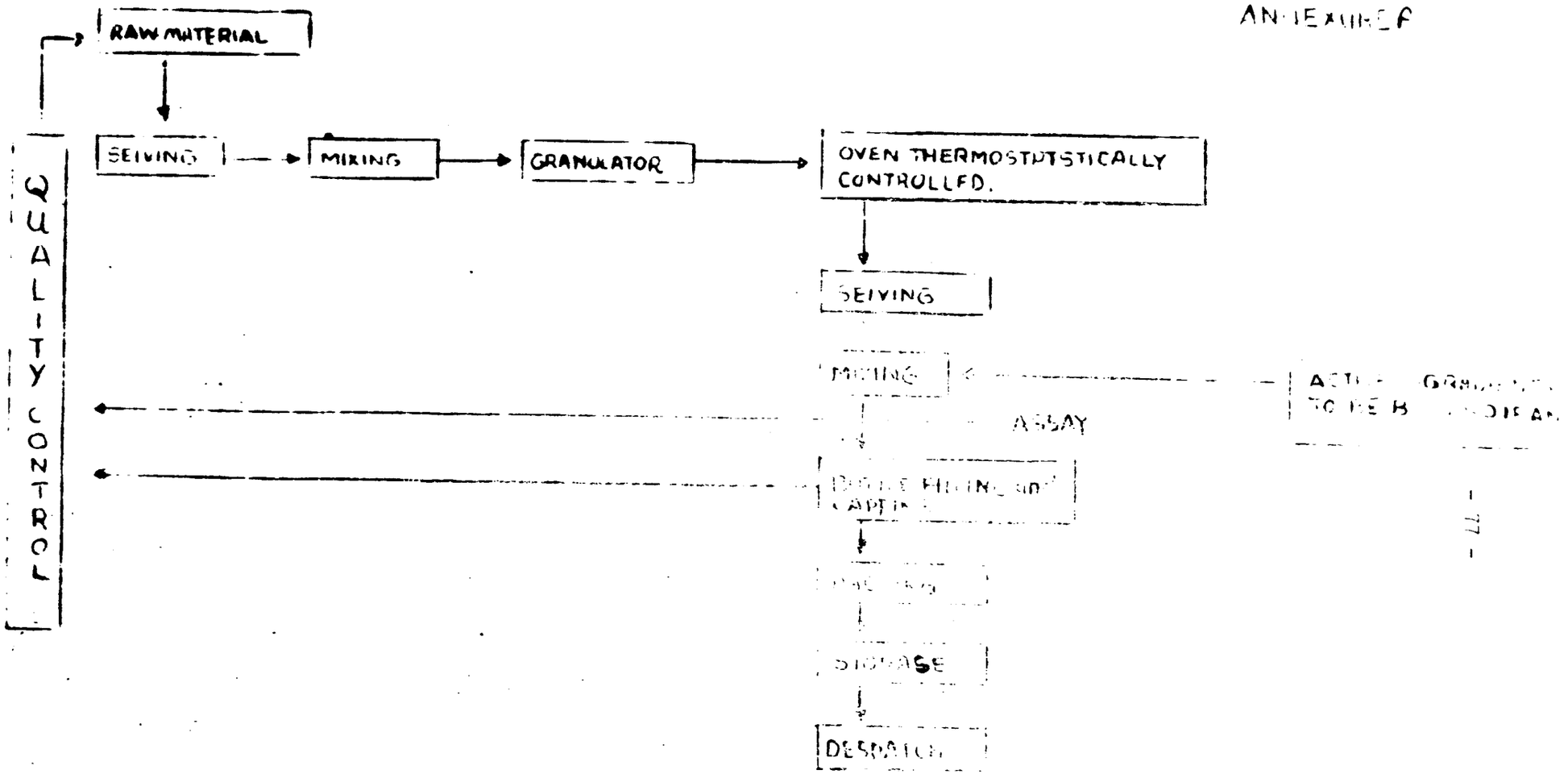

FLOW SHEET FOR POWDER FILLING

6.0 Section IV System of distribution of Drugs & Pharmaceuticals and measures for quality maintanance.

6.1 Practice in developed countries

In the developed countries, distribution of drugs and pharmaceuticals is considered to be a professional service with high responsibilities. This awareness has been translated in these countries in the implementation of certain controls and business terms that may not be possible in a developing countries.

A manufacturer or an importer distributes through a system of whole-salers who in turn supply to retailers.

The system of trade discounts leaves a margin of gross profit of 25% for the wholesaler and as much as 33% for the retailer. For imported drugs the importer also takes 10% on C.I.F. price plus duty.

The retailer has to have the services of a graduate pharmacist.

By virtue of their "development", the reaching of drugs and pharmaceuticals where they are needed and when they are needed does not pose much of a problem in developed countries. The net work of transport is highly efficient, specialised transport like refrigeration vans is available, the population is largely urban, better educated and the health services are better organised and better staffed.

6.2 Practice in developing countries.

A developing country like India faces a formidable task of transporting medicines over an area of the size of a sub-continent. The net work of transport, though improving every day, seems inadequate. The regualtions of various taxes and duties vary in different places. Unlike the distribution of consumer items, the drugs distribution costs in India are borne by the manufacturer. Traditionally he to take back what is not sold and reimburse any breakage in transit.

The non-availability of refrigerated vans also poses problems for distribution of drugs like Vaccine and sera. The normal procdeure is to transport such drugs in ice-boxes upto the District Towns, store them in refrigerators and supply to smaller places in vaccum flasks packed with ice. For other

products, proper stabilisation techniques are employed and periodic studies are conducted on the drugs after they reach their destination.

The drug industry in India has the following network at present :

1.	Licensed wholesale and retail chemists	1,00,000
2.	Hospitals and Dispensaries	15,000
3.	Primary Health Centres etc.	48,839
4.	Doctors' Dispensaries & Clinics	1,40,000
5.	General merchants having drug licenses	1,00,000

In the absence of a National Health Scheme, the health services in India functions under two broad-heads Government and Private.

The Government has a full-fledged Directorate of Medical Services with Directors in all states. Each district in the state has its own civil surgeon who presides over the civil hospitals and also a District Health Officer who administers the District Dispensaries and Primary Health Centres. These Govt. agencies purchase their requirements through ate contracts. To certain categories of Government servants, there is a system of re-imbursing the cost of the medicines prescribed by the authorised medical officer.

To cover a large numler of industrial workers, the Employees' State Insurance Scheme functions under a separate Directorate. The cost of the medical and health services provided to the workers covered under this scheme is borne by the employer and the Government. The worker contributes a very small percentage of his salary as a premium.

Large municipalities, Industrial Concerns and Corporations have their own systems of health care. They usually buy directly from the manufacturers.

To cater to the needs of the vast number of patients being treated by private doctors, there are more than 1,00,000 wholesale and retail outlets in the country. There are other 1,00,000 general merchants having restricted drug licences to sell comparatively safe "non-schedule" drugs that do not require a doctor's prescription.

A licensed doctor required the services of a qualified pharmacist.

Unlike the practice prevailing in the developed countries, these pharmacists are not required to be graduates of pharmacy. They could also be diploma-holders in pharmacy.

In developed countries, basic health care is accepted as a basic head. Since everyone appreciates the need and is able to spend for it, the istribution of drugs is even.

The developing countries, the urban people appreciate the need better and a fraction of them are able pay for it. So, the drug stores trend to get concentrated in urban areas. In these countries, doctors-who, by their prescriptions create demand are concentrated in urban areas. In villages, people resort to self medication and so a doctor is better off in a city in spite of the competition than in a village.

