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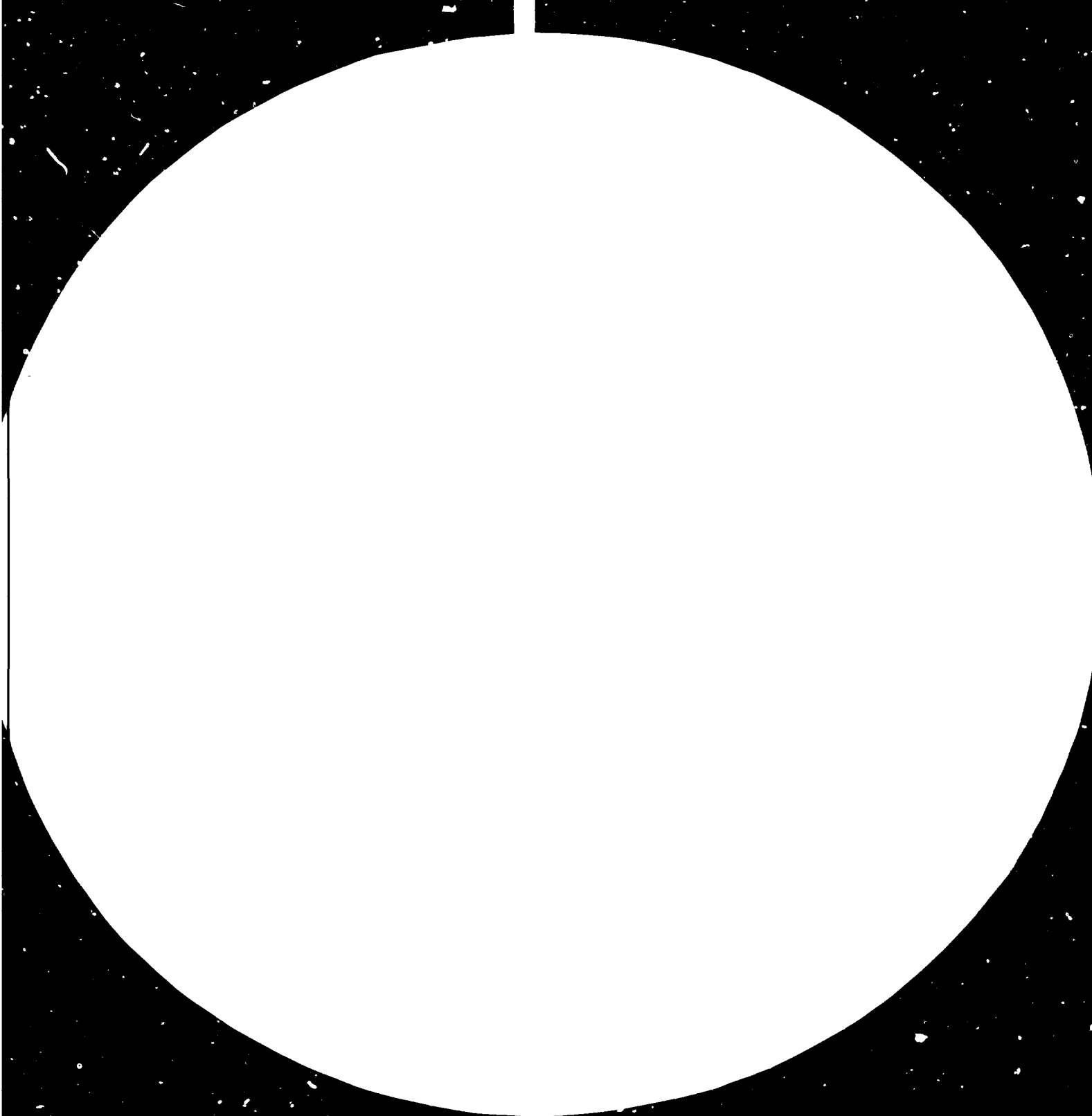
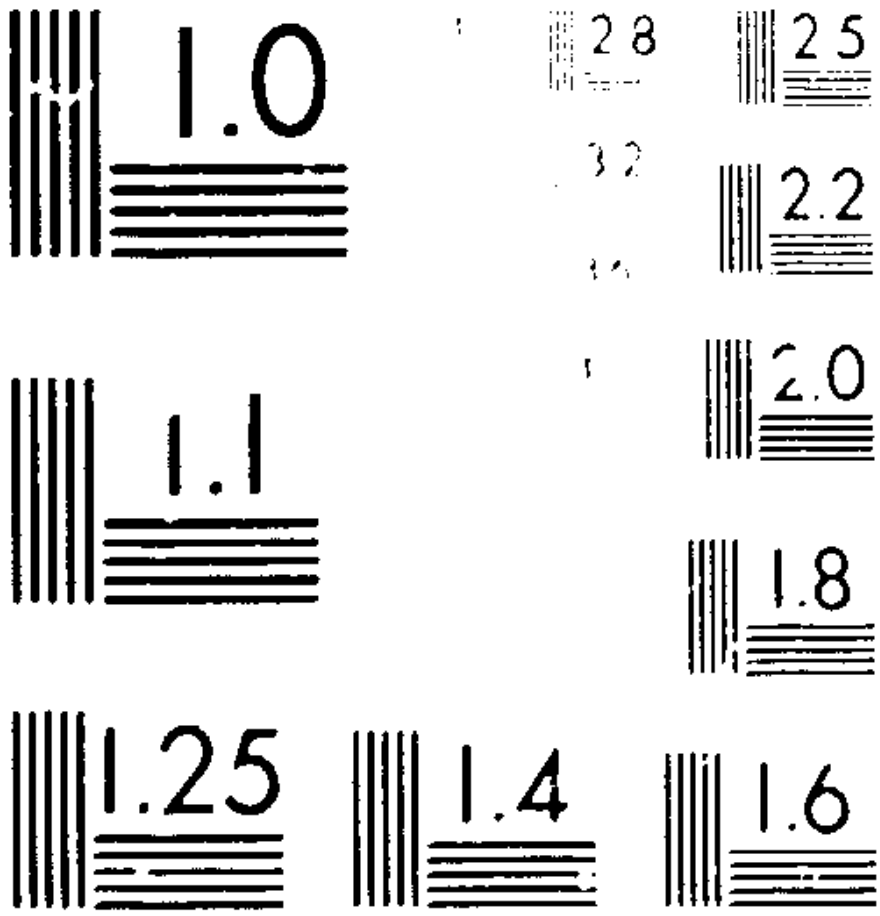
UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

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First Consultation Meeting
on the Pharmaceutical Industry

Lisbon, Portugal. 1 - 5 December 1980

GLOBAL STUDY OF THE PHARMACEUTICAL INDUSTRY (*)

prepared by the Secretariat of UNIDO

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GLOBAL STUDY OF THE PHARMACEUTICAL INDUSTRY

Addendum

Technical Cooperation among developing countries in the field of pharmaceutical industry *

prepared by the secretariat of UNIDO

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TECHNICAL CO-OPERATION AMONG DEVELOPING COUNTRIES IN THE FIELD OF PHARMACEUTICAL INDUSTRY

Introduction

The United Nations Conference on Technical Co-operation among Developing Countries convened in Buenos Aires in September 1978, adopted the Plan of Action for Promoting and Implementing Technical Co-operation among Developing Countries[1/]. The Plan of Action is a detailed blue print for major changes in approaches to development assistance and for a strong emphasis on national and collective self-reliance among developing countries as foundations for a new international economic order. The Buenos Aires conference also recommended that the entire United Nations development system and all its Organizations should play a prominent role as promoters and catalysts of TCDC. The United Nations General Assembly endorsed the above Plan in December 1978 and urged all Governments and elements of the United Nations system to implement its recommendations.

The Interregional Meeting to Prepare for Consultations on the Pharmaceutical Industry, convened in Cairo in January 1979, examined the opportunities for increased co-operation between developing countries.[2/] It was felt that countries with experience could provide useful assistance to other developing countries. The Meeting recognized that a major constraint on developing such co-operation was a lack of information on the capabilities developed in the more advanced countries in the pharmaceutical industry. The Meeting also suggested that UNIDO should help to identify opportunities for co-operation, receive project proposals, introduce suitable partners and, when requested, assist in the implementation.

1/ United Nations publications, Sales No: E78.II.A.II

2/ UNIDO document ID/WG.292/3

Why TCDC has become necessary in the Pharmaceutical Industry

The study of the Pharmaceutical Industry reveals that nearly 70% of the world's population reside in the developing countries and a large segment of this population has no access to the most essential medicinal products and that an urgent international action is necessary to alleviate this situation in these countries. The pharmaceutical industry, being the principal source of supply of medicinal products, has to play an important role in this action programme. The study of the pharmaceutical industry has also brought to the surface certain distortions in the development of the pharmaceutical industry in the developing countries:

(a) The technology involved in the formulation and packaging of drugs is relatively simple. Inspite of the availability of such technology for the production of pharmaceutical formulations within the developing countries there are nearly forty-five countries which do not have production facilities and have to depend on imports for their requirements of finished dosage forms;

(b) Indigenous production of bulk drugs still depends on imports of intermediates. The high cost of intermediates renders the manufacture of bulk drugs uneconomical;3/

(c) Non-availability of suitable technology for bulk drug production at a reasonable price is a major constraint on the development of an integrated pharmaceutical industry;4/

(d) Due to lack of local research and development efforts there has not been adequate technological base in assimilating and improving upon the imported technology. As a result, production of certain bulk drugs became uneconomic due to obsolescence in technology;

(e) Many developing countries have rich flora of medicinal herbs and plants. However, they export the medicinal plants to the developed countries because they do not have access to the technology to process them. Consequently, the developing countries have to import essential drugs based on medicinal plants which could have been indigenously produced;

(f) The growth of the pharmaceutical industry has been inhibited due to lack of harmonious national drug policies bearing on social priorities.

If the developing countries are to attain 25 per cent share in world pharmaceutical production by the turn of the

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3/ The Pricing and Availability of Intermediates and Bulk Drugs, ID/WG.331/4.

4/ The availability, terms and conditions for the transfer of technology for the manufacture of essential drugs, ID/WG.331/5.

century, the cost of imported technology would be so high that the developing economies could not stand the load.

Opportunities for TCDC

The study confirms that the current dependency on the imports of technology from developed countries could be avoided to a large extent since several developing countries in each region of Africa, Asia and Latin America have gained technical competence in pharmaceutical production and can provide valuable assistance to less developed countries in the region. They can also pool their capability and experience for planning large scale industry.

Technology for the entire range of pharmaceutical formulations is available within the developing countries. The state of development of pharmaceutical formulation industry in developing countries is given in Annex I. About seven countries are engaged in the manufacture of bulk drugs, which in general require relatively more sophisticated technology involving multistep processes. In all, about 50 of the essential drugs selected by WHO, are being produced in these countries (see Annex II). In addition, China has made considerable progress particularly in the field of basic drugs, contraceptives and utilization of medicinal plants. The aspect relating to suitability and availability of technology can be explored.

Better flow of technology by itself will not resolve the problem of technological dependency of the developing countries. Acquisition of technology is no substitute for indigenous research and development (R and D) efforts. The recipient country should be able to assimilate and improve upon the imported technology through its own R and D facilities.

Establishment of R and D for product innovations requires substantial resources and developing countries with limited resources cannot afford to undertake such research activities. It should, however, be noted that patents for most of the essential drugs required by the developing countries have expired and these can be produced without legal complications provided indigenous R and D efforts are capable of developing manufacturing processes from published literature.

TCDC in R and D is crucial, firstly in establishing R and D facilities in those countries which do not possess the same at present, and secondly to accelerate the progress of R and D in countries which already have such facilities.

TCDC makes it possible to draw a common R and D plan, avoids duplication of efforts and promotes free exchange of scientific information among the developing countries.

Lack of local industries suited to produce ancillary materials restricts the formulation activities in many developing countries. As the requirement of such materials in many developing countries individually is relatively small, establishment of joint ventures for producing ancillary materials can resolve the problem.

One of the solutions to the problem arising out of high prices of intermediates is the manufacture of such intermediates by the developing countries themselves. Unfortunately, manufacture of many of the intermediates is not economically viable unless done on a large scale. TCDC aims at not only solving the problems of non-availability of technology, but also that of economy of scale by extending the scope of planning beyond the national frontiers.

TCDC opens up the possibility of establishment of a common market for pharmaceuticals and related products by according preferential treatment to transaction between the developing countries as well as promoting joint ventures between them.

There are some distinct advantages in acquiring technology from other developing countries. Technology offered by them is likely to be of smaller optimum scale, use more labour intensive techniques and be better suited to supply conditions in developing countries than those offered by developed countries. The benefit also arises from the unpack nature of the technology offered.[5/]

Many pharmaceutical units in developing countries have successfully adapted imported technology to their specific needs and environments and some have even improved upon the productivity of the imported processes.[6/]

5/ S. Lall, Third World Technology Transfer and Third World Transnational Companies.

6/ Pharmaceuticals in the Developing World, Policies on Drugs, Trade and Production, Volume I.

With the experience gained in assimilating foreign technology, these units are in a better position to transfer technology to other developing countries compared to the original supplier.7/

As there are no unsurmountable language and emotional barriers to communication between the developing countries of the same region, training and consultancy services are expected to be more effective in TCDC.

Besides the direct economic benefit to the recipient country, TCDC offers indirect benefit to the developing countries as a group. It contributes to greater self-reliance and independence of the Third World countries and strengthens their position in purchase and transfer of technology. In the context of present negotiations on the New International Economic Order where the building up of common bargaining position by the developing countries is of prime importance, the growth of intra Third World trade in technology is of obvious signficiance.7/

Analysis

It becomes evident, therefore, that a framework of TCDC should be established for identifying alternative sources of supplies for the requirements of the pharmaceutical industries of the developing countries. UNIDO's assistance can be made available for implementing the following steps as a preliminary to the introduction of TCDC.

(a) Preparation of detailed documents with respect to:
- level of development of pharmaceutical industries in different regions, sub-regions and countries;
- availability of technology in the developing countries for transfer to other countries;
- evaluation of available technology for suitability in terms of process, scale of production, yield investment, etc.;
- assessment of existing facilities of raw materials, plant and machinery and auxiliary services;
- identification of the countries and the respective technical areas where technical assistance is needed;
- identification of product lines where regional and sub-regional co-operation would prove beneficial;
- preparation of programme for the utilization of country's natural resources;
- designing of appropriate R and D facilities according to product requirements of developing countries at regional and sub-regional level;

7/ S. Lall, Third World Technology Transfer and Third World Transnational Companies.

- preparation of programme for training of personnel;
- identification of discrepancies in the governmental policies that may hinder the success of TCDC and suggestions for their harmonization for an effective TCDC programme.

(b) In organizing a forum representing the Governments, national pharmaceutical and related industries of the developing countries in order to find ways and means of implementing TCDC programmes and specially to define the role of the Government in providing moral and financial support.

Annex I

State of development of Pharmaceutical Formulation Industry in Developing Countries.

Latin America

Argentina, Brazil, Costa Rica, Cuba, Mexico and Peru produce close to 100% of their requirement of formulations, other developing regions of Latin America manufacture, on an average about 75% of domestic requirements of the finished dosage forms. Only in Central America and CARICOM countries pharmaceutical formulation industries need considerable improvement.