The basic reason for these is that the income level is low and even this is not evenly distributed. Also, the doctors develop an urban orientation so that even if the income in urban and rural areas were to be equal, a doctor would rather like to line in an urban area than in a village. The relatively higher degree of self medication is also responsible for the kind of distribution of drug consumption obtaining in developing countries. Further, the people in rural areas are ignorant of the better and safer medical treatments available to-day.

It is clear therefore that if drug consumption is to be more evenly distributed, an all round development has to come about in these countries.

Meanwhile, some simple cures at least must reach the rural areas. In developed countreis like Australia, the rural people are catered to by flying doctors. A trained nurse in a remote area communicates the symptoms of the disease of the patient to a doctor through wireless and the doctor instructs what to do. Poor developing countries can not afford such methods. Even proposals like a doctor travelling in a van visiting a villages every week are considered too costly to set up and maintain. So a system which would require less investment and recurring expenditure and would make use of human resources available is called for.

In India, the rural health scheme now being implemented by the Govt. involves training a few colunteers on how to cure certain simple diseases and giving the volunteer drugs worth Rs 600 p.a.

The village head man, the school teacher, the postmaster, are some people who can be used for this purpose. The Govt. would have to guard itself to see to that these barefoot 'doctors' do not profess to know more than they do and cause serious damages and to see to that spurious drugs are not administered by these 'doctors'.

One important thing the governments of the developing coutries should bear in mind is the fact that the rural flok are, after all, using some medical methods of their own. The allopathic drugs are not necessarily the best for all diseases. So the Govts. need not be too pre-occupied with the idea of spreading use of allopathic cures. The Govts would do well to systeratically study the existing methods of cure and o modify them making them more effective. This strategy is likely to work because it be easy to develop on what is already familiar to the rural folk The doctors practicing these systems of medicine and the raw materials needed for these drugs would also be available in rural areas. So the rural health scheme of these countries should give considerable priority to these already acceptied systems of medicine.

Certain instances of family planning practices used by tribals of India being more effective than the popular allopathic methods have been reported. Obviously the Govts would stand to benefit exploiting such proven medicines and practices.

In developed countries, many competent organisations compete with each other. So competition can see to that the prices of drugs are low. The people are also more affluent and so can pay for the drugs.

In developing countries the number of competent manufacturers is relatively small. The people are striving hard even to get sufficient food and shelter. So, if the drug prices are let to be determined by market forces, monopolies will operate therby exploiting the people. So, the intervention of the Govt. is called for. India has a Drug Price Control system.

It should not be thought that the role of Govt. is negative-like imposing various regulations. Paradoxially, even the Govts. which want to keep the drug prices low impose various duties and taxes therby countributing to price rise. The govts.. can countribute to reduction in drug prices by providing inputs like raw materials, power, water, machinery at subsidised rates.

While fixing the prices of drugs, the govts. in developing countries try to keep the prices as low as possible because the ability of the consumers to pay is less. But this acts as a regarding factor in the supply end i.e. because the drugs are not profitable enough, entrepreneure invest their resources elsewhere and so the quantum of drugs produced remains small. Govts. should therefore try to keep the prices low by supplying inputs at a cheaper cost rather than by providing smaller profit margins.

6.3 Regulation of prices of Drugs in India

In India, the prices of drugs have been under control for over a decade. For the first time in 1962, an order was promulgated which required display of price lists. This was followed by an amendment to the (Control of Prices) Order, freezing the prices of medicines at the level prevailing on 1st April 1963. As the prices of various raw materials and other inputs were not frozen at the same time this order adversely affected the growth of the industry. Government introduced a system of selective increase of prices in 1966 and issued the Drugs Prices (Display & Control) Order in June, 1966 which made it obligatory for the manufacturers to obtain prior approval of Government before increasing the prices of any formulation. By subsequent amendements, new drugs developed through original research as well as items marketed under pharmacopoeial names were exempted from the operation of price control. Government also referred to the Taruff Commission for investigation of the cost structure of 17 selected essential bulk drugs and as a result of their study, the Commission recommended fair selling prices for these items.

The Drugs (Price Control) order, 1970, was promulgated on 16th May 1970. This order was subsequently amended from time to time in the light of the experience gained in its working and suggestions received from the industry and trade. The salient features of the Order are :

i) Selling prices of 17 essential bulk drugs, in various forms wherever applicable, were fixed by the Government taking into account the recommendations of the Tariff Commission.

ii) Selling prices of other bulk drugs were frozen at the level prevailing immediately before the promulgation of the Order, and manufacturers or importers etc. were not to be permitted to increase the selling prices of the bulk drugs without prior approval of the Government for which details were required to be furnished in the prescribed form.

iii) With regard to formulations, the retail price (Price to the consumer) of a formulation is arrived at after taking into consideration the ex-factory cost, which compresses of the material cost and manufacturing charges, based on the norms for conversion and packaging prescribed under the Drugs (Price Control) Order. On the ex-factory cost a variable mark-up is provided ranging from 75% in the case of formulations of essential drugs, 100% in the case of new formulations evolved by product development work to improve the therapeutic efficacy and 150% in the case of new formulations containing a new drug developed in India. An alternate scheme of pricing of formulations also provides higher mark-ups upto 150% in the case of formulations of other than essential drugs, provided the overall gross profit before taxes does not exceed 15% of the sales turnover.

16.4 Branding

One of the important aspects of marketing of pharmaceuticals being discussed today is whether or not the drugs should be sold by brand names like all other consumer durables and non durables. This question is of greater relevance in developing countries because

i) branding invloves a lot of promotional expenditure (which is avoidable), making drugs costlier.

ii) branding makes it difficult for demestic manufacturers to compete with subsidiaries of multinationals using their established brand names, thereby hindering the growth of indivenous industries.

iii) branding helps some firms to sell drugs at exhorbitant prices (much more than what is justified even by marketing expenses) though the drug may technically be just as effective as other sold under generic names.

iv) A lot of unnecessary combinations of drugs flood the markets.

In developed countries where "the game of survival of the fittiest" can be played without the consumers suffering much because competition is intense in those countries and the ability of the consumers to pay is also more. But in developing countries, the competition is not strong enough to see to that the prices are reasonable. So, if a firm, because of its marketing strength, is able to establish a brand name, it can exploit the advantage and the common man would suffer.

But proponents of brand name argue that the quality of drugs can not be ensured unless the drugs are branded. Sourious drugs can find easy entry and manufacturers will go unpunished.

Still, it is felt that at least in the case of medicines for common diseases should not be branded. The Hathi Committee, appointed by the Govt. of India, recommended, inter alia, abolition of brand names of drugs (Annexure) as an initial step. In the long run, the committee felt, all drugs should be sold under generic names.

Others developing countris can also initiate the process of de-branding.

6.5 QUALITY CONTROL OVER DRUGS IN INDIA

1) The drugs and Cosmetics Act, 1940 regulates theimport, manufacture, distribution and sale of drugs in this country. Under the provisions of this Act and Rules framed under this Act, quality control is exercised over drugs that are imported into this country as also over those which are locally manufactured. The nature of contorl exercised over imported drugs and drugs manufactured locally are described below :-

2) CONTROL Exercised over imported drugs :

All drugs which are imported into the country are inspected by the officers of the Drugs Control Organisation of the Central Government posted at the ports at the time of import. The labels of such drugs are scrutinised to see whether all the particulars required to be shown on them including the claims for the drugs are in conformity with the provisions of the Drugs and Cosmetics Act the Rules. In addition, samples of imported drugs are drawn and sent for test to the Central Drugs Laboratory, Calcutta. In case the samples ontest are found not to be comply with the prescribed standards, the drugs are not permitted to be imported. Labelling deficiencies are also got rectified before being permitted entry into the country.

Whereas the conditions mentioned above are required to be fulfilled by all drugs at the points of entry into this country before import is permitted, biological and special products like sera and vaccines, antibiotics, surgical ligatures and sutures, vitamins and hormones, glandular products, etc. are, in addition, required to be imported under a licence under the Indian Act. The importer has to submit an undertaking from the manufacturer abroad, whose products are to be imported to the effect that the conditions of manufacture required to be complied with under the Indian Act are being complied with by him and that the standards of drugs and other provisions of the Act and Rules will be complied with. Before granting licences for import, it is ensured that the importer has adequate storage facilities for storing bioligical and thermolabile drugs. The licensing scheme enables the Central Drugs Control Organisation to keep a check over the distribution of these biological products in the country subsequent to their import and in case any batch, during its movement in the

country is reported to have deteriorated, the importer (licensee) can be made to withdraw the defective drug from the market.

3) Control over drugs manufactured in the country :

Under the Drugs and Cosmetics Act, drugs can be manufactured only against a manufacturing licence. Manufacturers should satisfy the following pre-requisite conditions to be eligibe for a licence:-

i) Employ adequately qualified technical personnel to supervise the manufacturing operations;

ii) Maintain hygienic and adequate premises for the manufacture of the various categories of drugs covered by the licence:

iii) Maintain necessary equipments and appliences required for the manufacture of the drug proposed to be manufactured;

iv) Test the raw materials used for manufacture and every batch of the products manufactured and maintain records of the test reports. The testing unit should be independent of the manufacturing unit.

v) Maintain records and registers showing the distribution of the manufactured products.

Manufacturing licences are of two kinds. The conditions of manufacture are more stringent for biological products including sera, vaccines, etc. than for other drugs. Drugs Inspectors inspect the manufacturing premises and manufacturing licences are granted only if they are satisfied that the requirements of the legislation are complied with. Drugs inspectors are also empowered to visit the manufacturing establishment to see if the necessary safeguards to be observed during the process of manufacture are properly observed and can also take a samples for test.

4) Standards for drugs :

The standards laid down for drugs which are imported or manufactured are the same and according to the Schedule to the Act the Indian Pharmacopoeia is the sole book of standards for the drug included in it. For drugs not included in the Indian Pharmacopoeia, the standards laid down in the pharmacopoeia which the drug claims to be of, apply. For patent or proprietary medicines the standard is the formula or list of ingredients displayed in the prescribed manner on the label of container.

5) Control over New Drugs :

Under the provisions of the Drugs and Cosmetics Act control is exercised over New Drugs. Importers and manufacturers of New Drugs, have to submit applications giving medical literature including details of the pharmacological and toxicity studies carried out with the drug. The medical literature, clinical reports etc. are examined and where necessary opinions of expert bodies are also ascertained. After verification of the above details only these drugs whose efficacy and harmlessness are found satisfactory and which re being marketed in the country of origin are permitted to be marketed in this country. Additional caution is also taken by which the label or literature that is to accompany the drug are scrutinised and suitable caution note is required to be inserted in the label and literature. In case any adverse reactions are reported, the drug is not permitted to be marketed.

The regulatory measures under the Drugs and Cosmetics Act are in force for the last thirty years. Enforcement of the regulatory measure in respect of drugs which are locally manufactured or which are distributed in the country is the responsibility of the State Governments and the Central Govt. is responsible for making uniform rules and regulations for observance by manufacturers and importers, for laying down standards for drugs and also for regulating the quality of drugs imported into the country. In order to make sure that the standards of enforcement are uniform and that the conditions of manufacture are same throughout the country, the Central Government has established Zonal Offices and laboratories to assist States in toning Drugs Standard Control.

The testing facilities available with the Central Govt. have been placed at the disposal of the States and the intention is to assist the States to develop their own testing facilities. Several States are already having testing laboratories of their own.

There are 2,657 drug manufacturing firms in India, of which about 125 are in the large and medium scale sector and the remaining 2,532 in the small scale sector.

The total number of Drugs Inspectors in the country now including the Central Drugs Inspectors is 4545.

The turn over of the drug industry in India today is estimated to be of the order of Rs.7,000 million.

A programme for training for Drug Inspectors is conducted regularly in the country and so far 250 Drugs Inspectors have undergone such training. A training programme for Drug Analysis is also conducted at the Central Drugs Laboratory where training in the modern techniques of drugs manufacture is imparted. A training Programme is also conducted for the Drug Control Officers in the manufacture and testing of Sera and Vaccines at the Central Research Institute, Kasauli.

6.7 SECTION V : Constraints of Patent protections and Exclusive ownership of Process Technologies and R&D.

The drugs and pharmaceutical industry is highly research intensive, very competitive and secretive. There is a very high rate of obsolescence of products due to discovery of new and better drugs and the changing pattern of disease conditions. There is thus a constant need to develop new technology for the production of known drugs particularly for import substitution and self reliance and also to develop new drugs for disease conditions prevalent in the area.

Research requires much money and time. Many products should be screened before one commercially useful drug can be found. It involves a lot of uncertainty. From the identification to commercial exploitation it can take about eight years, if not more. One can understand the financial backing this would call for. Developed nations spend more than 5% of sales turnover on R&D. Since the sales turn over is high this represents a lot of money. In developing nations, where the sales turnover is low, the percentage spent on R&D is less than one percent. One of the main reasons is that the companies operating in developing countries are subsidiaries of multi-nationals. The multinational have a central R&D unit and do not encourage R&D expenditure in foreign subsidiaries. The developing nations lag so far behind in this field that it is not unusual for one to find a drug, which is fast on its way out in the developed world, being introduced in developing countries. So it is not rewarding for developing nations to invest their scarce resources in R&D to develop new drugs.

At present, R&D units in developing countries are engaged in process improvements and in process development. India has achieved some success in this regard. Even when a technically

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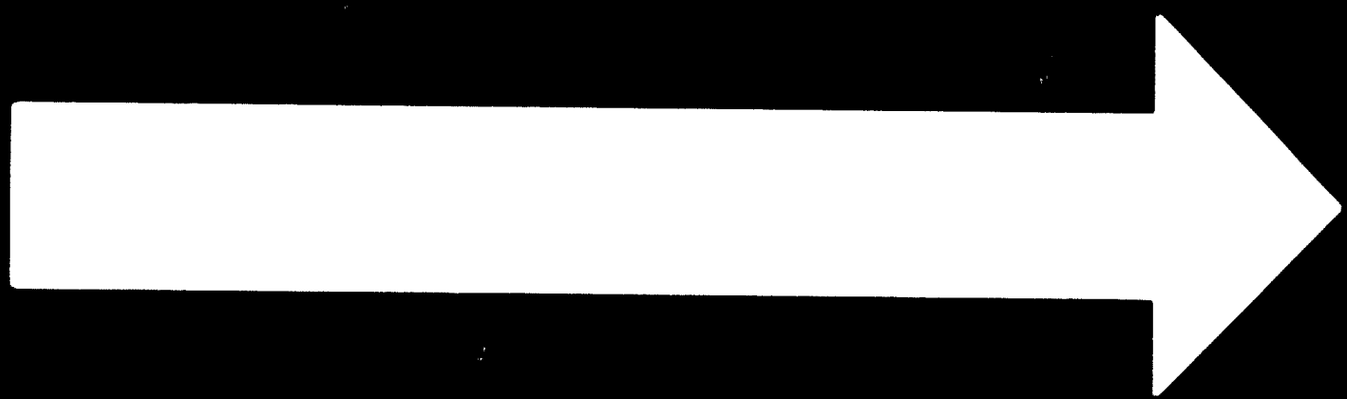