Asia

As in Latin America some of the countries in this region have achieved impressive stage of development. India, Indonesia, Pakistan, Philippines, South Korea and Thailand are nearly self sufficient in their requirement of pharmaceutical formulations. All other countries of developing Asia formulate 30-60% of national consumption. There are only few countries in the region such as Afghanistan. Bhutan, Nepal, Vietnam, People's Republic of Yemen and Democratic Republic of Yemen which are in their initial stages of development of pharmaceutical industries and need further improvement.

Africa

Development of Pharmaceutical Industry in greater part of this region remained stagnant. Egypt being the most advanced country in this field in the region produces 80% of its requirements of dosage forms. Algeria, Ivory coast, Kenya, Morocco, and Senegal have well established pharmaceutical formulation facilities.

The following countries in Africa have been listed by UNIDO for implementation of primary pharmaceutical industry - Botswana, Burundi, Cameroon, Chad, Gambia, Niger, Nigeria, Rwanda, Sudan, and Upper Volta.

Annex II

List of essential bulk drugs produced in the developing countries.[8/]

Name of the drug	Names of the countries producing the drug
1. Acetylsalicylic acid	Argentina, Bangladesh, Brazil, Colombia, Egypt, India, Mexico Turkey, Republic of Korea.
2. Ampicillin	Argentina, Brazil, India, Republic of Korea, Mexico, Peru.
3. Ascorbic acid	India
4. Benzyl Penicillin	Brazil, India, Mexico, Pakistan
5. Betamethasone	India, Pakistan
6. Chloramphenicol	India, Thailand
7. Chloroquine	Bangladesh, India
8. Codeine	India
9. Dapsone	India
10. Dexamethasone	India
11. Diethylcarbamazine	India
12. Digoxin	India
13. Emetine	India
14. Ephedrine	India
15. Erythromycin	Brazil, India, Mexico
16. Ethambutol	Brazil, India, Venezuela, Republic of Korea
17. Ethinylestradiol	Mexico, India
18. Folic Acid	India
19. Furosemide	Brazil, India
20. Glucose	India, Indonesia, Pakistan
21. Heparin	Botswana, India, Argentina
22. Hydrocortisone	India

8/ Information regarding suitability and availability of technology for transfer and the stage from which the bulk drugs are manufactured is not available in most cases.

Name of the drug	Names of the countries producing the drug
23. Insulin	Argentina, India
24. Isoniazid	Argentina, India, Republic of Korea
25. Metronidazole	India
26. Morphine	India
27. Nicotinamide	India
28. Paracetamol	Argentina, Egypt, India, Mexico
29. Phenobarbital	India
30. Piperazine	India
31. Prednisolone	India
32. Pyridoxine	India
33. Quinine	Guinea, India, Indonesia, Zaire
34. Reserpine	India
35. Riboflavin	India
36. Salicylic acid	Argentina, Egypt, India, Mexico
37. Streptomycin	Brazil, India
38. Sulphacetamide	India
39. Sulphadimidine	Egypt, India, Mexico
40. Sulphamethoxazole	India
41. Trimethoprim	India
42. Tetracycline	Argentina, Brazil, India, Indonesia, Iraq, Republic of Korea, Mexico
43. Thiamine	India
44. Vitamin A	Argentina, Brazil, India
45. Vitamin B12	Argentina, Brazil, India, Mexico

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INTRODUCTION

The study on the pharmaceutical industry endeavours to describe to developing countries a well-defined illustration of the industry in respect of all its components, and it aims to assist them towards a better understanding of what the industry is and which the means are to promote its growth in the developing world. Developed countries are still not fully aware of the urgent needs of developing countries. Previous studies accomplished by various sectors and/or institutions have failed to show the different parameters of the industry and how they affect or are influenced by the socio-economic environment.

The pharmaceutical industry is very sensitive to many inputs which have adversely affected its growth in the developing world, thus hampering the supply of drugs and therefore endangering the national health scheme.

None of the elements that have contributed to the stagnation of the pharmaceutical industry in developing countries could be considered independently because their contribution has so far been similar. It is imperative, therefore, to enumerate them and to clarify the inter-relationship between the health policies and the technological impact on the pharmaceutical industry. These two elements together could provide a wealth of initiative for the amelioration of policies to be adopted.

Developing countries must be very clear, nevertheless, in respect of how much they can expect from the establishment of a domestic pharmaceutical industry and what would thus be required for its implementation components. It is urgent, therefore, that all aspects relevant to the establishment of a pharmaceutical industry must be clearly defined so that developing countries could select a dynamic strategy that could be adopted by the policy-makers in the developing world. It also must be understandable to developing countries, that modern pharmaceutical technology is an element subject to continued changes and that domestic capabilities should be utilized for the improvement of said technologies.

This study is pointed towards the consumption, production and supply in developing countries of the essential drugs selected by WHO and is therefore not confined to the illustrative list of 26 essential drugs prepared by UNIDO in consultation with WHO.

(a) Definition of the pharmaceutical industry

The various stages through which developing countries are confronted when the implementation of a pharmaceutical industry is under consideration have been identified and grouped by UNIDO as follows:

Group I: countries that have no manufacturing facilities and therefore are dependent on imported pharmaceuticals in their finished form: countries with limited public health services and poor distribution channels. Steps to be taken:

(i) To establish procurement procedures to take advantage of purchasing in large quantities;

(ii) To develop quality control facilities to ensure quality of drugs purchased;

(iii) To establish units for repacking formulated drugs as training to help build the auxiliary industries of packing materials and to stnadardize their production:

(iv) To set up units for producing infusion solutions and simple formulations in hospital pharmacies or as separate units.

Group II: countries that are already repacking formulated drugs and are making simple formulations. Steps to be taken:

(i) To establish formulation units to convert bulk drugs into dosage forms such as tablets, capsules, liquid preparations, ointments and infusion solutions;

(ii) To establish facilities to control quality from the raw material to the finished product. In addition, to set up the requisite organization to frequently monitor the stability of the drug. In cases where products fail to meet specifications, they should be recalled from the market.

Group III: Countries that formulate a broad range of bulk drugs into dosage forms and that are starting production of simple bulk drugs from intermediates. Steps to be taken:

(i) To establish multipurpose plants to produce the bulk drugs required for health programmes by grouping products where production involves similar chemical reactions;

(ii) To set up units for extraction of active principles from medicinal plants, which grow wild or are cultivated in the country;

(iii) To set up centres to utilize slaughterhouse by-products, such as the extraction of active principles of glands and organs, to produce catgut, etc.;

(iv) To set up a unit to produce immunologicals both for prophylaxis and treatment.

Group IV: countries that produce a broad range of bulk drugs from intermediates and that manufacture some intermediates using local raw materials. Steps to be taken:

(i) To set up units for the production of antibiotics by fermentation;

(ii) To set up plants for intermediates also covering the needs of the other chemical-based industries.

Group V: countries that manufacture intermediates required for the pharmaceutical industry and that produce the plant and equipment required. They also undertake local research in order to develop new products and to improve manufacturing processes. Steps to be taken:

(i) To expand the range of intermediates and the volume of production to be able to meet other developing countries' requirements;

(ii) To expand the production of chemical plant equipment and machinery both for the production of dosage forms and the production of drugs from basic chemicals.

It is necessary to clarify a number of concepts which will provide developing countries with a clear definition of the pharmaceutical industry and its interrelationship and interdependence with the allied chemical industries.

The pharmaceutical industry consists of a branch of manufacture engaged to undertake various stages of production of drugs utilized in the prophylaxis, diagnosis or treatment of diseases endangering human and animal health. The main outputs of the pharmaceutical industry are bulk drugs and finished dosage forms. A drug is any substance in a pharmaceutical product that is used to modify or explore physiological systems of pathological states for the benefit of the recipient. Dosage forms are the forms of the completed pharmaceutical product, i.e. tablets, capsules, elixir, etc.

A pharmaceutical product is a dosage form containing one or more drugs along with other substances included during the manufacturing process. Drug formulation consists of the composition of a dosage form, including the characteristics of its raw materials and the operations required to process it.

Bulk drugs or active substances are the imputs of the pharmaceutical industry in terms of raw materials. They are mainly derived from substances of plant or animal origin; from bacterial or viral cultures, from substances produced in substrates during the growth of microorganisms, or chemical entities designated as late or early intermediates. The latter are provided by the chemical industry whereas the former are obtained from natural sources.

The chemical industry could be classified into two main groups: the industry of inorganic chemicals which produces inorganic acids, alkalies and miscellaneous compounds of relatively simple chemical structure. The output of this industry is used in most chemical processes and as reagents in analytical chemistry as well as in the agricultural industry. The second group of chemical industries derives from the petrochemical industry and the latter from the cracking of the petroleum. Their main outputs are fuels, pigments, polymers and a vast variety of chemicals used in all branches of modern life.

The main inputs to the basic pharmaceutical production, therefore, except for fermentation, plant and animal derivatives or biologicals are the pharmaceutical intermediates of common use in processes synthesis of bulk drugs.

The study aims, not only to define the pharmaceutical industry but to identify the constraints that hampered its growth in developing countries. The chapters encompassing the body of this study, as can be seen in the table of contents, mostly consist of the constraints to the growth of the pharmaceutical industry, policy options, pricing, availability of technology and the expected growth of the pharmaceutical industry in the years to come. An outlook to the year 2000 forms the conclusion of this study.

(b) Sources of information

A large amount of data on world statistics on pharmaceuticals has been reviewed in the preparation of this study. A wealth of information has been compiled from reports submitted by experts to the pharmaceutical industry who have undertaken missions for UNIDO throughout countries in the developing world. The study on the pharmaceutical industry prepared by the Union of the Hungarian Pharmaceutical Industry (TESCO) on production and consumption in terms of bulk drugs has been broadly used as reference. Likewise the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) has contributed a chapter to this study. WHO and UNCTAD have also contributed chapters on drug policies and trade respectively.

(c) Explanatory notes

In the chapters discussing production and consumption of pharmaceuticals the nomenclature "bulk drugs" has been adopted to define active substances. On the other hand the terminology "finished dosage forms" identified medicaments ready for consumption after the last stage of formulation operations has been completed.

This study encompasses observations on a number of grouped pharmaceuticals used in modern medicine: however, emphasis has been placed on the essential drugs identified by UNIDO and approved by WHO, since these drugs represent the most urgent needs for bulk drug production in developing countries[1/].

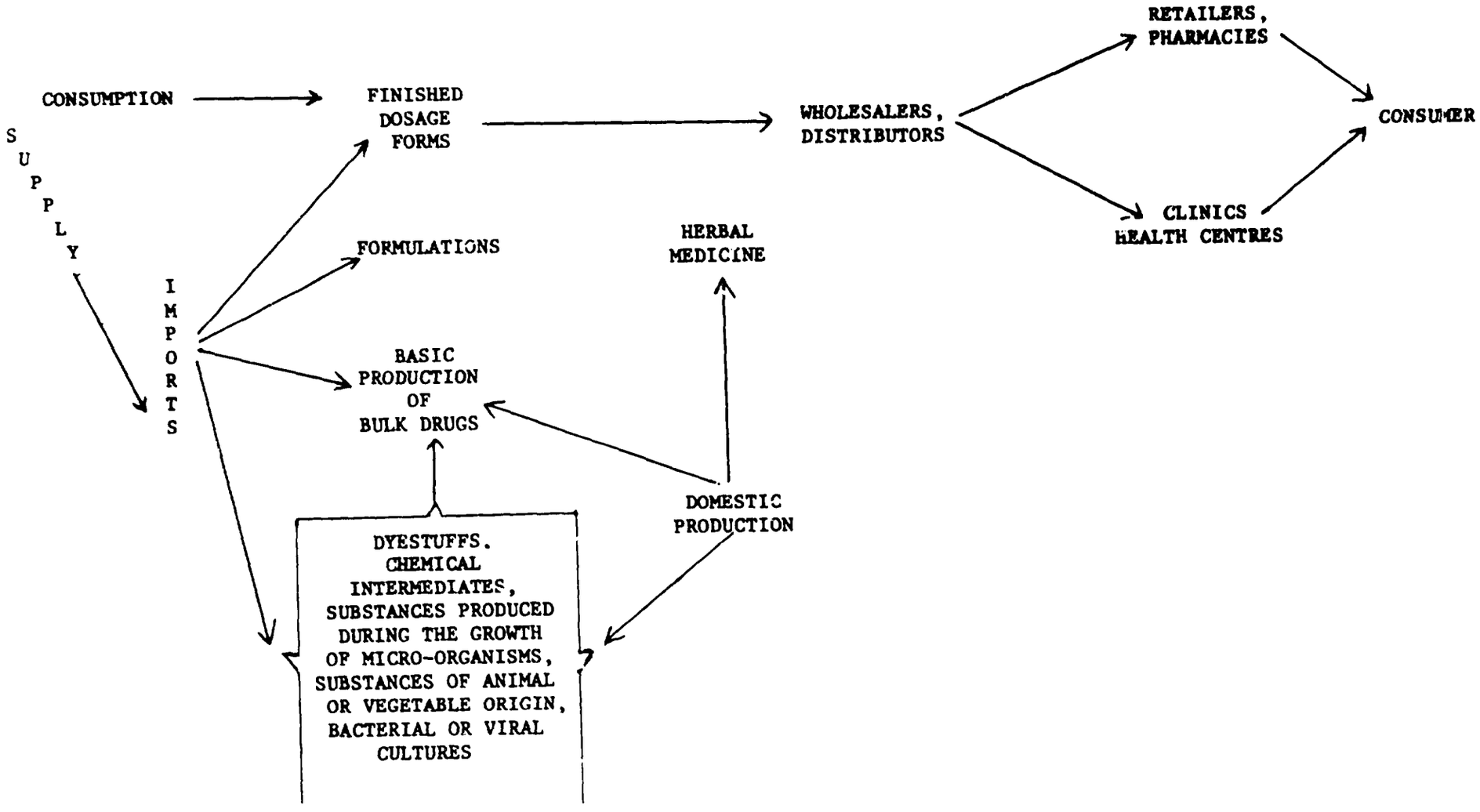
A large number of statements on production and consumption of pharmaceuticals has been confined to some extent to essential drugs in terms of weight of bulk drugs inasmuch as it has been thought that weight is a more precise indicator than value in assessing the growth of the industry or the drug requirements of developing countries. Furthermore, weight is less prone to distortions produced by price fluctuations or currency devaluation.

1/ UNIDO illustrative list of 26 essential drugs selected for local manufacture: acetylsalicylic acid, paracetamol, mebedazole, piperazine, ampicillin, penicillin-benzyl, erythromycin, streptomycin, tetracycline, sulphadimidine, diethylcarbamazine, dapsone, chloroquine, primaquine, ethambutol, isoniazid, propranolol, hydralazine, reserpine, furosemide, ethinylestradiol + norgestrel (levo), blood and blood fractions, retinol, hydroxocobalamine, ascorbic acid and insulin.

The framework of the pharmaceutical industry has been drawn in Figure 1 in a summarized diagram. This chart outlines the stages of pharmaceutical production which have been identified at the beginning of this chapter. The upper part of the diagram is concerned with consumption and distribution channels whereas the lower section of the chart exemplifies production and supply in drugs.