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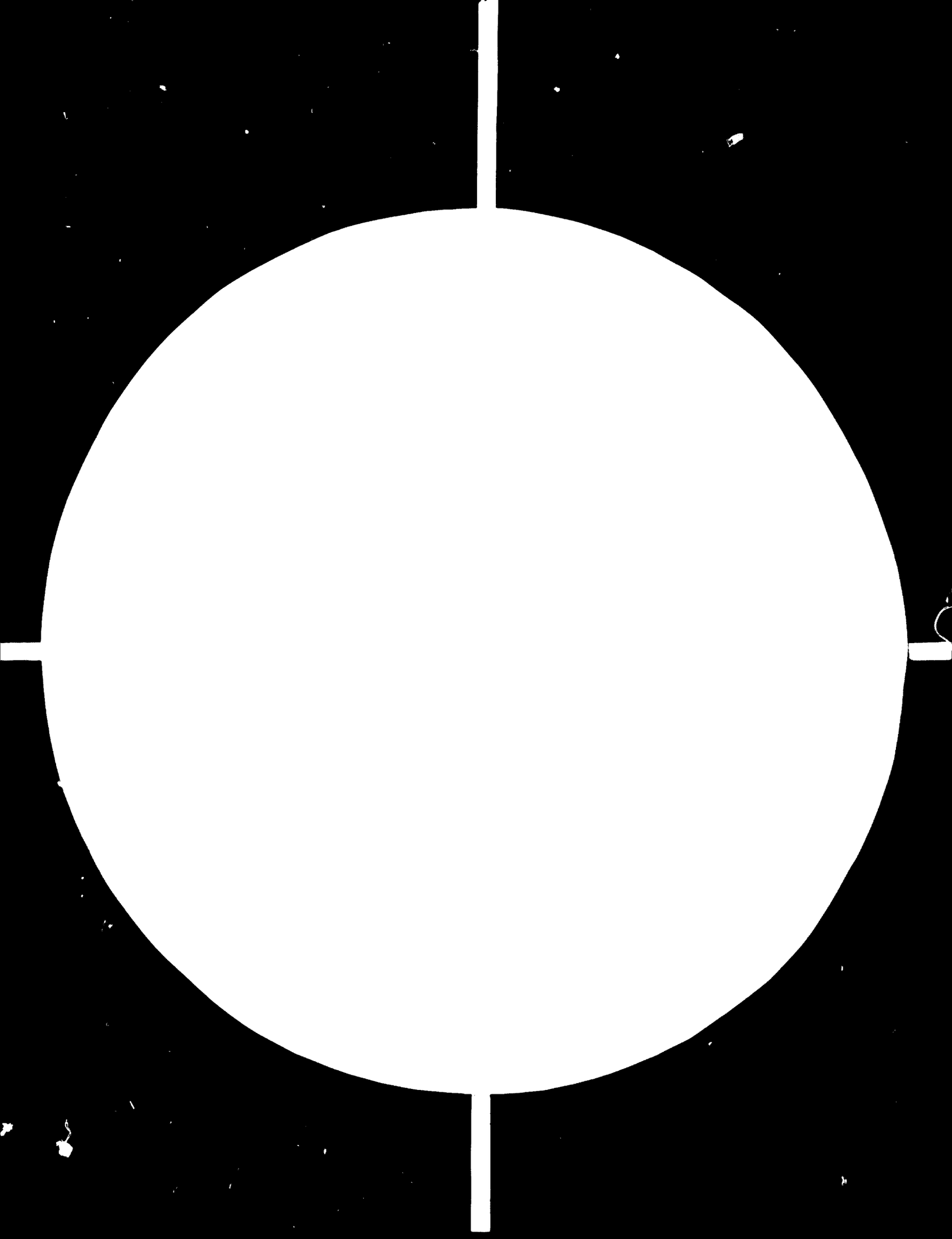

feasible process is developed, the cost of raw materials in developing countries render the process useless and the entire effort spent on developing the process will have to be written off.

Nevertheless, the developing countries have succeeded in developing their own technology for well known drugs and in improving upon the technology they imported. The very fact that these countries have set up facilities and have attained confidence to developed processes for "complex" drugs shows that given the resources, they would also be able to compete with R&D units in developed countries.

7.1 Research and Development in India in the Field of Drugs:

The Government of India has been laying considerable emphasis on the promotion of R&D and its utilisation by industry and has taken various steps in this direction. Apart from setting up its own laboratories, the Government has also given incentive to the industry in the form of income-tax relief for the establishment of R&D laboratories. In order to encourage commercialisation of technology developed by National Laboratories, the Government has recently taken a decision to exempt from licensing provisions any capacity which is established on the basis of a technology developed by a National Laboratory. This facility will be available in respect of sponsored research undertaken by such laboratories.

Research & Development in this field is carried out by three types of organisations -

1. Research and development units within the industry.
2. Government research laboratories.
3. Institute of Technology and Post-graduate departments of Universities.

R & D laboratories in the country have been set up mainly by some of the larger units in the organized sector. In

the public sector. Hindustan Antibiotics Limited and Indian Drugs & Pharmaceuticals Limited have their own full fledged R&D divisions. In the private sector, research laboratories like Sarabhai Research Centre, Ciba Research Centre, and those associated with Alembic Chemical Works Company, Unichem Laboratories, Ranbaxy Laboratories, Themis Group, Cadilla Laboratories, Bengal Immunity Research Institute, may be mentioned. The main emphasis of these laboratories has been on solving plant problems, process improvements, which includes recovery procedures, bye-product utilization, process control, import substitution of raw materials, enforcement of quality control measures and standardisation of process for production of new drugs. Some of the bigger research units are also working on development of new drugs. The overall investment in R&D is estimated to be about Rs.30 million, which is less than 1% of the turnover. But this figures is far too inadequate considering the high research needs of this industry. Amongst the Government research laboratories, the Central Drugs Research Institute, Lucknow, under the CSIR, is devoted exclusively to problems related to all aspects of pharmaceuticals and drugs research. It is one of the few laboratories in the country which has a strong scientific base and the whole range of infrastructural facilities necessary for new drug development. In addition, the following laboratories of the CSIR undertake problems connected with the development of technology for drugs and intermediates :

1. National Chemical Laboratory, Pune.
2. Indian Institute of Experimental Medicine, Calcutta.
3. Regional Research Laboratory, Hyderabad.
4. Regional Research Laboratory, Jorhat.
5. Regional Research Laboratory, Jammu.
6. National Botanic Gardens, Lucknow
7. Central Indian Medicinal Plants Organization, Lucknow.

These laboratories have helped the industry by (i) standardizing technology for the production of known drugs and intermediates; and (ii) establishing proper agronomic conditions

for the cultivation of medicinal plants and evolving new varieties of plants. A large proportion of work in these laboratories is sponsored by the industry.

7.2 Constraints of Patent protection and exclusive rights to know-how on over-all development :

Patents are granted to inventors so that the organisation which has spent money for the purpose would have exclusive rights to use the invention for a particular period during which it can recover the money spent and can earn a reasonable profit. This kind of protection fostered development of new machines and processes. But it can also be argued that the inventor firm is allowed to have a monopoly and thus exploit the community.

Patent laws differ from country to country. The US provides protection to processes and products. In India patents are given to processes only. In general, more the protection, greater is the development activity in a country.

The developing countries do not suffer more due to patent protection given to a company than a rival company in the developed country itself. In fact, the patent laws should not be of much concern to developing countries at least for quite sometime to come. The time lag between the time at which a new drug is patented in a developed country and the time at which the drug finds sufficient market in a developing country so as to warrant indigenous production, is at least as long as the protection period. Therefore, in effect the patent laws are not a major hurdle to Drug industry at least today. There are many cases in which the patent period has expired long since but still the know-how is not available at a reasonable price. A few companies who have the technology use various factics like charging very high price for intermediates and outright refusal to sell the technology so that the developed country finds it cheaper to import the finished products. What the developing

countries have to fight is this kind of collusion between international manufacturers. It is only by intervention of Govts. of developed countries that such problems can be solved.

The foregoing refers only to the patent protection granted to processes and products in developed countries. As regards the patents granted in developing countries, if the protection does not exist, no entrepreneur or subsidiary of a foreign company will introduce a process. So there must be some protection to the processes developed.

Since the aim, after all, is to see to that better drugs are available to the society at reasonable prices, the Governments should use controls which would ensure adequate supply and reasonable prices. Price controls are already existent in some of these countries. If the Government feels that the demand for a drug is more than the quantity a company which holds the patent is willing to sell (or is capable of producing) the Government may force the company to transfer the know-how to another which is willing to produce it, seeing to that the company which holds the patent is able to sell the amount it intends to sell.

7.3 Need to organise R&D activity directed towards bridging technology gaps.

As already said, R&D is a costly and time consuming activity. Developing countries which have less than adequate resources can not afford to waste money or time. So, the governments of these countries have a responsibility not only to see to that individual research units do not duplicate efforts or engage in non-priority drugs, but also to pool their resources together and develop drugs and know-how which they need. Left to themselves, the R&D units may engage in drugs of low-volumes-high-value luxury drugs which have no priority in these countries.

It is essential therefore that the governments in these countries draw up a national priority list and allocate work on each drug to a few R&D units. In this manner, duplication can be avoided and the resources could be used better. Secondly, these governments can form a consortion of "Concorde" type so that the burden of research is shouldered by more than one country and the benefits also spread to more than one country.

8.0 SECTION - VI : INDUSTRIAL AND INSTITUTIONAL DEVELOPMENT NEEDED FOR DEVELOPMENT OF D & P INDUSTRY

Drugs and Pharmaceutical Industry is essentially a consumer product industry. Like all consumer product industries, it is it-self a consumer of a lot of industrial raw materials and services. Thus, it is dependent very on chemical (including starch) industry for raw materials, on engineering industries for machinery and equipment (for manufacture, storage and transport), and on packaging industry. It requires expert main power to design, fabricate, operate and maintain the machinery and for R&D in process development and improvement. So the following are some the essential infrastructure needed for setting up a viable pharmaceutical industry :

a) A well established fine chemical industry

b) Packaging industry

c) Engineering industry

d) Engineering institutions-both educational and consultancy

e) R & D institutes.

A brief description of the status of engineering industry is presented as Annexure-I. The design skill India has acquired has been is described below :

8.1 Detailed Engineering :

Detailed engineering of a project involves the conversion of the basic engineering data or process package obtained from the process licensor into designs and drawings needed for the procurement and construction work. Various disciplines involved in this work basically relate to civil and structural, mechanical, heat exchangers and vessels, piping and layout, electrical and instrumentation.

In a professional organisation specialising in the implementation pf projects (Engineering Contractors) these diverse activities are carried out by specialist functional groups.

In general the activities of the various functional groups are as follows :

a) Civil & Structural : This group is responsible for finalising the site development, architectural features and detailed design of buildings, detailed design of equipment foundations and preparation of documents for civil and structural contracts.

b) Mechanical : The mechanical department provides specialist service for the selection of bought-out equipment such as pumps, compressors, conveyors etc. and furnishes design specifications for custom made equipment such as vessels, agitators, heat exchangers, etc. They also check the drawings and performance data furnished by the equipment suppliers and fabrication contractors.

c) Piping : The piping group is responsible for preparing the equipment layout drawings, piping layout drawings, specifications for pipes, valves and accessories, quantity estimates for the installation materials, specifications for thermal insulation, painting etc. Scale models of plants which are now-a-days extensively used for finalising the plant layout, piping routing, valve locations etc. are also prepared under the control of the piping group.

d) Electrical : The electrical group is responsible for the preparation of specifications for bought-out items such as transformers, switch gears, cables, lighting fittings etc. single line dia-grams, power distribution layouts, lighting layouts, and schedules and quality estimates for the installation materials.

e) Instrumentation : The instruments group prepares specifications for all the instruments, instrument layout drawings, layout drawings for instrument panels and quantity take-offs for the installation materials.

8.2 Consultancy, Process Engineering, Design and Project Management

About two decades of technological planning have brought us now to an intermediate stage in technological development which can be considered as a take-off stage for achievement of self-reliance in the Chemical and Pharmaceutical machinery industry. The country should now be prepared to be self-sufficient in all aspects of new project management. New project management involves a number of activities like :

a) Market Survey

b) Selection of Location.

c) Selection of right process and know-how.

d) Planning for finance.

e) Detailed process Engineering and Design for equipment and plant.

f) Procurement of right materials and planning for equipment fabrication.

g) Man-power planning recruitment and training.

h) Installation of equipment.

i) Test Run and start-up of Plant.

j) Regular routine production.

While all these activities are paris of successful Project Management, the main problems that are faced in a developing country like ours centre around the selection of the right process know-how and process engineering and design of equipment. These are the crucial activities which ultimately make

- firms.

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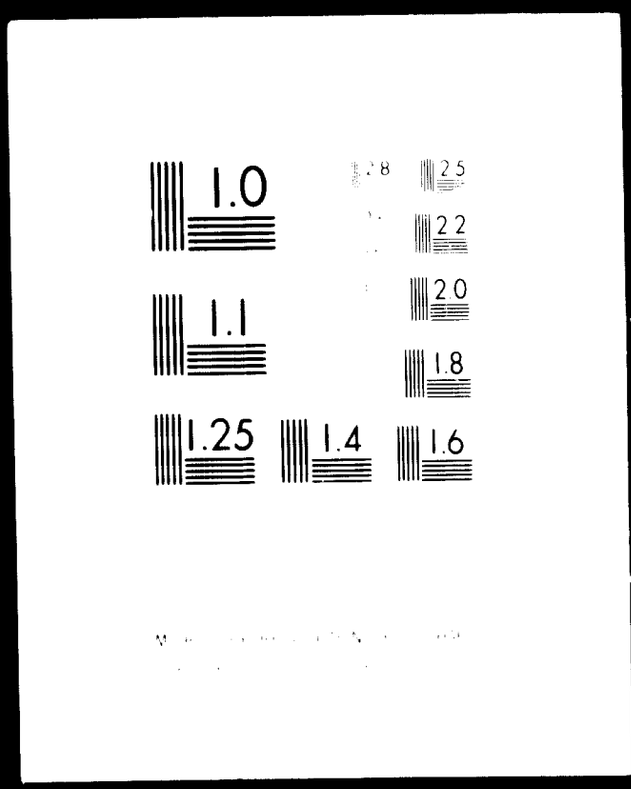

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the project a success or otherwise. Even where a good process know-how is available, the next important factor for the success of any project is proper process engineering and design. The problems faced in the country in regard to process engineering and design are formidable. Hardly and process data are available for design purposes. This situation heeds immediate attention. Creation of "data banks" should be taken up immediately for all processes that are available at present and for the new processes that will be developed in future. This applies to both for processes developed in the country as well as those purchased from overseas.