The calculation of the world-wide rate of growth of consumption/production of pharmaceuticals in value as well as in weight - the latter refers only to active substances - has not followed an homogeneous pattern. Uncertainty of price increases and unpredictable consumption/production pattern over a twenty-year time span made it difficult to foresee with accuracy the magnitude of the world-wide pharmaceutical consumption/production by the year 2000. An additional complexity arisen during the preparation of this study was the attempt to split the data on the dimension of the pharmaceutical world into production of bulk drugs/formulations. In achieving these objectives, estimates have been projected by considering a consistent attainable reality. The dimension of the consumption of elements used in traditional systems of indigenous medicine, a sizable segment in developing countries, has not been quantified since data are sparse. It is expected, however, that the demand for this type of products be urged and that it will also accompany the path of the population increase.

Fig. 1 Flow chart of pharmaceuticals



II. STRUCTURE OF HEALTH

Benjamin Disraeli, the noted British statesman, said: "The health of the people is really the foundation upon which all happiness and all their powers as the State, depend."

However, one quarter of the people on this earth have no access to any health care whatsoever. High morbidity and mortality rates exist among the rural populations that constitute the majority of the world's population, including some 800 million people that still suffer from absolute poverty. Malnutrition, communicable diseases and parasitic infections continue to take heavy toll of lives, especially among infants, children and other weaker groups. The staggering statistics of mortality and disease in the Third World are a chilling reflection of human tragedy on a global scale. 15.6 million children under five years of age will die each year on this earth, out of which 15.1 million will be from developing countries. Of these, 12 million could probably be avoided. Hundreds of millions of people in the Third World contract parasitic diseases each year for which adequate therapy is not available when and where it is needed. Millions of people continue to suffer from symptoms which can be alleviated, die from diseases which can be treated and develop diseases which can be prevented entirely. What is really needed is the building of a primary care infrastructure in each country, built by the individual country adjusted to its particular needs.

(a) Disease patterns in developed and developing countries

In spite of the significant economic growth and technological progress following the Second World War, the same basic complex of infectious parasitic and respiratory diseases compounded by nutritional deficiencies remain the causes of most of the world's mortality. There has been an increase or resurgence of certain communicable diseases such as schistosomiasis and malaria. One could have expected greater progress in respect of tuberculosis or sexually transmitted diseases. Cardiovascular disease and cancer continue to be the greatest problems of the industrialized countries, with many middle-income countries following suit. About 800 million people in the developing world live

in conditions of abject poverty devoid of basic nutrition and access to services essential to a healthy life. Nearly 450 million people have less food than is necessary for basic survival. There is a positive correlation between socio-economic factors, well being and levels of health. Morbidity in the less developed regions is primarily associated with a large incidence of infectious, parasitic and respiratory diseases.

In the 1970, world population increased at an annual rate of 1.9 per cent and exceeded 4000 million in 1977 as against 3600 million in 1970. Population, rate of increase, birth and death rates, density, GNP per capita and medical team density for the world, continents and geographical regions are shown in Table 1. The differences between developed and developing countries as reflected in the population growth rates illustrate the differences between them in levels of fertility and mortality. The average infant mortality in the developed countries is a little over 20 per mil, while in the least developed countries it is over 150. The national expenditure on health as percentage of GNP is indicated in Table 2.

It is obvious from Table 2 that health matters have low priority in developing countries. In general, developed countries spend 5-8 per cent of GNP on health care, out of which the expenditure on pharmaceuticals accounts for 10-20 per cent. In contrast, the expenditure on health care in many developing countries is below 2 per cent of the GNP which up to 50 per cent represents expenditure on pharmaceuticals.

Major health problems of developing countries are illustrated in Table 3. It can be seen from Table 3 that malaria and diarrheal diseases are prevalent in all the regions. Leading causes of death in a more developed and a less developed group of countries are shown in Table 4.

Although accidents are among the three leading causes of death, they represent a much smaller proportion of all deaths in the less developed than in more developed countries. This is the result of the greater incidence of infectious, parasitic and respiratory diseases in the less developed countries, which have been controlled or eliminated in the more developed countries.

The differences in consumption patterns between some developing countries and developed ones are indicated in Tables 5 and 6. While systemic antibiotics and vitamins lead in developed countries studied, psycholeptics are prominent in some developed countries. Comparative rankings of the leading ten therapeutic classes in selected developed and developing countries are given in Table 7 and these reveal some distortions in the usage of pharmaceuticals. For example, tropical diseases are big killers in tropical countries. However, it can be seen from Table 7 that in six of the more advanced developing countries, antiparasitic drugs account for only 1 to 2 per cent of total drugs consumed.

(b) Supply of drugs

Medicinal products play an important role in protecting, maintaining and restoring the health of the people. Although medicinal products constitute essential tools for health care, it is observed that drug policies are often directed towards industrial and trade development. The pharmaceutical supply system involves various activities, such as the procurement, production and control of drugs and vaccines, research and development, distribution to the health services and the public and monitoring of marketed product. The need for developing countries to formulate appropriate drug policies to reflect true health needs is well recognized. The main aim of the national drug policies should be to make the most effective and safe medicinal products of established quality accessible at reasonable cost to all people. WHO has drawn up a list of essential drugs considered adequate to cater to the bulk of ailments which facilitated the rationalization and proper use of essential drugs by developing contries to meet their real health needs and in the local production and quality control of such drugs, where feasible.

The Lima Declaration and Plan of Action on Industrial Development and Co-operation adopted by the Second General Conference of UNIDO in 1975, specified the need for a better balance in the structure of world production and set the goal of increase in the share of the developing countries in total world industrial production from 7 per cent to at least 25 per cent by the year 2000.

The share of developing countries in 1977 in the world production of pharmaceuticals was about 11 per cent. The per capita consumption of drugs in some of the developing countries amounted to a meagre $ 1 compared to a corresponding figure of $ 50 in some of the developed countries, as can be seen in Table 8. These clearly show the wide gap which exists between the developed and developing countries in the matter of supply of drugs and highlight the urgent need for measures to substantially improve the availability of drugs to the vast majority of the world's population living in conditions of abject poverty, devoid of basic nutrition and access to services essential to a healthy life. In view of this and in line with the Lima Declaration and Plan of Action, UNIDO developed a series of policies with a view to promoting the growth and development of pharmaceutical industry in developing countries. These include production policy, basic principles for transfer of technology, strategy on replacement of synthetic chemicals by locally available natural products and multipurpose plants.

The development of a national quality control system linked with procurement and local production are important elements in national drug policies. There are significant differences in the types of medicinal products needed for health care in developed and developing countries. In the former, the demand is on the increase for certain products used for chronic diseases of the adult or aged population, or for mental illness. In developing countries, the demand is for medicinal products for the control of major communicable diseases, such as products against malaria and other parasitic diseases prevalent in tropical areas.

(c) Preventive medicine and pharmaceuticals

Preventive medicine is an important branch in modern medical care.

Immunization is one of the best weapons of preventive medicine. It is a process of increasing resistance to infection whereby micro-organisms or products of their activity act as antigens to stimulate certain body cells to produce antibodies with a specific protective capacity.

The process of antibody formation is known as active immunization and may be a natural process following recovery from an infection, or an artificial process following inoculation with a vaccine or toxoid. It is a slow process dependent on the rate at which the antibody

formation can be developed. Immediate protection of short duration may be achieved by passive immunization in which immune serum containing antibodies of the required type, antiserum is administrated.

Vaccines are preparations of antigenic materials which are administered with the object of inducing in the recipient a specific active immunity to infection or intoxication by the corresponding infecting agents. They may contain living or dead micro-organisms, bacterial toxoid, or purified products derived from bacteria.

Antisera are native (unconcentrated) sera, or preparations from native sera, containing substances that have a specific prophylactic or therapeutic action when injected into persons exposed to or suffering from a disease due to a specific micro-organism.

A number of medicinal agents used in preventive medicine are commonly named biologicals. Many communicable diseases have already been eradicated or kept under control in many areas of the world, nevertheless, developing countries have not achieved a substantial progress in preventive medicine either because they lack the financial resources to provide mass immunization of the population, or they do not have the technology to become engaged in local production of biologicals.

The research carried out on preventive medicine has been fruitful in the sense that the incidence of a number of communicable diseases has been curtailed lately. Smallpox, yellow fever, cholera, plague, typhoid-paratyphoid fever, rabies, typhus, polio, tatanus, diphtheria, measles and mumps exemplify a broad range of communicable diseases which, to a large extent, could be prevented nowadays. Unfortunately, the usefulness of preventive medicine is mostly a privilege of developed countries.

A number of reagents also made from cultures of micro-organisms assist to detect or to rule out a number of communicable diseases. The following diagnostic reagents are illustrative: Widal for typhoid fever, Dick test for scarlet fever, Schick test for diphtheria, Mantoux test for tuberculosis and Frei test for lymphogranuloma venereum.

As a part of the scheme of human preventive medicine, the immunizing agents used in veterinary medicine should not be excluded,

not only because some animal diseases could be transmitted to humans but also because healthy livestock constitute an important protein source for humans.

Another important segment of preventive medicine comprises the production of antivenom sera since poisonous ophidians or deadly arthropods are common in most developing countries.

(d) Drug policies and essential drugs in developing countries[2/]

The Alma Ata Conference on Primary Health Care declared that the health status of hundreds of millions of people in the world today is unacceptable, particularly in developing countries. More than half the population of the world does not have the benefit of proper health care.

In view of the magnitude of health problems and the inadequate and inequitable distribution of health resources between and within countries, and believing that health is a fundamental human right and world-wide social goal, the Conference called for a new approach to health and health care, to close the gap between the "haves" and the "have nots", to achieve more equitable distribution of health resources, and to attain a level if health for all the citizens of the world that will permit them to lead a socially and economically productive life.

The Conference considered primary health care to be essential care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination. It forms an integral part both of the country's health system, of which it is the central function and main focus, and of the overall social and economic development of the community. It is the first level of contact of individuals, the family, and the community with the national health system, bringing health care as close as possible to where people live and work, and constitutes the first element of a continuing health care process.

The Conference reaffirmed the importance of establishing and further developing a comprehensive national health system of which primary health care is an integral part, encouraging the full participation of the population in all health-related activities.

2/ Contributed by WHO

Primary health care requires the development, adaptation and application of appropriate health technology that the people can use and afford, including an adequate supply of low-cost, good-quality essential drugs, vaccines, biologicals and other supplies and equipment, as well as functionally efficient supportive health care facilities, such as health centres and hospitals. These facilities should be reoriented to the needs of primary health care and adapted to the socioeconomic environment.

Drug supply and health care in developing countries

Urgent international action is required to alleviate the situation in developing countries, where large segments of the world's population do not have access to the most essential drugs and vaccines that are indispensable to ensure even minimum health care. In fact, for many diseases affecting millions of people in these countries, effective prophylactic and therapeutic agents already exist, but are not available in sufficient quantities and are not effectively distributed or utilized.

In the coming decades, the development of primary health care systems in the developing countries will require the concomitant development of pharmaceutical supply systems, including local production wherever feasible, adapted to the real needs of the majority of the population. Efforts will also be required in information, education, and training in the proper use of drugs in the communities.

Pharmaceuticals cannot be considered isolated from health care systems. In many developing countries, health services are concentrated in urban areas, based in city hospitals which may utilize 80 per cent of national health expenditure but only cater for the needs of 20-30 per cent of the population.

The basic principle of a drug supply system in a country or region should be to secure an easy and permanent supply of essential medicines of acceptable quality and reasonable price to people.

Expenditure on drugs, in both the private and public sectors, is much lower in absolute terms in developing countries than in developed countries but is much higher in relation to the total health expenditure. The need to optimize expenditure in drugs is therefore vital in developing countries. Resources are often wasted in purchasing expensive drugs that are only marginally useful or even irrelevant to the solution of a country's health needs, where large segments of the population are in

urgent need of essential drugs for disease control and primary health care.

There is an urgent need to ensure that the most essential drugs are available at a price that countries can afford and to stimulate research and development to produce new drugs adapted to the real needs of developing countries. This pharmaceutical sector combines drug requirements with health priorities in national health plans within the context of socio-economic development. It also calls for international co-ordination in the medium and long-term programmes for research, production, legislation, distribution and utilization of essential drugs and, finally, for control of diseases prevalent in developing countries.

WHO has made significant contributions towards raising the drug standards and assisting countries in improving drug quality, safety and efficacy. It is now important to co-operate with countries in formulating and implementing national drug policies.

The WHO Action Programme on Essential Drugs is aimed at stimulating broad international co-operation among governments of both developed and developing countries, interested agencies, development aid organizations and the pharmaceutical industry in order to alleviate the situation, particularly in the public sector, of developing countries where large segments of the population do not have access to the most essential drugs, including vaccines, that are indispensable in ensuring a minimum of health care.

Selection of essential drugs

In October 1976, an informal consultation was convened in Geneva to advise the Director-General on the selection of essential drugs which would correspond to health requirements, bearing in mind the situation in developing countries where the main objective was to extend primary health care coverage to the population. The report of this consultation was circulated for comment to WHO regional offices, health administrators, experts and non-governmental organizations in official relations with WHO. The comments received were analysed and made available to assist a WHO Expert Committee on the Selection of Essential Drugs convened in Geneva in October 1977. In addition, the following guidelines were proposed to the Expert Committee:

(a) The extent to which each country implements schemes or establishes lists of essential drugs is a question of individual national policy.

(b) As far as health services in developing countries are concerned,

organized procurement and use of essential drugs has many advantages in terms of economy and effectiveness. However, the concept of essential drug lists must accommodate a variety of local situations if the lists are ever to meet the real health needs of the majority of the population.

(c) These are convincing justifications forWHO to propose model or guide lists of essential drugs as a contribution to solving the problems of those member States whose health needs by far exceed their resources and who may find it difficult to initiate such an endeavour alone.

(d) Such guide or model lists should be considered as a tentative identification of a common core of basic needs with universal relevance and application. The further local needs move from the core, the more health authorities or specific sectors of the health services will have to adjust the lists. Therefore, any list proposed by WHO should set out to indicate priorities in drug needs, with the full understanding that exclusion does not imply rejection. A list of essential drugs does not imply that other drugs are not useful but simply that in a given situation these drugs are most necessary for the health care of the majority on the population and therefore should be available at all times in adequate quantities and in the proper dosage forms.

(e) The selection of essential drugs is a continuous process, involving changing priorities in public health activities and epidemiological conditions, as well as progress in pharmacological, pharmaceutical and therapeutic knowledge. Selection should be accompanied by a concomitant effort in educating and training health personnel in the proper use of the drugs.

(f) Finally, the WHO programme on essential drugs should provide a focus for an organized and systematic investigation of this approach. It should also identify plans of action and research at national and international levels to meet the unsatisfied basic health needs of populations who at present are denied the most essential prophylactic and therapeutic substances.

The report of theWHO Expert Committee on the Selection of Essential Drugs contains proposed guidelines for establishing a list of essential drugs, suggestions for drug information and educational activities and a "model" list of essential and complementary drugs which can furnish a basis for countries to identify their own priorities and to make their own selection.

This list should be regarded as a contribution to solving the problems of those member States whose health needs far exceed their resources and who may find it difficult to initiate such an endeavour on their own. The Executive Board, at its Sixty-first Session, having reviewed this report, requested the Director-General to continue to identify the drugs and vaccines which, in the light of scientific knowledge, are indispensable for basic health care and disease control in the vast majority of the population, and to update periodically this aspect of the report.