Development of accurate data on process heads extensive Research and Development activitity and Pilot Plant studies. Here again, facilities in the country are very meagre. Further Research and Development and Pilot Plant studies are not well planned and directed towards definite objectives.

Even where design data are available, non-availability of right kind of material for fabrication of equipment and lack of development of sophisticated manufacturing techniques for specialized equipment pose serious problems.

Firms taking up projects for manufacture of chemicals prefer to choose a short cut in in buying the entire know-how, process, design and engineering details and even equipment when they contract for transfer of foreign technologies to this country. These firms, justificably or not, want to avoid even the slightest of risk factors involved in supporting and developing indigenous design capabilities.

Not only there is a market absence of desire to encourage local talent for engineering and design activities but local design engineers are not even associated in the technology buying process. This shows that managements involved are not innovation minded. They also do not have the desire to work with the Indian design and engineering firms. However, the recent trend in Government policies towards self-reliance is quite encouraging and it is hoped that Indian engineers would be associated in all phases of new project activities starting from market survey, engineering, design, construction and operation. Only with a bold policy of taking certain calculated risks, it is possible to develop local talent for undertaking new projects in all their aspects.

It can be added that even if a country has to buy a new technology, it should have capable engineers with a experience in a variety of design and developing activities to bargain and get the best technology and know-how from foreign countries.

8.3 **Training :**

It has been emphasised that pharmaceutical industry is technically more complex. Apart from the operation of machinery, there are complex tasks like testing of in process material, which can be performed only by personnel qualified to do this.

As a long term measure, developing countries will have to set up educational institutions in the fields of chemical engineering, Chemistry, Pharmacy etc. When talents for even teaching are hard to find in a country, those for running an industry, will have to be imported for some time. Where the talents are not there at all, experts from other countries can be taken on a short term contract and during their stay, local personnel can be got trained. Also, qualified nationals can be sent to factories of reputed firms in countries where this industry is developed, for a short term on the job training.

Developing countries who do not have either the pharmaceutical industry or educational institutions catering to this industry, should start both on a limited scale without wasting any further time. Only when such a start is made countries lagging behind can hope to become self reliant in a foresceable future.

It is worth pointing out at this point that some countries which are developing in the sence that their percapita incomes are low are fairly well developed in this regard. For example India has a good institutional set up for education in most fields of science and technology. Also, Indian Pharmaceutical Industry is also developed to such a level in which it has competance and confidence of handling complex machinery and processes. In the field of R&D not only have Indian firms been able to improve upon imported technology but also to develop economical processed for many known drugs. For a late

comer with less than adequate resources this achievement is commendable. It hardly needs to be pointed out that countries of the developing world can use the experience India has gained, to their benefit. Co-operation in the field of technical training between developing countries would be cheaper and the knowledge gained by a trainee would be more relevant in his country than that gained in a developed country.

Apart from this kind of co-operation between two countries, some countries of the developing world can enter into regional co-operation and set up a pharmaceutical plant management centre in a relatively more developed country of the third world in that region. A proposal to set up a Pharmaceutical Industry Development Centre in India with unaid is being discussed. Such centres, needless to say, would go a long way in helping the under developed countries especially those lagging behind in Pharmaceutical Industry in becoming self reliant in man power within the foreseable future.

Section VI (a)

CHEMICAL PLANTS AND PROCESS EQUIPMENT

Type of Equipment	Present status
1.a) Vessels, pressure vessels, storage tanks, silos, bins etc.	At present there is adequate manufacturing facility as well as design capability in the country for fabrication of this type of equipment in MS. Monel, Copper, Aluminium and S.S. One of the shops even offers fabrications in tantalum, zirconium, tungsten etc.
b) Specialised equipment glasslined, rubber lined plastic coated and fibreglass based equipment.	There is adequate capacity for rubber lined equipment and the quality is also satisfactory. Glasslined steel equipments are available indigenously from some manufacturers. However, only one unit has been developing in an organized way. Even this unit needs a lot of experience before it can make and deliver satisfactorily equipment specially for high temperature pressure operations.
c) Agitators of various types with reduction gears and various other mixing equipment	A number of companies fabricate all types of these equipments to customers' design and specifications. Some manufacturers offer designing facility also.
2. Transfer equipment such as pumps make of SS, rubber lined, PVC, MS, CI or Bronze blowers, conveyors elevators and other material handling equipment.	Most of the types of pumps are manufactured within the country. SS Castings and forgins activities have also started and this has facilitated development of indigenous manufacture of

	SS Pumps. Diaphragm pumps with rubber, Neoprene or Teflon diaphragms are made extensively by a numb r of companies. All types and sizes of conveyors, blowers, elevators, travelling cranes and other meterial handling equipment are made indigenously.
3. High vacuum Molecular Distillation Equipment.	Laboratory size molecular distillation equipment is available.
4. Vacuum Equipment like water ring vacuum pumps, steam ejectors and high vacuum pump.	Water ring pumps, ejectors and other high vacuum systems are indigenously available.
5. Separation equipment including filter presses, centrifuges, screens and cyclones dust collectors, clarifiers, liquid/liquid extractors.	Plate and frame filler presses in wood, CI & SS etc are made indigenously. Also made are SS pressure filters of sparkler type. All types of batch vertical centrifuges and fully automatic sugar centrifuges are made in the country. So also dust collectors cyclone and clarifiers and most of pollution control equipment.
6. Heat Exchangers, Distillation columns, Evaporators and Crystallizers.	All types including shell and tube, fin-tube and plate heat exchangers are made in the country. Design for some are proprietory and restricted for use. Evaporators and crystallisers can be obtained of standard sizes or built to customers' designs.
7. Thermal equipment including rotary vacuum dryers, fludized bed dryers spray dryers, drum dryers, etc.	Most of the equipment has been fabricated indigenously.

8. Size reduction equipment including crushers, ball mills, tube mills, harding mills, pebble mills, hammer mills reductionzers etc.	Quite a number of companies have developed design capabilities and fabrication of all types of size reduction equipment. Of recent development is the fabricationof refuctionizers.
9. Electrical equipment including motors, generators, diesel generators, electrical transformers, switchgear, various types of starters, cables, explosion proof motors and accessories.	All types of electrical equipment including diesel generators upto a size of 150 KVA are being made within the country and the fabrication capacities are also adequate.
10. Pipes, valves and fittings of various types and of different materials of construction.	A large number of companies are manufacturing pipe fittings and valves made of CI, Rubber lined, Polyethylene lined valves SS valves of different types and glasslined valves necessary for the drugs and pharmaceutical industry are available.
11. Ventilation equipment including fans, blowers and air handling equipment etc.	A large number of companies are manufacturing these to customers sizes and in some sizes there are standard designs also.
12. Services equipment like steam boilers, refrigeration compressors and oil free air compressors cooling towers etc.	There are 3 to 4 companies making well designed package boilers of different sizes. Manufacture of refrigeration compressors upto about 500 tonnes had just been started. Production of oil free air compressors from 3000 to 5000 cft. per minute has been started by one or two companies. There are one or two companies

	There are one or two companies who are able to undertake designing and building cooling towers to customers' needs.
13. Water deionisation, softening and effluent treatment plants.	There are number of companies manufacturing water softening and deionisation plants. Resins required for deionisation and delkalisation are being manufactured within the country. At least two or three units have designing and installing capability for effluent treatment plants.
14. Hydrogen Cells-Electrolytic cells to produce hydrogen etc.	There is one company making electrolytic cells to produce hydrogen and they also offer turn-key services.

9.0 SECTION VII

Policy Imperatives-need for clear cut National Health Policy-specifying boundary limits to the Industry.

9.1 National Health Policy

For any programme to succeed, a defenite objective is a must. Only then the personnel in charge of implementation will have a clear idea of what their job is. Also, such a statement would enable the evaluation of the progress and corrections and remedial measures to be taken whenever needed. So a definite National Health Policy is called for, if the Govt. seriously wants its citizens to get the basic health needs

The national health policy should spell out the kind of facilities the citizens are to be provided freely, the extent of coverage intended, the priority health care is be given in national planning and drugs which are considered essential and therefore must be available at reasonable prices, the minimum health standards the Govt. would try to provide to every citizen, the percentage of national income to be spent on health etc. Such a statement would help the Govt. and others to estimate the demand for drugs and thus help in planning. It would also give the Industry a sense of stability and clear direction. The officials would be able to function with a clear direction.

9.2 National Science and Technology Policy

The S&T policy of the Govt. sets the direction of research in more than one way. Firstly, it sets the output expected out of the research efforts. Secondly, it sets the priority among various research projects. Thirdly, it specifies what kind of technology (e.g. labour-intensive, automatic etc.) the Govt. is looking for. A clear understanding of the view of the Govt. regarding these in the minds of administers of R&D laboratories is a must if the resources spent on R&D are to yield any useful results.

In the Indian context, the Govts. emphasis on R&D in Drugs Industry is on developing indigenous technologies for drugs which are of an epidemic nature in India like chloroquin and primaquin for malaria. As for as other fields are concerned, the Govt. wants its laboratories to develop technologies which would use the resources available in the country like man power, cattle, minerals, coal etc.

9.3 Administration of National Health Programme

Security of citizens from deseases is one of the primary tasks of any Govt. The task of Govts. of developing countries is more difficult because the poor incomes of the people compel them to like in unhygienic conditions and have unhealthy food habits thereby creating conditions facourable to attack and spread of diseases. Unfortunately, the disease prone people can not afford to pay for their health care. Govt. hospitals are the only source of remedy to most people.

Many factors complicate the task of these Govts. Unhygienic conditions of living and unhealthy food habits have already been referred to. The innocence arising out of illiteracy is another major factor. The population of the developing countries is huge relative to their resources and is spread over vast areas.

The Indian Govt. has a full fladged Ministry of Health and Family Welfare whose activities include not only cure or prevention of diseases but also to administer nutrition programme, family planning, medical research and regulation of dealing in drugs.

Health is a concurrent subject in the sense that both state and Union Govt. together administer health programme. Each district headquarters has a Govt. Hospital with specialised facilities. Apart from these there are various Govt. hospitals supplementing these hospitals. Employees of State and Cenral Govts. are covered by employees state insurance scheme and Central Government Health Scheme, in which a nominal amount is collected from all employees and any amount of medical service needed is provided by Govt. hospitals to the families

of these employees. For the general public, most health services are free or are provided at a nominal cost.

Most Government hospitals are located in urban and semi-urban areas because only in those areas, the infrastructure required for maintaining good hospitals is available. But in any developing country, due to the agricultureal orientation, more than 70% of the people live in rural areas. Thus only a small part of the population has easy access to the modern health facilities the Govt. offers.

It is to remedy this situation that the Govt. has embarked on a Rural Health Scheme.

This scheme involves training a few volunteers in identifying diseases from external symptoms and dispensing simple medicines. The idea is that at least those disease which show easily recognisable symptoms and for which well established medicines exist should be cured as a first step. The volunteer who is trained is not purported to be a doctor at all. The volunteer gets Rs. 600 worth of medicines free every year.

ANNEX VIII

Systematic Development of Pharmaceutical Industry.

The development of pharmaceutical industry in any country has, of necessity, to pass through several distinct phases. The phasing would of course depend upon a number of factors, such as the status of the supporting fine and heavy chemical industries, production of equipment and ancillaries and available expertise, public health measures and in addition the resource position :

The pattern of phasing of development of pharmaceutical industries in developing countries could be :

Phase I

i) Initiation of national health scheme, including family planning programme.

ii) Identification of essential drugs

iii) Import of formulated drugs, including vaccines and sera

iv) Evolution of distribution system

v) Drug control organization for enforcement of quality control for the drugs imported

Phase II

i) Import of bulk drugs

ii) Production of heavy inorganic chemicals

iii) Production of packaging materials

iv) Production of simple family planning devices, such as conduoms, IUD's etc.

v) Production of formulated drugs, including creams and jellies for family planning programme from imported bulk drugs

vi) Production of vaccines and seras

vii) Expansion of activities of the drug control organization to cover licensing of production units.

Phase III

i) Production galenicals, phyto-chemicals and simple animals' products, such as liver extracts.

ii) Import of penultimate intermediates and production bulk drugs therefrom

iii) Production of simple pharmaceutical processing machinery

iv) Heavy Inorganics.

Phase IV

i) Production of synthetic bulk drugs, including oral contraceptives from basic stage

ii) Production of heavy organic intermediates

iii) Production of sophisticated pharmaceutical machinery

iv) Production of antibiotics and [illegible]

v) Production of sophisticated formulations, such as sustained release preparations

Production of phytochemicals involves relatively simple technology and can be easily taken up in the first phase of development of the pharmaceutical industry. Even if some of the plants used as raw material are not indigenous to a particular country, they can be introduced if the agro-climate is suitable. The equipment required for the production is also not sophisticated. It is true that over the years the number of plant drugs used has declined greatly, due to replacement by more potent synthetics and antibiotics. Yet, there are a sufficient number of them still in use in modern medicine to sustain a reasonable sized industry. These are :

i) Ephedrine

ii) Caffeine

iii) Morphine

iv) Codeine

v) Rutin

vi) Strychnine and brucine

vii) Sennosides

viii) Digoxin

ix) Berberine

x) Ergot alkaloids

xi) Emetine

xii) Quinine and quinidine

xiii) Papaverine

xiv) Xanthotoxin

xv) Vinocamine

xvi) Glycyrrhiza products

Moreover, some phytochemicals are used as starting materials for the production of various drugs. Such plants could be cultivated for the isolation of starting materials for further processing within the country and perhaps also for export. These include Diosocorea spp. Solanum spp., Costus. In fact the production of simpler steroids such as testo-storone and progesterone, and some intermediates for more complex steroid drugs, can be easily taken up by those countries which can grow Dioscorea spp. or Solanum spp. Some plants are also the source of some pharmaceutical auxillaries, such as mucilages and gums.

Both from the economic as also from the public health point of view, effective use of sera and vaccines is in the long run a much better insurance against disease. Therefore, considerable emphasis should be laid on the production and mass use of immunologicals. Even in the research institutes greater emphasis should be laid on the development of immuno-diagnostic and prophylactic agents.

In addition to these drugs accepted in modern medicine, a number of plants are used in every country in their traditional systems of medicine. In fact, use of traditional house-hold

remedies is strongly entrenched in many developing countries. If one were to estimate the amount of money spent on modern medicines and traditional medicines in different countries, the money spent on the latter would far exceed the expenditure on the former. It is, therefore, necessary for those countries which have well developed indigenous systems of medicine to consider these problems and to try to integrate proven traditional remedies into modern therapeutics. After all the basic purpose is to provide medical relief at a price which the people and the country can afford. What perhaps could be done is to standardise the methods of production and formulation of traditional remedies and prescribe specifications of quality and thus promote their wider use.