The notion that the number of necessary drugs is relatively small is supported by experience in both developing and developed countries where limited lists and formularies are successfully used, for example, in hospitals. Limited drug lists have several advantages, particularly in developing countries:

- reduction in the number of medicinal products to be purchased, stored, analysed and distributed;
- improvement in the quality of drug utilization, management, information and monitoring;
- stimulation of local pharmaceutical production.

As drugs and vaccines are major strategic components in preventive and curative health care, it is necessary to draw up a list or lists of priority drugs which can always be available at different levels of health care. The countries' resources being generally limited, any kind of health action necessitates establishing priorities.

The range of medicinal products marketed in various countries varies from more than 30 000 to less than 2 000. The figures refer to dosage forms in a particular strength from a particular manufacturer and not to the active substances they contain and do not include herbal remedies. From the point of view of "health needs"[3/] of the majority of the population, three main types of medicinal products can be considered, although it is recognized that the distinction is not clear cut and may not apply in every situation:

- essential drugs of priority medicinal products used on the basis of scientific and clinical data;

3/ "Health needs" are described as scientifically (biologically, epidemiologically) determined deficiencies in the health of the population. Essential and complementary drugs can prevent or influence a health condition in a predictable fashion and can be considered as efficacious and safe if properly used because their expected risks and benefits in specific indications have been evaluated on the basis of adequate scientific and clinical data.

- complementary drugs[4/] or medicinal products to complement a list of essential drugs;
- remedies used on the basis of long experience, but for which adequate scientific and clinical data are being accumulated.

The following principles were considered by the WHO Expert Committee to be a foundation on which to establish a list of essential drugs:

(a) Adoption of a list of essential drugs is part of a national health policy. This implies that priority is given to achieving the widest possible coverage of the population with drugs of proven efficacy and safety, in order to meet the needs for prevention and treatment of the most prevalent diseases.

(b) Only those drugs for which adequate scientific data are available from controlled studies should be selected.

(c) Each selected pharmaceutical product must meet adequate standards of quality, including when necessary bioavailability.

(d) Concise, accurate and comprehensive drug information drawn from unbiased sources should accompany each list of essential drugs.

Criteria for the selection of essential drugs are intended to ensure that the process of selection will be unbiased and based on the best available scientific information, yet allow for a degree of variation to take into account local needs and requirements. The following guidelines are recommended:

(i) Each country should appoint a committee to establish a list of essential drugs. The committee should include individuals competent in the fields of clinical medicine, pharmacology and pharmacy, as well as peripheral health workers. Where individuals with adequate training are not available within the country, assistance from WHO could be sought.

(ii) Drug selection should be based on the results of benefit and safety evaluations obtained in controlled clinical trials and/or epidemiological studies.

(iii) The international non-proprietary (generic) names for drugs or pharmaceutical substances should be used whenever available. A cross-index of non-proprietary names should initially be provided to the prescribers.

4/ These drugs provide : (a) treatment in rare disorders; (b) alternatives when infectious organisms develop resistance to essential drugs; (c) special pharmacokinetic properties, etc.

(iv) Regulations and facilities should be available to ensure that the quality of selected pharmaceutical products meets adequate quality control standards, including stability and, when necessary, bioavailability. Where national resources are not available for this type of control, the suppliers should provide documentation of the product's compliance with the requested specifications.

(v) Cost represents a major selection criterion. In cost comparisons between drugs, the cost of the total treatment, and not only the unit cost, must be considered. In addition, the cost of non-pharmaceutical therapeutic modalities should be taken into account.

(vi) Local health authorities should decide the level of expertise required to prescribe single drugs or a group of drugs in a therapeutic category. Consideration should also be given to the competence of the personnel to make a correct diagnosis. In some instances, while individuals with advanced training are necessary to prescribe initial therapy, individuals with less training could be responsible for maintenance therapy.

(vii) The influence of local diseases or conditions on pharmacokinetic and pharmacodynamic parameters should be considered in making the selections: e.g., malnutrition, liver disease.

(viii) When several drugs are available for the same indication, select the drug, pharmaceutical product and dosage form that provide the highest benefit/risk ration.

(ix) When two or more drugs are therapeutically equivalent, preference should be given to:

(1) the drug which has been most thoroughly investigated;

(2) the drug with the most favourable pharmacokinetic properties, e.g. to improve compliance, to minimize risk in various patho-physiological states;

(3) drugs for which local, reliable manufacturing facilities for pharmaceutical products exist;

(4) drugs, pharmaceutical products and dosage forms with favourable stability, or for which storage facilities exist.

(x) Fixed-ratio combinations are only acceptable if the following criteria are met:

(1) clinical documentation justifies the concomitant use of more than one drug;

(2) the therapeutic effect is greater than the sum of the effect of each;

(3) the cost of the combination product is less than the sum of the individual products;

(4) compliance is improved;

(5) sufficient drug ratios are provided to allow dosage adjustments satisfactory for the majority of the population.

(xi) The list should be reviewed at least once a year and whenever necessary. New drugs should be introduced only if they offer distinct advantages over drugs previously selected. If new information becomes available on drugs already in the list that clearly shows that they no longer have a favourable benefit/risk ratio, they should be deleted and replaced by a safer drug. It should be remembered that for the treatment of certain conditions, non-pharmacological forms of therapy or no therapy at all, may be preferable.

Review and updating of the model list of essential drugs and selection of pharmaceutical forms

(a) The first report of the Expert Committee (WHO Technical Report Series, No. 615, 1977) contained recommendations for the review and updating of the model list of essential drugs, therefore the first report of the Committee was sent, with requests for comments, to all members of the WHO Expert Advisory Panels on Drug Evaluation and on the International Pharmacopoeia and Pharmaceutical Preparations, to the WHO regional offices, to national health authorities, and to interested international and non-governmental organizations. The replies to this request were collated and presented to a preparatory meeting convened in 1978.

The Second WHO Expert Committee on the Selection of Essential Drugs (Geneva, 2-6 July 1979) considered the proposals and the necessary modifications were made by the addition or deletion of substances, on the basis of the latest available knowledge and informed opinion.

(b) The same Committee set up guidelines for the selection of pharmaceutical forms as follows:

The purpose of selecting dosage forms and strengths for the drugs in the model list was to identify the most appropriate pharmaceutical forms and to give advice to countries wishing to standardize or minimize the number of preparations in their own drug lists. As a general rule,

pharmaceutical forms were selected on the basis of their general utility and their wide international availability. In many instances, a choice of preparations was provided, particularly in relation to solid dosage forms. While the cost factor should be taken into account, the selection should also be based on a consideration of pharmacokinetics, bioavailability, stability under ambient climatic conditions, availability of excipients, and established local preference.

In a few instances, exemplified by acetylsalicylic acid and paracetamol, a range of dosage strengths was provided from which suitable strengths should be selected on the basis of local availability and need. When precise dosage is not mandatory, the scoring of tablets was recommended as a simple method of making dosage more flexible if so required and, in some instances, to provide a convenient paediatric dose. Specific paediatric dosages and formulations were included in the list only when indicated by special circumstances.

Bioavailability was re-emphasized as a general problem in the quality of pharmaceutical forms and their utilization, particularly for certain drugs, such as digoxin and phenytoin. It was felt that governments should be aware of possible shortcomings in the quality of pharmaceutical formulations when selecting drug products either of local manufacture or of foreign provenance.

The second report of the WHO Expert Committee was published as WHO Technical Report Series No. 641, 1979.

Transfer of information

The need for accurate and objective information on each drug in the national lists of essential drugs, which should be appropriate to the needs of consumers and all levels of professional personnel involved with drug procurement and use, was underscored in WHO Technical Report Series, No. 615. Comprehensive drug information sheets - similar to the model presented in that report - which are approved by responsible national drug regulatory agencies are required as a condition of the licensing of products in several countries; abstracts of information from these sources that are relevant to drugs of international interest are included in Drug Information - a bulletin issued periodically by WHO in the form of a mimeographed document.

Having regard to the rapid development of this source of national documentation and to the widely varying conditions under which drugs are licensed and used in different countries, the Expert Committee felt that many problems of harmonization would arise in adapting this information in a comprehensive manner to subserve international needs. It was therefore considered that the transfer of information on essential drugs generated at the international level should focus predominantly on the rationale for the selection and the recommended use of each drug included in the model list.

Finally, the Expert Committee also stressed the importance of an exchange of information with the pharmaceutical industry on the drugs included in the model list, in order to ensure the availability of raw materials and of the most appropriate and economic pharmaceutical forms to meet the health needs of developing countries.

Quality assurance and regulatory control

The objective of quality assurance in pharmaceutical supply systems is to ascertain that all pharmaceutical products have adequate quality characteristics "built-in" in their process of manufacture and retain them through all the stages of distribution until they reach the patient. At various levels of production and distribution specific quality assurance procedures have to be applied, and for years the World Health Organization has been advising member States on the most appropriate approaches to achieve these aims. Although these recommendations are addressed to all countries, many of them are directed towards specific situations in developing countries.

Quality of the drugs can only be assured if the testing of the finished products is supplemented by production control at all stages of manufacture, including the testing of starting materials, proper storage of raw materials and semi-fabricated products, and continuous monitoring of each step of the manufacturing process.

The implementation of drug legislation is a highly complex matter, especially for developing countries where only limited and scattered financial, technological and human resources are available. In many developing countries the following could be considered as priority areas requiring appropriate legislation:

(a) Drug control

- procedures for the selection of essential drugs for health needs and strengthening of quality control of these products
- use of generic names whenever possible
- registration (or licensing) of pharmaceutical products on the basis of evaluated information obtained through regional agreement or from international organizations, particularly WHO.

(b) Development of drug production

- incentives for development of local production
- regulation of foreign investment in the pharmaceutical sector
- adequate regulation of elements of industrial property, such as patents and trade names

(c) Pharmaceutical distribution

- regulations on multisource international procurement (e.g. tenders), especially in the public sector
- legal definition of drug distribution within the country, giving clear responsibility to each level of the network, i.e. central, regional, subregional and peripheral

At the manufacturing stage, the aim is to ensure that all manufacturers, domestic or foreign, comply with good manufacturing practices. At the distribution level, the aim is to ensure that the quality of all drugs, particularly those imported, has been properly assessed and that adequate control exists over transportation, storage and rotation of drug supplies, including customs, warehouses, and other places where drugs are stored befores they reach their final user. This also includes procedures for the recall of unsatisfactory drugs when considered necessary.

A government analytical drug control laboratory carries out tests and assays required to establish whether the products in question conform to the claimed specification.

Under certain circumstances technical co-operation among developing countries (TCDC) may be useful, grouping countries to pool their efforts towards the institution of a regional central laboratory. In other circumstances, a fully established national drug control laboratory can serve neighbouring countries.

Quality specifications comprise a set of properly selected standards with associated methods of analysis that may be used to assess the integrity of drugs and starting materials. Adequate specifications for a particular drug in its dosage forms for identity, purity, strength, performance and other characteristics are a pre-requisite for the assurance that all batches of a drug have uniform quality. Quality can then be achieved by strict adherence to the specifications. Thus, once the efficacy and safety of a drug have been established, the quality of products available in commerce is judged by the conformity to specifications.

A pharmacopoeia includes normally the general methodology of testing monographs on pharmaceutical raw materials, including active and inactive ingredients of pharmaceutical products, and in many cases, monographs on the most widely used dosage forms to make the test methodology more uniform, as well as to decrease the unnecessary diversity of quality requirements for identical drugs.

Besides the question of identification of pharmaceutical substances, another problem of great importance, especially in tropical countries, is the degradation of pharmaceuticals during storage and transportation. The expiry date which sometimes serves as an adequate safeguard in temperate countries, may be misleading in tropical areas even when adequate containers are provided. Simplified analytical techniques to ensure the absence of gross degradation should be developed. Such tests should be introduced first of all for essential drugs used in general health care.

The quality of pharmaceutical products depends on correct performance of all manufacturing operations and must be "built-in" from the beginning of the manufacturing process. The main approach to maintain desired quality levels in intermediate and final products is quality control of production. The principles for quality control procedures that should be applied to drug manufacturing practices are designated "Good Practices in the Manufacture and Quality Control of Drugs". These principles are general guides which, whenever necessary, may be adapted to meet national needs, provided the established standards of drug quality are still achieved. Manufacturing establishments with a limited product line need only utilize relevant parts of the requirements.

The WHO Certification Scheme on the Quality of Pharmaceutical Products

Moving in International Commerce, when used, will provide valuable data required for pharmaceutical quality assessment of imported drugs.

The Scheme permits the control authorities of importing countries to obtain information on imported drugs. In this context, it is desirable to obtain similar information relative to the quality and manufacturing conditions of imported drugs as could be obtained if the same product were manufactured locally. The extent of information required may vary depending on the category of the drug and the control procedure in the importing country.

Every drug product has a finite shelf-life during which its quality may be expected to remain within acceptable limits. Improper storage conditions can seriously shorten the shelf-life. There is a need, therefore, to ensure especially in adverse climatic conditions, that during all phases of distribution adequate conditions of storage, such as light, temperature and humidity, are maintained and permissible periods of storage and expiration date are not exceeded.

Drug evaluation, safety and efficacy

One important drug policy issue concerns the evaluation of the risk/benefit ratio of new drugs to be introduced on the market. Regulatory demands for the introduction of new medicinal products are becoming stricter in many countries and the question has been raised as to whether, in some respects, they are becoming too stringent, leading to excessive delay in the introduction of some new compounds and, in the longer term, to curtailment of drug research and development.

On the other hand, the assessment of the long-term safety of new compounds still presents intractable difficulties, since the occasional fallibility of animal models as indicators of hazards to man and the difficulty of identifying infrequent and delayed adverse reactions to drugs already in widespread use are problems that resist routine investigational approaches.

As a result of the rapid development of drug epidemiology and the demands now placed upon many of the highly-evolved drug regulatory authorities to review all currently available drugs within their jurisdiction, the safety and efficacy of many established drugs are now subject to re-examination. As a result, the terms under which many of these drugs are registered in various countries have been modified and others

have been withdrawn from use. Different national authorities have, however, sometimes taken divergent action over identical drugs either as a result of disparate assessments of the available evidence, or because of varying risk/benefit considerations arising from differing disease patterns from country to country. These cases highlight a need for rapid and efficient transfer of technical information underlying important decisions between national drug regulatory authorities in both the developed and the developing world. Current procedures for the evaluation of the safety and efficacy of drugs, although greatly improved during the past decade, still leave much to be desired. Therefore, no matter how well performed, it is necessary to emphasize that there can be no guarantee of absolute safety. The WHO Scientific Group on Principles of Pre-Clinical Testing of Drug Safety summarized the situation as follows: "The administration of biologically active substances to human beings must always be accompanied by some element of risk that cannot be avoided by the most careful and exhaustive scientific study of the drug before it is introduced.

Any situation, including the introduction of new drugs, that may involve some hazard to an individual or to a community should be judged from an evaluation of the balance between benefit and risk. This balance implies that the therapeutic aims of the drug be considered in relation to the possible risks demonstrated by the early studies to be discussed in this report. Two aspects of the intended therapeutic effects of the drug must be considered. First and most important, the laboratory studies of the efficacy of the drug must be such as to demonstrate that there is a real therapeutic interest sufficient to justify the trial of the drug in man. Second, the intended purpose of the drug is also important, since the possibility of toxic effects may be acceptable in a drug for treatment of a severe disease whereas the same potential toxic effects would prevent the trial of a drug for treatment of a relatively minor condition or one for which other drugs of greater safety already exist."

Drug information

The success achieved by modern marketing techniques in fostering the demand for pharmaceutical products has raised problems from the public health point of view in serving mainly to increase drug consumption without necessarily meeting health needs. For example, in countries where

a number of similar or identical products are marketed under different brand names each manufacturing company promotes its own products, incurring considerable marketing expenses because of the close competition; these expenses are from the public health point of view unnecessary and are finally supported by the consumers or the national health services or health insurance schemes.

International non-proprietary names, INN (Generic names)

The role of trademarks and generic names in medicine shows that generic names have become an established fact that the need to identify each pharmaceutical substance by a unique and universally available generic or non-proprietary name does not have to be further demonstrated.

After acceptance of the Procedure, the General Principles for Guidance in Devising International Non-proprietary Names for Pharmaceutical Substances were established. As mentioned earlier, these guiding principles are regularly revised.

INNs are no longer solely used to identify a substance but also more and more for what is referred to as generic marketing. In this context it is interesting to note that in a resolution on the "Action Programme on Essential Drugs" adopted by the last World Health Assembly, member States are urged to enact legislation as appropriate covering amongst other things the use of prescription of drugs by generic names.

III. WORLD CONSUMPTION OF PHARMACEUTICALS

Consumption of pharmaceuticals has shown an upward trend since the beginning of the twentieth century. The discovery of chemotherapeutic drugs and of a broad variety of therapeutic agents to treat a number of pathologic conditions, and the launching of medicaments utilized to treat or to cure a large number of ailments produced a strong impact on the world consumption of pharmaceuticals. Many diseases for which there was no cure or even alleviation until recently can now be treated through the utilization of a broad range of drugs mainly dispensed by medical prescription. The extensive use of analgesics and of an assortment of miscellaneous preparations providing symptomatic relief to the common cold increased the consumption of pharmaceuticals to levels perhaps beyond the health requirements of the world population.

In developed countries ethical drugs are not purchased out of choice by the consumer but only at the criteria of the physicians' selection of a particular drug. The growth of consumption of ethical drugs in developed countries depends wholly on the promotion impact of the pharmaceutical industry on the medical profession. The trend of consumption of non-ethical pharmaceuticals in industrialized countries grew parallel to the sizable advertising outlay displayed by pharmaceutical companies. Nevertheless, in a number of developing countries the situation is otherwise. Since a broad range of ethical drugs is dispensed over the counter, the growth of the consumption of a number of ethical pharmaceuticals does not reflect the morbidity pattern of many developing countries but the collateral demand for a variety of drugs which grew under the umbrella of self-medication. Therefore, the increase in consumption of pharmaceuticals in developing countries could well be attributed to the fact discussed above in addition to the population increase, the improvement of the socio-economic level of the people and the expansion of public health systems. It must be emphasized, nonetheless, that large segments of the population in developing countries have no access to essential drugs so far.

The environment of the pharmaceutical industry is under complex interactions of economic constraints such as the economic environment in the form of increasing demand for social services, recession, unemployment, inflation and devaluation. The political environment with its concern over high cost of social services and health care systems also gravitates over the environment of the pharmaceutical industry. The commercial environment is also influenced by Government constraints on prices and promotion aimed at lowering the costs. All these affect the demand for pharmaceuticals. The technological environment likewise outweighs the pharmaceutical industry in a way of reduction in funds available for innovation.

a) Situation in developed and developing countries

Consumption of pharmaceuticals is closely bound to socio-economic components. This reality spells out the disparity between developed and developing countries as regards the consumption of drugs.

The consumption of drugs in industrialized countries in 1978 in terms of value represented 82.45 per cent of world pharmaceutical consumption. Consumption of medicaments in developed countries is mainly confined to the public system of health insurance. A large segment of the supply of medicines is channelled through the private network of pharmacies from which prescription drugs and over-the-counter preparations are purchased by the consumer. It should be observed, nevertheless, that a large ratio of the cost of medicines purchased directly by the consumer in sales outlets in developed countries is subjected to partial reimbursement through the private system of health insurance. This procedure assists to increase the drugs' consumption. Another large source of consumption of medicaments in developed countries is the system of medicare which at the beginning supplied drugs free of charge or at a minimum cost. The pharmaceutical industry has largely become the only private sector supplier of medicaments in health care delivery in industrialized countries. It could be stated, therefore, that consumers in developed countries have unrestricted access to pharmaceutical requirements.

Consumption of drugs in the developing world unlike the industrialized countries is attached to a number of constitutents besided the economic constraints such as availability and high cost of finished dosage forms. The share of developing countries on world consumption of pharmaceuticals in 1973 was about 13 per cent. Their share, nevertheless increased in 1978 to 17.55 per cent of world drugs consumption.

The outstanding growth in consumption of pharmaceuticals in the Latin American region is illustrated by its contribution to the achievement of the ten largest market economies in 1978 which attained a total value of US$ 34.55 billion representing 60.7 per cent of world pharmaceutical consumption. Argentina contributed with US$ 971 million and Brazil with US$ 1.37 billion equivalent to a combined 4.1 per cent share on the ten leading market economies consumption. The share of the Latin American region of world pharmaceutical consumption in 1978 was 7.81 per cent which is slightly above the region of Developing Asia whose share in 1978 was 6.89 per cent of world drug consumption. Consumption of medicaments in Least Developed Africa in 1978 only represented 2.33 per cent of world consumption.

b) Structure of world consumption by therapeutic classes

The structure of world consumption of pharmaceuticals by therapeutic classes presents a similar pattern in a large number of countries. As a matter of fact, the incidence of a broad variety of microbial diseases leads the path to place the antimicrobials, and out of this group, the antibiotics , as the leader in world consumption. The latter shares 13 per cent in the world market and 19.5 per cent in developing countries.

The second largest therapeutic class identified is the group of analgesic-antipyretics that share 9.4 per cent of world demand for medicinals. This class is formed by a wide range of over-the-counter preparations in whose compos. one or two ingredients are common to the majority of the existing formulations. In this class the share of developing countries is about 6.4 per cent of total drug consumption.

The third largest group pertains to vitamin preparations which share 5.8 per cent of total worldwide consumption. A large segment of this group refers to ascorbic acid whose world consumption dimensions is measured by the thousands of tons. Under this therapeutic class the share of developing countries is about 12.3 per cent of world total consumption. The following therapeutic class, the hormones, share 4.3 per cent of world market and about same share in developing countries. The main component of this group is contraceptives.

When analyzing the morbidity pattern in developing countries in conjunction with the prescription habits and the impact of promotion the sequence of antimicrobials and analgesic/antipyretics lead the

consumption pattern in almost every region of the world. In some areas the latter group is identified mostly as cough and cold preparations. From the former two leading groups down, the true morbidity patterns come to be reflected in the consumption pattern in developing countries. The therapeutic classes of skin disease products, anthelmintic drugs and anti-inflammatory agents follow the sequence of therapeutic classes of broad use in developing countries.

Although anti-hypertensives, diuretics, psychotropic drugs and antidiabetic products are of common use in all regions of the world, their utilization is more frequent in the industrialized countries.

c) World consumption of essential bulk drugs

World consumption of a selection of essential drugs in 1977 in terms of value was US$ 994.4 million. Projected consumption of those drugs for 1980 and 1985 has been estimated at UD$ 1.36 billion and US$ 2.10 billion respectively. The share of developing countries in 1977 in terms of weight, ranges from 0.84 per cent for ascorbic acid to 40 per cent for ampicillin as compared with world consumption of said drugs. Consumption of acetyl salicylic acid and paracetamol in developing countries is 28 per cent and 20 per cent of world's total. Consumption of the latter drugs illustrates the impact of sizable promotional campaigns of the private sector aimed to expand the demand for analgesics and antipyretics in developing countries.

Consumption of chloroquine corresponds in almost 99 per cent to developing countries which reflects that the incidence of malaria is confined to the developing world. The low consumption of ascorbic acid of less than one per cent in a universe of 36.000 tons estimated for 1980 exemplifies the potential consumption for this medicament in developing countries in the years to come.

The dimensions of world bulk consumption of the 26 essential drugs for 1980 in terms of value could be estimated in US$ 1.55 billion. This estimated value should be considered only as indicator because drug consumption in many areas of the least developed countries has not even attained the level of primary health care as regards large segments of the population.

d) Share of the public sector

The share of the public sector in developing countries with respect to consumption of pharmaceuticals varies among developing regions. In state-planned economies in the developing world they can be exemplified by Cuba where the public sector wholly shares the consumption of medicaments. With respect to the developing countries market economies, the data is fragmented and therefore it is difficult to come up to an accurate assessment of the portion of consumption of drugs channelled through the public sector. Furthermore, neither the acquisition nor the distribution of medicinals is centralized in most developing countries and therefore consumption of medicaments through the public sector is carried out through a number of agencies within the public sector.

As regards the Latin American region the following examples will illustrate the participation of the public sector as compared to the countries' consumption of medicinals. In Peru the programme of basic medicaments shared about 14 per cent of country's consumption in 1977. A similar programme was established by the public sector in Mexico where the social security shares about 28 per cent of national consumption of drugs. It is estimated that consumption of medicaments by the public sector in Argentina represented about 6.26 per cent of the country's consumption in pharmaceuticals in 1977. Public sector in Venezuela shares about 32 per cent of medicinals consumption. In Uruguay the public sector shares 16 per cent in pharmaceutical consumption.

With respect to the Asian region it could be illustrated by India where the public sector shares 24.3 per cent of pharmaceutical consumption. In Thailand the contribution of the public sector to pharmaceutical consumption in 1977 in terms of value was US$ 17 million. Total acquisition of drugs and surgical equipment in Singapore in 1977 by the public health sector was valued in US$ 6.2 million. Public sector consumption of medicaments in Malaysia[5/] in 1978 amounted to US$ 38 million, and 27 per cent of this consumption corresponded to antimicrobials.

5/ United Nations Asian and Pacific Development Institute (UNAPDI): Malaysia country case study 1980

Tables 9 to 20 show the consumption of pharmaceuticals in developed and developing regions:

Table 9 - Production and Trade in Pharmaceutical Products in Selected Countries 1973

Table 10 - Value of Worldwide Consumption of Pharmaceuticals and Share of Developing Countries

Table 11 - Percentage Contribution to Combined Total Sales of the Five Leading Pharmaceutical Companies in Selected Therapeutic Categories in 1973

Table 12 - Consumption of a Selection of Essential Bulk Drugs

Table 13 - World Consumption of Pharmaceuticals by Regions

Table 14 - Consumption of Pharmaceuticals in Ten Largest Market Economies in 1978

Table 15 - Pharmaceutical Consumption in the Americas

Table 16 - Pharmaceutical Consumption in Europe

Table 17 - Pharmaceutical Consumption in Asia

Table 18 - Pharmaceutical Consumption in Africa and Oceania

Table 19 - Consumption of Essential Bulk Drugs in India 1978-1979

Table 20 - Average Share of Consumption of Main Therapeutic Groups at Retail Level

IV. STATUS OF THE PHARMACEUTICAL INDUSTRY

The medicaments supplied by the pharmaceutical industry have been an outstanding component in the progress of medicine. An improved quality of life with reduction in sickness or suffering has been the impact produced by the discovery of new drugs. **Although it is fully recognized that the research arms of the large pharmaceutical houses have been a source of new medicaments a number of drugs whose discovery has been attributed to the industry were infact derived from discoveries which had been made by academic and non-industrial scientists.**

The pharmaceutical industry is remarkable in the sense that it is marked by an uncommon degree of market penetration symbolized by the concentration of production within a small number of industrialized countries. Some developing countries feel, however, that a small number of pharmaceutical companies dominate the drugs price scheme in the whole world. The concentration of production within a few developed countries illustrate the dependence of developing countries on a few developed countries.

Transnational corporations emerged as the major producers and suppliers of drugs since early this century. They are congregated in a few market economies, and through subsidiaries, joint ventures and affiliated companies they share a large segment of drug production in developing countries. In contrast to this situation the developing world accounts for a small proportion of the global output of pharmaceutical production.

Sizable efforts spent in research and development by pharmaceutical houses have been designed to produce drugs of large consumer market potential or those to conform with consumption and disease pattern of industrialized countries. It could be admitted therefore, that the pharmaceutical industry did not orient the research efforts towards a number of diseases prevalent in many developing countries.

As it was observed in the preface of this study production of pharmaceuticals could be arranged in two main groups: formulation of finished dosage forms and production of bulk drugs. World-wide statistical data separating production of pharmaceuticals in either group is unpublished. Therefore an attempt to quantify the share of world production in formulated and bulk drugs appears unfeasible at this time. Hence, the remarks on production will only aim to illustrate the disparity between local production in regions of the developing world as compared to industrialized countries.

a) World production of pharmaceuticals

World production of pharmaceuticals attained the value of US$ 64.52 billion in 1977. The share of developing countries was only 11.43 per cent of world-wide production. The share by developing regions was 5.61 per cent for Asia, 5.26 per cent for Latin America and about 0.56 per cent corresponded to Africa.

The largest concentration of pharmaceutical production is placed in Western Europe where 32.84 per cent of the world's pharmaceutical production is accomplished, followed by South America with 22.26 per cent and by the centrally planned economies with 19.10 per cent.

It is undeniable that the pharmaceutical industry has attained an outstanding growth in two regions of the developing world, Asia and Latin America. It is believed, however, that a large share in pharmaceutical production in developing countries is alloted by pharmaceutical enterprises whose target has always been the obtention of high returns on investments and the utilization of tactics to consolidate the market control. It is stated that transnational pharmaceutical corporations exercise a power of predominance to safeguard the care of their monopolistic interest.

The growth of pharmaceutical production in the developing world as it has been stated above is illustrated by two regions: Latin America where the leading producing countries are Argentina, Brazil and Mexico, and Asia where India and South Korea exemplify the world's most advanced developing countries inproduction of pharmaceuticals. These four countries formulate close to 100 per cent of their medicaments requirements. A greater number of developing countries in South America meet with local production about 70 per cent of their formulation needs. Bolivia and Paraguay, nevertheless, formulate less than 50 per cent of their requirements.

Production of finished dosage forms in Central America and in the CARICOM[6/] countries still requires considerable improvement.

The outlook for expanding production of bulk drugs in Latin America is promising. Basic production of bulk drugs such as antibiotics, steroids and a number of synthetics is accomplished in the region although the latter are produced from imported intermediates. Value of the production of pharmaceuticals in the region in 1977 was about US $ 3.4 billion. Assuming that 10-30 per cent of the sales price of medicinals is represented by the cost of bulk drugs, then it could be estimated that US $ 340 million-1.02 billion illustrate the approximate value of bulk drugs contribution. This parameter, nevertheless, does not allow **the estimation of the value of the local production of the latter.**

In spite of the advancement of the industry of production of bulk drugs in Latin America the status of the pharmaceutical industry in this region is rather fragile since it depends to a great extent on imputs of imported intermediates. As long as developing countries fail to grant serious consideration to the manufacture of their essential drug requirements they will continue to maintain their dependency on imports from foreign sources.

The development and the growth of a backward integrated pharmaceutical industry is illustrated by India. Its finished dosage forms production value in 1978-79 was about US $ 1.3 billion. Production of bulk drugs meet 60 per cent of the country requirements. **The essential drugs identified by UNIDO are produced** in India except primaquine although some drugs are produced in insufficient quantities to meet the needs of the country.