Choice of Technology

Pharmaceutical technology is one of the most highly developed and sophisticated of technologies among chemical based industries. There is no denying the fact that developed countries have greatly contributed in this field both in terms of development of new drugs as also development of technology for their formulation and dosage forms. Therefore, ideological considerations should not be allowed to stand in the way of availing of such technology and expertise from firms in developed countries. What is necessary is to take due care in delineating and selecting the areas where technological collaboration with firms in developed countries is inescapable and then to regulate and direct the operation of such firms. This should of course, be restricted mainly to bulk drugs. And out of various forms of technology acquisition outright purchase leads to least subservience to foreign technology as has been shown by the experience of countries like Japan.

For promoting technological development, the decision-maker in a developing country is sometimes faced with a difficult choice.

On the one hand, there is need to develop quick production of an item, on the other it is equally important to develop self-sufficiency and self-reliance. Development of all technology by a country on its own would not be advisible because of the time and cost factors involved. It would be necessary to import technology into the country for certain products, but at the same time create an R&D organization which would be able to receive the technology, assimilate, modify and build upon it. Terms and conditions for the import of technology should be such as not to lead to economic subservience. Outright purchase of technology with the usual performance guarantees would be best in most circumstances.

In this matter cooperation and technological sharing between developing countries can be of great advantage. Firstly, the experience of a developing country is likely to be more applicable to the situation in another developing country, rather than the experience of a developed country with its much different socio-economic background. Secondly, the type of technology which is suitable to a developing country may be quite different from the requirements of a developed country.

Although the aim of any developing country should be to achieve self-sufficiency in production, there cannot be any absolute self-sufficiency, particularly in a field like pharmaceutical production. The discovery and introduction of new and better drugs, with consequent obsolescence of existing drugs, is a common phenomenon which has to be reckoned with. Therefore, a certain amount of dependence on imports for new drugs and new technology is unavoidable. All that a country can strive for is to develop self-reliance in technology and to produce the majority of essential drugs required in large bulk, but to allow import of these drugs whose indigenous production may be uneconomical due to low demand and other factors.

The growth and development of the pharmaceutical industry, particularly of basic production , is intimately linked with that of the chemical industry, bulk drug manufacture in fact is an extension of the fine chemical industry. It is, therefore, necessary to integrate and interface the development plans of the pharmaceutical industry with that of the chemical industry. There cannot be any set pattern of such interfacing the pattern will depend upon the availability of primary raw materials and the status of related industries. In countries with rich coal resources, the industry would naturally have to be mainly coal-based, while in countries with large oil and gas reserves, the industry would naturally depend on petro-chemicals. Similarly, countries which have a large base of mineral and vegetable resources would draw more on these raw materials for their chemicals production.

It is well-known that multi-national drug firms and their associates often exercise monopolistic control over the production of some key intermediates. They can hamper the development of a new bulk drug industry which is dependent on imports of such intermediates by charging artificially high prices or even by not selling such intermediates. The example of chloroquine is illustrative. Although technology for its production is available in India, non-availability of the intermediates at a reasonable price in the world market has made its indigenous production uneconomic. This furhter emphasizes the importance of developing a strong base of the heavy and fine organic chemical industry to feed the pharmaceutical industry.

REPORT ON THE DEVELOPMENT OF THE DRUGS AND PHARMACEUTICALS INDUSTRY IN DEVELOPING COUNTRIES

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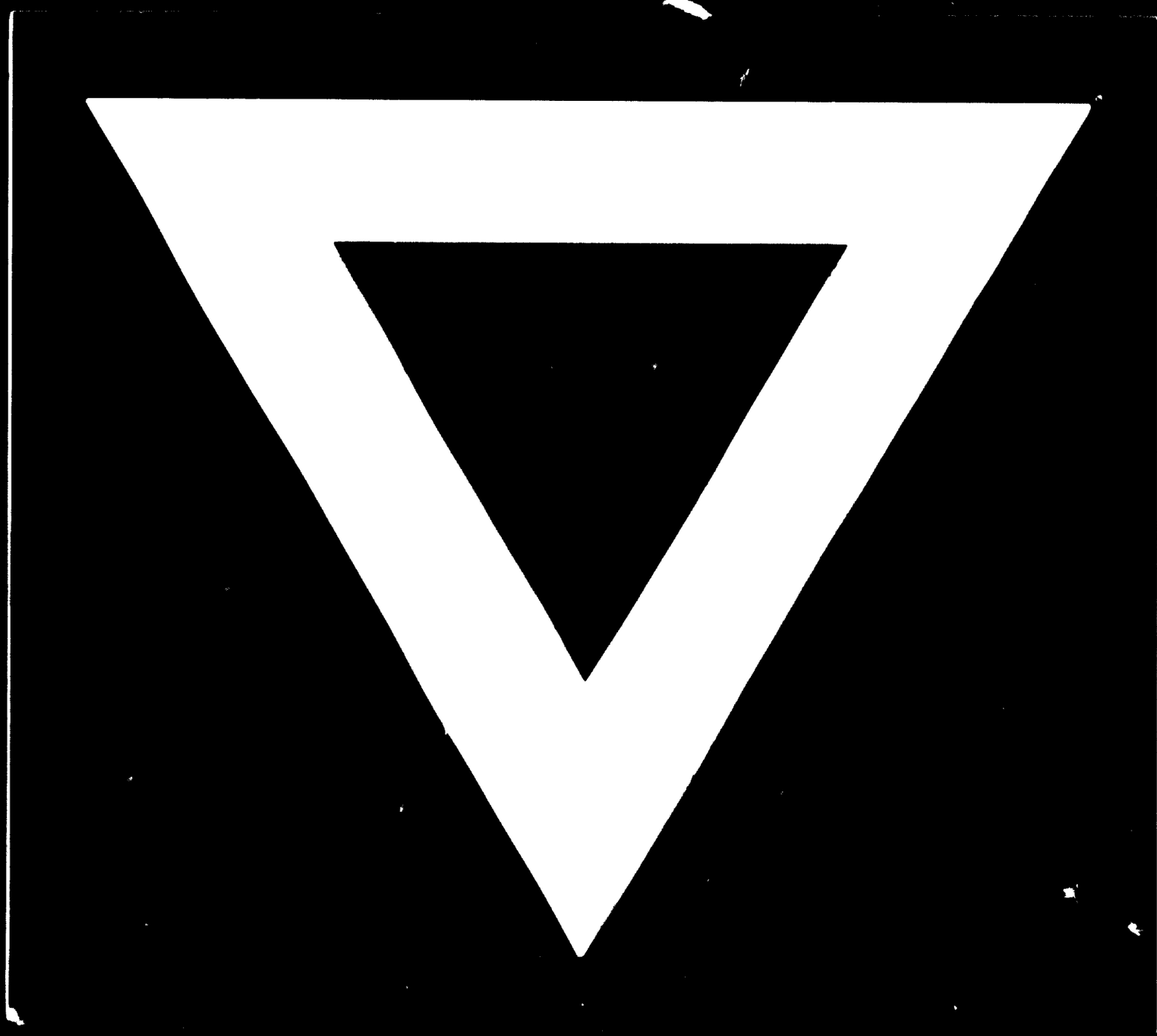

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