Production of pharmaceuticals in developing Asia attained the value of US $ 3.62 billion in 1977 representing 5.61 per cent of world pharmaceutical production. **Indonesia, Pakistan, the Philippines and the Rep.of Korea formulate** close to 100 per cent of the domestic requirements. All other countries of developing Asia formulate about 30-60 per cent of national consumption. **A considerable improvement is foreseen** in the formulation output in this region with the increasing involvement of the public sector in pharmaceuticals' manufacturing.

6/ Caribbean Community

Basic production of a number of bulk drugs is undertaken in Indonesia, Pakistan, Rep. of Korea and Singapore. Bangladesh produces all its requirements of chloroquine phosphate. Basic production in Thailand is confined to small amounts of a synthetic antibiotic. It must be observed, nevertheless, that in most instances bulk drugs production in the region in inadequate to meet the domestic requirements.

The region of least developed Africa has remained stagnant as regards production of pharmaceuticals. It is believed that socio-economic components and colonialism have precluded this region to share the growth of the pharmaceutical industry as it ocurred in the two other regions of the developing world. Pharmaceutical production of Africa is negligible since its contribution to world-wide pharmaceutical production in 1977 was 0.56 per cent. Formulation of domestic requirements ranged in average 0-30 per cent of national requirements except for Egypt which formulates 80 per cent of the country's needs.

b) Contribution of multinational corporations

Multinational companies have made a valuable contribution to the discovery of new drugs of common use in modern medicine. Some 100 pharmaceutical houses supplied about 90 per cent of world shipments of pharmaceuticals valued US $ 48 million in 1977. Two thirds of this amount was supplied by 50 leading pharmaceutical companies in market economies.

Among the large pharmaceutical companies, United States based corporations are dominant in a number of companies and in sales achievement. F.R. of Germany and Switzerland rank second and third countries respectively.

Besides their sizable domestic operations, transnational corporations share an important segment in the production and consumption of drugs in developing countries. Whenever the size of the market warrants, multinationals enter developing countries with promotion and distribution outlets. Formulation operations have been established by multinationals' subsidiaries in a number of countries sometimes under the pressure of local legislation enforcing local manufacture. Basic production is mostly established by multinationals only in large consumer markets or in countries where the bulk drugs output could be exported to other consumer markets. Ten world leading pharmaceutical companies sell 37-98 per cent of the total output to markets outside the country headquarters.

As regards the three world leading countries producing pharmaceuticals, United States-based transnational corporations hold the largest share of the foreign-owned sector in Brazil, Canada, France, F.R.of Germany, Italy, Japan, Mexico, Spain and the United Kingdom. On the relatively small foreign share of the United States pharmaceutical market (about 16 per cent) over 75 per cent is held by Swiss pharmaceutical companies.

No one will deny the contribution made by transnational pharmaceutical companies in the development of new therapeutic weapons to combat disease. New drugs have greatly increased the social and economic well-being of most countries. Direct benefits from drug therapy can be measured in two areas: reduction in morbidity, and mortality, and contribution to economic productivity and savings in medical care expenses resulting from a more rapid cure of illness.

Sulfonamides and antibiotics cut the death rates from diseases such as rheumatic fever and childbed fever. The discovery of ethambutol, streptomycin, para-aminosalycylic acid, isoniazid and rifampicin reduced the mortality rates of tuberculosis. A large number of other ailments which can be prevented, treated or cured could also be exemplified. The industrialized countries and the developing countries as well have granted full credit to those institutions which one way or the other contributed to discover a variety of essential medicaments. It is regrettable nevertheless, that neither all types of medicaments are currently available to developing countries nor their cost of acquisition is at the reach of large segments of the population.

Transnational pharmaceutical corporations establish market dominion by investing sizable resources in promoting their brand-name pharmaceuticals to the medical profession or featuring the non-ethical products through the mass media. This strategy has led to proliferation of brand-name products.

The strongest point which permits the domination of transnational pharmaceutical corporations is rooted in the patent and brand-name systems. These barriers of entry into the pharmaceutical industry, and the main constraints to the growth of the pharmaceutical industry in some developing countries will be discussed in subsequent chapters of this study.

c) Share of developing countries (basic manufacture, formulations)

Production of pharmaceuticals in developing countries has been increasing at a rate far below the expectation of those countries. The share of developing countries in pharmaceutical manufacturing in 1977 was 11.4 per cent of world-wide pharmaceutical production. If it is assumed that a steady 15 per cent annual growth rate in constant monetary terms in production of pharmaceuticals in developing countries in a 20-year span is attained, the share of world-wide output would be only about 17 per cent which would be, however, far below the Lima target.

The largest geographical area with a concentration of pharmaceutical production in the developing world is in India but also of a large dimension in the Latin American region. The value of the combined overall pharmaceutical production of Argentina, Brazil and Mexico in 1973 was $ 1.160 million. As it has been stated elsewhere in this study there is no practical way to indentify what share of production values corresponds to bulk drugs, what share conforms to finished dosage forms and what amounts of raw materials are met by imports. Table 28 nevertheless shows a listing of essential bulk drugs produced in developing countries; their estimated annual output and cost were computed at average international market prices.

The developing regions of Latin America manufacture in average about 75 of the domestic requirements of finished dosage forms. The countries of the region in which basic production has not yet been established are fully dependent on imports to meet their manufacturing requirements. Foreign companies hold a large share in production of pharmaceuticals in this region. In spite of its advancement in pharmaceutical production its share in world-wide manufacturing of pharmaceuticals is only about 5.2 per cent.

The region of developing Asia ranks top in pharmaceutical production with 5.6 per cent of world-wide production. Excluding China and the least developed countries, the region produces about 65 per cent of its finished dosage forms for domestic requirements. The world's largest ampicillin plant established in a developing country is in operation in this region although the destination of most of its output is to developed countries.

With respect to basic production, India is a large producer of essential bulk drugs although production does not meet yet the domestic requirements. Pakistan produces about 50 per cent of the country's needs of benzylpenicillin. Pakistan is also a large exporter of santonin and ephedrine and a potential producer of morphine.

Indonesia is self-sufficient for its domestic requirements of quinine and it is the world's largest exporter of this drug. Indonesia produces rifampicin, ethambutol and diazepan derivatives in small quantities far below the country requirements and it is starting to produce tetracycline from imported crude base.

The share of least developed Africa on the world production of pharmaceuticals of less than one per cent is insignificant. A majority of African countries depend on imports of finished dosage forms to meet all their pharmaceutical requirements. Zaire and Guinea produce quinine which is exported in crude form. Basic production in Egypt is confined to a small assortment of drugs synthesized from imported late intermediates. As it has been cited in this study, Algeria is expected to enter antibiotics production in the near future.

In spite of the scant statistical data it has been explained in this study that current share of developing countries in pharmaceutical production is below reasonable levels and, therefore, a strategy must be formulated to augment their share in the production of essential drugs.

d) Production policies

The second half of the twentieth century has observed an outstanding growth of the pharmaceutical industry, thus providing a significant support to the progress and the development of modern medicine. This spectacular growth could be attributed in part to the expansion of public health programmes instituted in industrialized countries and to a lesser extent in the developing world. The total world pharmaceutical output in 1977 was about US $ 48 billion. Sixty-eight per cent of this total corresponded to the developed countries, 20 per cent to centrally planned economies and 12 per cent to the developing countries. The existing disparity is noticeable between developing countries and the rest of the world.

It has to be admitted that essential pharmaceuticals are unavailable in many developing countries, whereas in some regions of the developing world, their cost of acquisition is beyond the reach for many segments of the population. The burden of the pharmaceutical import bill of developing countries is far beyond their availability of hard currency. The establishment of domestic pharmaceutical industries in the developing countries, therefore, is a priority issue to which primary attention should be granted in order to provide medicines that local population can afford.

The dynamic role of UNIDO in the establishment of a modern pharmaceutical industry has been remarkable. In 1974, UNIDO had only one pharmaceutical project valued at US $ 90 thousand, while in 1979 UNIDO had about 50 projects representing a total value of US $ 10 million.

UNIDO's pharmaceutical projects have a two-fold significance. They are helpful to developing countries in the sense that they initiate manufacturing processes of a highly specialized and technology-based industry, and contribute to providing developing countries with high quality, low-priced essential drugs. The latter displays a profound social element since the expansion of programmes of health care could hardly be materialized without a fair supply of inexpensive medicaments.

The strong dependence of developing countries on imports of bulk drugs or finished dosage forms is being ameliorated thorough the broad programmes on the pharmaceutical industry under study by UNIDO or in the stage of implementation. Developing countries imported 51.8 per cent in pharmaceuticals whereas industrialized countries only imported 11.7 per cent and southern European countries 20.7 per cent.

UNIDO is assisting developing countries not only in the implementation of domestic pharmaceutical industries, but also in the issuance of drug policies, basic elements for the transfer of modern pharmaceutical technology, in the establishment of a system oriented to substitute some chemical raw materials by products from natural sources, such as the extracts from medicinal plants, and the concept of versatile multipurpose plants to synthesize a number of modern drugs of common use in developing countries. UNIDO has promoted a system aimed at attaining pharmaceutical self-sufficiency at sub-regional and regional levels. The strategy of UNIDO in respect of the establishment of a pharmaceutical industry in developing countries is firmly oriented towards backward integration to undertake chemical synthesis from intermediates and indigenous raw materials.

The strategy of establishing the basis for research and development in developing countries through the creation of Pharmaceutical Centres is another phase of the aims of UNIDO towards a compact system of technical co-operation among developing countries.

A broad range of project proposals suggested by UNIDO comprising all phases and stages in pharmaceutical production is as follows:

1. Formulation and packaging of finished dosage forms. The following countries have been listed by UNIDO for implementation of a primary pharmaceutical industry:

In Asia: Afghanistan, Bhutan, Bangladesh, Nepal, Sri Lanka, Vietnam, People's Republic of Yemen, Democratic Republic of Yemen

In Africa: Botswana, Burundi and Rwanda, Cameroon, Chad, Gambia, Niger, Sudan, Uganda and Upper Volta

In Latin America: Dominican Republic, El Salvador, Haiti, Honduras and Nicaragua

2. Basic production of bulk drugs from intermediates and establishment of multipurpose plants.

Countries selected for this activity are:

In Asia: Nepal

In Africa: Tanzania

3. Production of drugs from medicinal plants and from various natural resources.

Countries under consideration for this type of pharmaceutical activity are:

In Africa: Botswana, Burundi, Central African Empire, Cameroon, Guinea, Guinea-Bissau, Madagascar, Rwanda, Senegal, Zanzibar

In Asia: Afghanistan, Bhutan, Nepal, Thailand, Vietnam

In Latin America: Bolivia, Ecuador, Haiti, Honduras, Nicaragua

Three Pharmaceutical Development Centres are on the way to be established by UNIDO. A centre is being planned in Upper Volta, financed by the Belgian Government. Another centre will be implemented in India and another centre in Latin America for the Andean Group Countries, both under UNDP financing. UNIDO's plan calls for another centre to be established in Tanzania.

UNIDO's Pharmaceutical Unit is fully equipped to provide technical assistance to developing countries in respect of any matters related to development of pharmaceutical industries in the Third World.

e) The role of medicinal plants in the pharmaceutical industry

Higher plants have been one of the main sources of medicines since the very beginning of human civilisation almost in all parts of the world. It is because of this reason that folk medicine derived more than 90% of their drugs from higher plants. As a result of screening carried out by scientists, a number of plant drugs used in traditional medicine have been adopted in modern medicine during the 19th and 20th centuries. In spite of the fact that there has been considerable development in synthetic drug chemistry during the last four decades, plants still constitute one of the major sources of medicine, in both the developing as well as developed countries.

According to an estimate, 25% of all the prescriptions issued in the United States every year contain one or more drugs from plants. American public pays each year more than 3 billion dollars for the cost of drugs solely derived from plants (calculated on the over-the-counter price).

In the absence of sufficient statistical information, an assessment of the world market for medicinal plants and their derivatives is not possible. However, the developed countries have been the major importers and users of them and the total imports of such products into the OECD countries, gives a rough indication of the international market for this product 1/. The value of imports of plants seeds, flowers and parts of the plant primarily used in perfumery, pharmacy of for insecticidal or fungicidal purpose, etc., into OECD countries had increased from $ 52.9 m. in 1967 to $ 71.2 m. in 1971 and to $ 217 m. in 1976. The principal botanical drugs that have been finding a good market in these countries are: Aconite, Aloes, Ammi, Belladona, Benzoin, Buchu, Cinchona, Dioscorea, Digitalis, Ephedra, Ergot, Ginseng, Hyoscamus, Hydratis, Ipecac, Liquorice, Opium, Papain, Podophyllum, Psyllium, Pyrethrum, Rauwolfia, Rhubarb, Senna, Strammonium, Valerian, Vinca, etc. Developing countries have been leading suppliers of medicinal plants. They have been the sole producers and exporters of a number of plants that do not grow elsewhere, e.g. cinchona, ipecacuanha and rauwolfia species. In the case of other medicinal plants such as camomile and liquorice, which also occur elsewhere but which are difficult

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1/ Seminar on export potential, Export Promotion Council, India, 1980.

to obtain in sufficient quantities from traditional suppliers owning to manpower scarcity and rising production costs, developing countries are increasingly providing new sources of supply. Since medicinal plants in high demand may be grown in developing countries some of which possess arable land and manpower resources permitting them to produce and sell at competitive prices, a further increase may be expected in the developing countries' share in exports of medicinal plants on the world markets.

Because of its large area and variation in climate and soil, India is one of the few countries where most of the plants used in modern medicine can be cultivated in one or another region of the country. It is because of this reason, India is one of the countries which has a prosperous medicinal plants industry with an annual turnover of more than US$ 125 million supplying crude drugs as well as finished products to the entire world.

The large-scale cultivation of medicinal plants for profit, however, depends on careful consideration of a number of factors, because the value of a medicinal plant depends on its active principle content and not on it luxurious growth, which makes it somewhat different from the principles of production of agricultural crops. It is also often found that the same plant grown in different localities differs widely in its medicinal value ; for this reason, medicinal plants collected from different regions are found to differ in quality. Several factors, such as soils, rainfall, altitude, method of cultivation, time of collection, storage, marketing, etc. and maintenance of the farm as well as research and development play an important part for commercial success of large scale cultivation.

Having considered to some extent the world trade and cultivation of medicinal plants, it would be worthwhile going into some details of the world trade in the derivatives active principles of medicinal plants like vegetable saps/extracts, enzymes, alkaloids, hormones and glycosides.

In 1976 USA, F.R. Germany, UK, France, Switzerland and Japan, which are considered the world's leaders in pharmaceuticals, had a total import of medicinal plants of US $ 163 million but an export of only US $ 63 million. Estimated total local production is equal to or slightly less than local consumption. There is about US $ 90 - 100 milliom worth of medicinal plants which provide the pharmaceutical industry with extraction of purified or pure active principles. Switzerland offers an illustrative example: in 1976 the import of medicinal plants accounted for US $ 5,1 m. and alkaloids for

US $ 9.7 m. with a total sum of US $ 14.8 m. whereas the export of medicinal plants was US $ 1.6 m. and alkaloids US $ 162.8 m., totalled US $ 164.4 m., i.e. the value of the export of this item has increased over 10 fold by the processing the medicinal plants.

Dealing with the exports of derivatives/active principles of medicinal plants by the six countries France, F.R. Germany, Japan, Switzerland, UK and USA totalled US $ 752.5 m., the major exporter being F.R. Germany with US $ 251.5 m., followed by Switzerland with US $ 207.8 m. and the USA with US $ 140.7 m. The major item of export was alkaloids US $ 324.6 m., followed by hormones with US $ 234.4 m. and vegetable saps/extracts US $ 119 m., Switzerland was the largest exporter of any single group of items mentioned above, her exports in respect of alkaloids being US $ 162.8 m.

Another aspect of the medicinal plants is the extent and the way in which they are used in developed and developing countries. In developed countries the medicinal plants are mainly used in purified forms, as pure alkaloids and glycosides, etc., by processing the plant material, whereas in developing countries the medicinal plants, owing to the lack of appropriate technology, are used as such or as simple unstable extracts which generallly means inaccurate dosage.

It should also be pointed out that in developing countries, on an average 15 - 20% (maximumm) of the population can afford "western medicine", while the rest of the population use the tradicional medicine with its simple preparations.

Several research stations and laboratories in developing countries are working on the extraction procedures for medicinal plants. In many cases this means a duplication of what is already done in developed countries. A direct transfer of technology is therefore highly recommended.

Although considerable progress has been made during the last 30 years there is an urgent need for intensifying research and development and organizing both internal and external marketing facilities so as to increase the future production of medicinal plants and their products. Major emphasis will have to be laid to chalk out a strategy in which drugs are not exported in crude form, but they are processed inside the production country and only finished products are allowed to be exported this would not only provide job opportunities to the people in the rural areas, but would also increase the export earnings of developing countries.

f) Trade, distribution and technological development in pharmaceuticals[8]

Developing countries depend on import of pharmaceuticals from developed countries, since their domestic production is very limited. Some 50 - 60 transnational drug corporations account for the bulk of the world pharmaceutical output. By virtue of their large sizes, considerable research and development activities, extensive promotional and marketing efforts and the protection afforded by the industrial property system, particularly patents and trade marks, these corporations possess an exceedingly high degree of market power.

Developing countries can counter the economic and technical strength of these corporations by formulating an integrated national pharmaceutical policy package which would first reduce their import bill by 50 per cent or more and in the longer run strengthen their technological capacity in this vital sector.

From 1968 to 1973, developing countries more than doubled their drug imports bill from US $ 777 million to US $ 1,566 million. Since then the average annual growth rate in the imports has been in the region of 15 to 17 per cent. At this rate of increase the import bill of these countries will exceed US $ 9 billion in 1985.

Assuming the total import bill for the developing countries is about US $ 9 billion in 1985 a rational procurement policy would immediately bring about a saving of more than US $ 4 million. This saving could be utilised to import more pharmaceuticals to cover a larger per cent of the population and to finance the investments that developing countries would wish to undertake for the production of pharmaceuticals, for training of personnel and for establishing research and development and technological capacity.

The major elements of a new policy framework would include: i) marketing and distribution of pharmaceuticals; ii) revision of the industrial property system and iii) transfer and development of technology.

8/ Contributed by UNCTAD.

i) Marketing and distribution of drugs:

Centralised procurement agency

There is inadequate appreciation that it is within the power of developing countries to formulate new policies, which, when implemented, would enable them to reduce their import bills by as much as one third or more, simply by entering into a bulk purchasing system. For example Sri Lanka and Guyana were able to reduce their import bills by 30 - 40 per cent by pooled procurement. Several other developing countries have now established national centralised procurement agencies.

The major objectives of pooled procurement system are to ensure a steady supply of high quality drugs at the lowest prices obtainable in the world market and their delivery at specified times. The system necessitates the preparation of a list of the required drugs in their generic names, their quality specifications and quantities wanted and 'shopping around' internationally by means of open tender.

The establishment of a centralised procurement agency could be phased, starting with public sector requirements and increasingly covering the whole spectrum of import requirements of the country including raw materials for the private sector.

Co-operative regional pooled procurement

The total drug requirements of small developing countries are too small to take advantage of the economies of scale by just centralising their procurement system at the national level. A way of solving their problem would be for such countries to pool their drug purchases at subregional and regional levels.

The Caribbean Community (CARICOM) started its pooled procurement programme in 1977. The members of the South Pacific Bureau for Economic Cooperation (SPEC) are investigating the possibility of pooled bulk purchase of drugs.

Marketing and distribution

Most medical practitioners in developing countries have very limited access to objective information on drugs and therapeutics. They depend to a very great extent on information supplied by the industry.

There is, at present, heavy promotional activity by the private pharmaceutical industry directed towards the practising doctor which strongly influences the latter's prescribing habits.

An adequate system of marketing and distribution should take effective measures to provide objective information on drugs and therapeutics. All information given by the private sector must be monitored and controlled. National formulary committees could provide these services.

ii) Revision of the industrial property system

The role of patents is of great significance in the pharmaceutical industry which is now perhaps the only major industry which depends on patents to protect its innovations. Almost 99 per cent of the pharmaceutical patents granted by developing countries are owned by transnationals. None of these are exploited in their countries but are used to acquire import monopoly, and to prevent the import of cheaper products from alternative sources.

Trademarks (brand names) have become a source of market power in the pharmaceutical industry perhaps of greater importance than patents. Patents have a finite life but brand names last for all time and have a restrictive effect on the development of the pharmaceutical industry in developing countries.

A critical analysis of the economic, commercial and developmental aspects of the industrial property system as it operates in the developing countries reveals that the existing system has a detrimental effect on the growth and development of the pharmaceutical sector in these countries.

A fundamental assessment and revision of the industrial property system as an instrument of policy in the interest of developing countries is urgently needed. Appropriate policies on patents and trademarks in the pharmaceutical sector depend very much on the specific features of the sector in each country the main variables being the degree of local manufacturing, the participation of foreign subsidiaries and local firms and the purchasing system adopted by the public sector.

Many developing and some developed countries have already attempted to modify their national laws on patents and trademarks. Several studies made by the UNCTAD secretariat have dealt with the impact of the industrial property system, particularly patents and trademarks, on the technological development of developing countries. From the country experiences and UNCTAD studies it could be observed that the following options are open to developing countries:

Patents

a) Exclude both pharmaceutical products and processes from grant of patents;

b) As a minimum first step grant process patents only, but provide adequate safeguards aimed at ensuring satisfactory working of the patented invention. These safeguards would be:

   i) specify that importation does not constitute working of the patent;

   ii) provide for an expeditious system of compulsory licensing;

   iii) use forfeiture or revocation of the patent on specific grounds;

   iv) shorten the duration of the patent and use it to ensure satisfactory working of the patented invention.

Trademarks

a) Withdraw brand name protection to pharmaceuticals and replace the use of brand names by generic names;

b) Grant brand name protection but include adequate safeguards in the trade mark legislation;

   i) provision for the revocation of the trade mark, or for compulsory licensing;

   ii) suitable tax on trade marks based on economic criteria;

   iii) regulate the licensing of foreign owned trademarks.

iii) Transfer and development of technology

Acquisition of technology

Developing countries have acquired pharmaceutical technology in one of several ways. At one end of the spectrum is direct foreign investment

which supplies the various elements of technology as a package leaving little room for local participation. At the other end of the spectrum is the public sector enterprise which attempts to acquire the various technological elements from different sources at most advantageous terms, conditions and costs. Between these two extremes a number of mixed forms, essentially consisting of joint ventures have evolved ranging from nearly absolute control by foreign enterprises to an increasing degree of ownership and control by the national enteprises.

Control of technology transfer

In an effort to promote industrialisation, developing countries introduced protective tariffs and offered various incentives to new industries. Transnational drug corporations exploited the situation to establish affiliates, subsidiaries and branches in many developing countries for the final processing of drugs. The parent firms exported raw materials to their subsidiaries at very high prices and nowhere else was the opportunity greater for this practice of transfer pricing.

As the knowledge about the high incidence of transfer pricing and high level of profit began to be known, some developing countries initiated a movement towards developing their own independant national industry through technology transfer. Such initiatives were faced with formidable obstacles. To begin with, the transnationals were not prepared to establish any kind of pharmaceutical industry in developing countries without ensuring control of it. It is only in the very recent period, particularly in countries like India, Egypt, etc., that greater attention began to be paid to transfer of technology agreements.

In the negotiations of these transfer agreements, it soon became obvious that the licensing of patents, trademarks and know-how was burdened with several restrictive conditions. They are, among others: restrictions on volume of production, domestic sale and export; tying of the supply of raw materials, intermediates, spare parts and capital goods; excessive royalties and know-how fees; payment of royalties on unexploited patents; transfer pricing; contribution to domestic technological capabilities; training local personnel; use and processing of domestic resources; automatic grant back clauses for the results of R and D undertaken by the licensee; horizontal transfer of technology, not to mention strengthening of the technological capacities of these countries.

The problems connected with health in general and the critical role of pharmaceuticals in particular are such that attention could now be given to devising a code on trade, distribution and transfer and development of technology in pharmaceuticals.

Technology planning in the pharmaceutical sector

To devise a technology plan, a country, irrespective of its size and level of development, should first attempt to formulate an integrated policy for health and pharmaceuticals. This would be greatly facilitated by preparing a plan for the development of pharmaceutical supplies. In many cases such a plan may have a modest begining, for example the final processing of drugs from imported raw materials. On the other hand a country may decide to begin the manufacture of raw materials. This would require a fairly large domestic market, a well-established chemical industry and technological infrastructure. It is here that pharmaceutical planning can extend beyond national frontiers and encompass the idea of collective technological self-reliance.

iv) New standards governing the trade and input of technology in the pharmaceutical sector

Of particular significance is to explore the possibility of a new set of criteria governing the trade and the import of technology in the pharmaceutical sector. Public authorities in developing countries have accepted full responsibility for the health of the population. The implementation of this policy is difficult when some 40 to 60 per cent of the health budgets have to be used in imported pharmaceuticals. Programmes under way are oriented towards meeting the health requirements for all the population before the end of the century. A part of the technological knowledge required for manufacture of pharmaceuticals is now in the public domain. The time is therefore ripe to use the lessons of experience of developing countries in working out new standards for the exchange of technologies among countries in this sector. Of particular relevance in this connexion is the experience gained by UNCTAD in international negotiations on a code of conduct on transfer of technology. Attention needs to be given to devising a code on trade, distribution and transfer and development of technology in pharmaceuticals.

g) World trade in pharmaceuticals

The market economy countries had a positive pharmaceutical trade balance of US $ 1.54 million in 1973, whereas developing countries had a trade deficit in pharmaceuticals valued at US $ 1.44 million. It is remarkable to observe, nevertheless, that the largest world trade value in pharmaceuticals is effectuated among industrialized countries. The largest number of pharmaceuticals' producers in the United States obtain their sales from the domestic market; three Swiss drug companies realize over 90 per cent of their sales abroad while three large Japanese drug producers only sell about 7 per cent of their output abroad.

Total exports of pharmaceuticals in 1973 represented about 0.9 per cent of world exports and 10 per cent of the total chemical exports. It can be assumed that the position is held at present.

Imports of pharmaceuticals by developing countries increased by 78.69 per cent between 1975-1977. Imports by the Latin American region increased about 9 per cent, meanwhile Asian imports increased by 67 per cent during the same period. The African region import bill in pharmaceuticals during 1977 was US $ 731 million or 39 per cent of the total imports of developing countries. Imports of pharmaceuticals in 1977 by developing countries was 39 per cent of total world imports. In the same year, trade balance of pharmaceuticals in developing countries was US $ 1,528 million and US $ 227 million in centrally planned economies. These figures illustrate the dependency of the pharmaceutical world imports from market economies.

The tables 21 to 25 illustrate the trend of pharmaceutical imports and exports in a number of developing countries;

Table 21 - Direction of pharmaceutical exports of large producer countries in 1973

Table 22 - Trend of pharmaceutical exports of major producers 1973

Table 23 - Imports of essential bulk drugs in five Asian developing countries

Table 24 - Imports of pharmaceutical products in selected African countries

Table 25 - Imports and exports of pharmaceuticals 1975-1977

The tables 26 to 30 relate to estimated worldwide production of pharmaceuticals for 1980-1990 in terms of value and share in pharmaceutical production by developing countries:

Table 26 - Estimated value of world production of pharmaceuticals for 1980, 1985, 1990

Table 27 - Production of pharmaceuticals and share by regions 1977

Table 28 - Production of a selection of essential bulk drugs 1977

Table 29 - Imports and Exports of pharmaceuticals (in millions of dollars)

Table 30 - Value of production for bulk drugs and formulations (in millions of dollars)

V. OVERVIEW OF THE PHARMACEUTICAL INDUSTRY[9/]

(a) Characteristics of the pharmaceutical industry

The pharmaceutical industry comprises 3 main market sectors: prescription medicines, over-the-counter preparations and animal health products. This chapter will focus attention on the prescription medicine sector.

There are two broad categories of manufacturers of prescription medicines, namely, the manufacturer of standard drugs and the research-based manufacturer of pharmaceutical specialties. The standard drug manufacturer performs the functions of manufacturing and selling standard drugs, namely, drugs which are not novel and have been established on the market for some time.

The research-based pharmaceutical manufacturer undertakes a closely integrated and interdependent complex of functions, which include, in addition to the manufacture and sale of drugs, the discovery and development of new drugs, the testing and evaluation of those drugs, the assembly of detailed scientific and clinical data about their properties and use, and the communication of those data to physicians and other health professionals. The research-based manufacturer may also manufacture and sell some standard drugs, but this does not usually constitute a significant part of his business.

The manufacture and preparation of modern drugs is undertaken in distinct phases. In all countries, the formulation of pharmaceutical dosage forms such as capsules, tablets, ointments and injectable dosage forms, is recognized as one constituent phase of pharmaceutical manufacture, and the packaging or repackaging of the finished pharmaceutical dosage forms is accepted as another. In some countries, the basic manufacture of pharmaceutical chemicals, by fermentation, synthesis or extraction, or by a combination of these processes, is also regarded as a constituent phase of pharmaceutical manufacture. In other countries it is treated as a chemical manufacturing operation, providing the raw materials for drug manufacture but not forming an integral part of it.

The facilities required for basic manufacture normally involve advanced technology and substantial capital investment, and production is normally semi-continuous or undertaken in relatively large batches. Accordingly, in this phase of manufacture, economy of scale is important.

9/ Contributed by the International Federation of Pharmaceutical Manufacturers Association (IFPMA).

In the formulation and packaging of pharmaceutical dosage forms, economy of scale is less important than it is with basic manufacture, although, even here, the economic benefits of long runs can have a significant effect on cost.

In all phases of manufacture, a sophisticated system of quality control is required, with careful attention being paid to the analysis and storage of raw materials, in-process quality checks and maintenance of detailed batch records. Again, in all phases and especially in the phases of pharmaceutical dosage form formulation and packaging, the "Good Manufacturing Practice" regulations laid down by the National Drug Regulatory Authorities on the basis of World Health Organization recommendations must be strictly observed.

(b) Pharmaceutical TNC's and market concentration in world pharmaceuticals

If only because of the high and increasing cost of research and development which can only be justified on an international as distinct from national scale of operations, nearly all the major pharmaceutical companies can be described as transnational corporations (TNC's). Another major characteristic of these pharmaceutical TNC's is that they are nearly all highly diversified with widely varied activities outside the pharmaceutical industry.

As an example of the contribution that these pharmaceutical TNC's have made to the innovatory process, it is estimated that the leading 20 pharmaceutical companies were spending some 80% of the total world expenditure in pharmaceutical research and development (R and D) in 1978.

However, in the total worldwide market for prescription drugs, the market is fragmented and the market ranking of individual companies is volatile. Taking five major pharmaceutical markets - **France, F.R.of Germany, Japan, France, UK and USA** of the leading five companies in each country only one company appears in as many as three of the lists and only two companies appear in two of the lists.

The largest pharmaceutical company in the world has little more than a 4% share of the total world market and the top twenty companies in the world account for well under half of the total world's market.

The degree of concentration in the pharmaceutical industry as a whole is low compared with other high-technology manufacturing industries. Thus in the world automobile industry, the largest manufacturer had an estimated

25% of the market in 1977 and the leading ten companies accounted for some 80% of the total. Similar higher concentrations of market share compared with the pharmaceutical industry, can be seen in other high-technology industries such as computers and aircraft manufacture.

(c) Research and development carried out by pharmaceutical TNC's and the international pharmaceutical industry and its relation to the disease patterns of developing countries

The research-based pharmaceutical manufacturers (which are usually but not always TNC's) in those industrialised countries which have free market systems have, during the past 40 years, been highly successful in innovation, and have proved themselves to be the best qualified instruments for the discovery and development of new drugs. The vast majority of new drugs which have become available during that period have been derived from research-based manufacturers in those countries. Academic research has been very successful in developing understanding and extending knowledge of biological processes and of the aetiology of disease.

The discovery and development of new drugs is a very difficult and risky entrepreneurial activity, which requires a large investment of money and effort expended over a long time-span, with no certainty of ultimate success. It is estiamted that the international pharmaceutical industry spent about US$ 4.5 Billion (N.B. 1 Billion = 1000 million) on research in 1978 and nearly all of this was spent by companies based in the United States, Western Europe and Japan.

The uncertainty of success results from the extreme unpredictability of behaviour of new compounds in animals and humans and is manifested in the very high attrition rate in the screening of compounds prepared in the course of research projects. For example, in 1970, member companies of the Pharmaceutical Manufacturers Association of the United States prepared, extracted or isolated 126,060 substances, while, in the same year, only 16 new compounds (which were, of course, derived from research conducted in previous years) actually reached the market. The degree of risk is magnified by the fact that it is not normally possible to tell whether an improved and marketable product will eventually emerge from a project until its closing stages, by which time a great deal of money and effort will have been invested in it.

The expense, complexity and difficulty of pharmaceutical R and D have increased steeply in the past 15 years, due partly to the increasing sophistication and elaboration of testing procedures, and partly to the actions of the drug regulatory authorities in expanding their demands for data. These authorities have also become increasingly reluctant to accept any risks of adverse reactions as the price for progress in the treatment of disease, and (in some countries) have been reluctant to accept the evidence of pre-clinical and/or clinical trials conducted elsewhere than in their own country, and have insisted on the costly duplication of those trials within their own borders.

Research carried out by the international pharmaceutical industry on such matters as heart disease, cancer and pneumonia is as applicable in the Third World as in developed countries. Extensive needs exist for such products as analgesics, major and minor tranquillizers, diuretics, anti-inflammatories and hormones (all of which are the subject of current industry research) in industrialised countries but also in many developing countries.

Nevertheless although most diseases such as tuberculosis, cross national boundaries, some are confined to, or are more prevalent in certain geographic regions and require specialised research. Many major diseases are endemic only in developing countries. These diseases, as well as new technologies to prevent or cure them, must be studied under the conditions and in the population in which they occur. Such efforts by the research-based pharmaceutical industry have resulted in numerous products to prevent or treat yellow-fever, malaria, smallpox, cholera, bubonic plague and many parasitic diseases which occur mainly in the less developed countries. As examples of what has been achieved in recent years, the following major products - all the result of pharmaceutical industry research, have been introduced for the treatment of tropical diseases:

-proguanil, pyrimethamine - for malaria

-niridazole, hycanthone, oxamniquine and, as the most recent example of current industry research activities, praziquantel - for schistosomiasis

-clofazimine, thiambutosine, acedapsone, rifampicin - for leprosy

amongst many others.

The research-based drug manufacturer normally relies on the sales of the products developed by him to help him recoup his expenses and provide him with a fair return on his investment in R and D. In the case of

tropical disease research however, it is difficult for the manufacturer to obtain this return on his investment, as the people who suffer from the disease are usually too poor to buy the drug themselves, and there may be no or inadequate local government funds to buy the drug for supply to them. The solution to this problem may lie in the channelling of official foreign aid funds into the purchase of drugs for use in the treatment of tropical diseases.

A similar problem exists in relation to vaccines, which play such an important role in the prevention of infectious diseases. Vaccines exist which are suitable for widespread use against measles, poliomyelitis, pertussis, diphtheria and tetanus. However there is a need for new vaccines to tackle the infectious diseases such as malaria that only exist in specific geographical areas. The problem here is that, in the vaccine field, it is difficult to find in the technology used, an invention which is both patentable and not so narrow in scope as to be easily avoidable. Both for these reasons and also because of the heavy potential problems on product liability manufacturers are reluctant to invest heavily in the development of new vaccines, as they know that, even if their development efforts are successful, the likelihood that they will be able to recoup their investment and earn a fair return on it will be small.

(d) World production and world trade in pharmaceuticals

There are over 10,000 pharmaceutical manufacturers in the world today, but it has been estimated by the Stanford Research Institute USA that only some 3,000 of these companies can be described as fully competent pharmaceutical manufacturers by global standards and probably no more than 200 of these companies can be described as significant international research-based companies. These figures do not take into account the many government owned pharmaceutical factories that exist in centrally-planned economy countries such as the USSR, Eastern Europe and the People's Republic of China.

These companies produce a wide variety of products, though the number of active substances they contain is relatively small ranging from 750 to 1200 in most developed countries.

The key statistics of worldwide pharmaceutical trade relate to consumption, production, exports and imports. No reliable statistics are available on these subjects for the following reasons:

Problems of definition:

In some countries sera and vaccines and/or veterinary products may be included or excluded from the quoted figures. A similar situation arises in the case of bulk sales of active substances. There are also problems of definition because of the inclusion or exclusion of OTC and proprietary medicines. In addition, trying to put these statistics into a common currency form provides additional problems because of violent foreign currency exchange variations that have occurred, especially over recent years.

However, an attempt has been made through the International Federation of Pharmaceutical Manufacturers Associations and its member associations, to arrive at reasonable trade estimates, based on US$ conversion, for each year in question, at manufacturers' price levels. This last factor is particularly important as many statistics quote sales at retail pharmacy levels which include distribution margins (often quite substantial) for wholesalers and pharmacies.

Based on these figures, it is estimated that 1972 and 1977 consumption figures amounted to US$ 33.5 and US$ 60 billion (excluding China) respectively. These totals were made up as follows:

	1972	1977
	in Billion $	
Developed "free market economy" countries	22.5	39
Centrally planned economy countries	7.0	12
Developing countries:		
Africa	0.5	1
Asia	1.5	4
Latin America	2.0	4
Total	33.5	60

There is some evidence to show that whilst pharmaceutical consumption in the 1970 s was increasing at the rate of over 10% p.a., this rate of increase is now slowing down to about 6.5% p.a.

Taking account of the fact that (excluding China) the population of developing countries in Africa, Asia and Latin America now constitutes well over half of the world's total population of 4 billion people, it is obvious that there is an unsatisfied need for pharmaceuticals in these countries. Africa alone, which has a current population of 472 Million

is clearly underserved as far as pharmaceuticals are concerned.

No country is entirely self-sufficient as far as pharmaceuticals are concerned. To illustrate this, even a market as large and sophisticated as the USA, currently (1980) imports pharmaceuticals at the rate of over $ 400 million p.a. The UK too, provides a typical example of a major pharmaceutical producing country where imports form a significant proportion of domestic pharmaceutical trade. See following table:

U.K.

Year	Exports	Imports
	in million £'s	
1979	650.8	256.9

Source: ABPI Annual Report 1979/1980.

The seven countries which have the highest positive trade balance (that is to say where pharmaceutical exports exceed imports)are as follows: **Denmark, France, Federal Republic of Germany, The Netherlands, Switzerland, UK and USA.**

It should be added that the fact that a country has a high figure of production does not necessarily mean that it is a large exporter. For instance, Japan which is the world's second largest manufacturer of pharmaceutical products does not appear amongst the seven major exporting countries which are as follows: **Italy, France, Federal Republic of Germany, The Netherlands, Switzerland, UK and USA.** A more recent development has been the appearance of such developing countries as India, **Malaysia, Rep.of Korea and Singapore** as significant pharmaceutical exporters.

The industry is therefore a truly international one as seen by both the manufacturers themselves and purchasers. The products are usually not bulky so they are easy to transport: the need for them is usually universal and finally, the companies that have made large investments in research and development and/or in capital intensive plants are anxious to ensure that their products reach as large a world market as possible in as short a time as possible.

VI. CONSTRAINTS ON THE GROWTH OF THE PHARMACEUTICAL INDUSTRY

The growth of the pharmaceutical industry in the developing world is hampered by a number of constraints. These constraints have been identified by UNIDO, and the developing countries have agreed that unless said constraints are removed, the possibilities of growth of the pharmaceutical industry are dim. The main obstacles to the development of the pharmaceutical industry are high cost and limited or non-availability bulk drugs, intermediates and raw materials; difficulties in securing modern technology adaptable to the environment of the recipient country; lack of highly qualified and trained personnel; inadequate infrastructure; scarcity of financing, available on terms and conditions suitable for the industry; and lack of well defined national policies to promote the growth of the industry.

It can be ascertained that the constraints impeding the growth of the pharmaceutical industry are not alike on all developing countries. It should be taken into account, therefore, that different constraints would be applicable depending on the stage of development attained by a developing country as regards the prevailing conditions of the pharmaceutical industry. In this context, UNIDO likewise has identified three main groups of countries: (a) developing countries with little or no pharmaceutical activity; (b) developing countries with installed facilities to formulate a number of drugs; (c) and developing countries with facilities to produce bulk drugs as well as to formulate finished dosage forms. With respect to the third group of developing countries, their main interest is to expand the magnitude of the bulk drugs produced from late or early intermediates. Hence, common constraints are the unavailability and the high cost of imported intermediates and the acceptable conditions under which technology transfer could be negotiated.

The main constraints decelerating the growth of the pharmaceutical industry in developing countries have been identified as follows:

- Price disparities
- High cost and availability of intermediates and raw materials
- Availability terms and conditions for transfer of technology and restrictive clauses in licensing agreements
- Lack of infrastructure and trained personnel
- Lack of national policies
- Inadequate regional co-operation

a) Price disparities

Price disparity is an obstacle to the growth of the pharmaceutical industry in developing countries. Developing countries feel that pharmaceutical houses based in industrialized countries have maintained unreasonably high prices with respect to bulk drugs, intermediates and other raw materials. According to them said attitude has proven to be very harmful to the economies of developing countries since financial resources of said countries, which could have been used to expand the health schemes in poor countries, have not only been wasted but they have assisted transnational pharmaceutical companies to effectuate indirect hard currency remittances and at times avoid local taxation in some cases. Furthermore, said price disparity has created utter confusion in the domestic pharmaceutical industry in developing countries. The scheme of price uncertainty brought into being by the industrialized countries placed in developing countries the dilemma to the latter in such a way that developing countries did not know either where to buy or from whom to buy their essential requirements at equitable prices in order to establish or to keep running their pharmaceutical industries. Price disparities had been monitored by several developing countries and they have reached the public to the extent that a number of developing countries have established regulations restricting imports of bulk drugs unless billing prices are at least equal to the lowest world market prices. This ceiling price policy, nevertheless, is not yet followed by a large number of developing countries and, therefore, price disparity continues

to exist to the detriment of the growth of the pharmaceutical industry in the developing world, thus constituting a serious constraint on the growth of the pharmaceutical industry.

b) Price and availability of intermediates and raw materials

The pharmaceutical industry in developing countries encounters other serious problems conflictive to its growth like for example, excessive proliferation of branded products promoted by the large pharmaceutical houses. This problem could be and should be overcome by enforcing a national list of essential drugs. This option and the advisability of establishing systems of central procurement have been discussed in another chapter of this study.

Various inquiries carried out in countries of developing regions lately have proven that a large disparity in prices of bulk drugs exists. Although the pharmaceutical companies based in industrialized countries are now more cautious after the incident which brought out the exorbitant billing price of chlordiazepoxide some time ago, price disparities of bulk drugs continue to exist. Overbilling in essential bulk drugs contributes to worsen the drain of foreign exchange resources of developing countries and therefore reduces the health expenditures budget and disminishes the health coverage within large segments of ailing population.

Price disparity is not only confined to the cost of bulk drugs. In Indonesia, diazepan is produced locally by two pharmaceutical companies from imported intermediates; however, there is a large discrepancy in prices of the two manufacturers producing the same bulk drug with identical standards of quality.

No price control on imported pharmaceutical intermediates exists in most developing countries. The range of synthetic drugs produced in developing countries by national producers from imported late intermediates is relatively small. Except for India and Rep. of Korea, a majority of the synthetics produced in the advanced developing countries is manufactured by affiliates of transnational pharmaceutical corporations. Thus the availability of intermediates and other raw materials is confined to a large exent, to the subsidiaries of the transnational corporations and the national wholly-owned firms which maintain close links with foreign pharmaceutical houses. Intermediates and other sophisticated raw

materials are not available either to small independent producers or to the public sector. When and if said intermediates are offered by pharmaceutical houses based in industrialized countries, the prices are so high that domestic basic production would be unfeasible due to the small margin between the cost of the intermediates and the international world market price of the bulk drug. Therefore developing countries feel that they are pushed into the dilemma of buying intermediates at unequitable prices and simultaneously to pay an unreasonable price for bulk drugs which jeopardize not only the budget limitations of the public health campaigns but also with all principles of sound marketing.

Developing countries therefore, have only one alternative to accelerate the growth of pharmaceutical industry: the elaboration of a price scheme encompassing essential bulk drugs and intermediates to make it feasible for a domestic basic production.

c) Industrial profiles

A study on the pharmaceutical industry could not be considered exhaustive unless industrial profiles are discussed. This is precisely why one preliminary cost breakdown and industrial profile of one essential drug has been embodied to this study as an illustration. (See Annex I) .This industrial profile has been worked out from data obtained from developing countries. It should be observed, nevertheless, that detailed industrial profiles provide the elements leading to demonstrate the rate of feasibility of bulk drug production in developing countries and show the break even point of a product and its rate of return with respect to the investment. In the model of an industrial profile included in this study, the cost of intermediates and other raw materials, utilities, direct and indirect labor, overhead, financial charges, etc. has been taken into account. Due to a lack of detailed data, some of the cost elements have been grouped under the caption of conversion cost. This schematic industrial profile aims to prove that with equitable prices for intermediates and other raw materials, developing countries are in a position to become engaged in basic production of a number of essential drugs.

Developing countries, therefore, expect to be able to work out more complete industrial profiles for all essential drugs when a second assesment of the pharmaceutical industry is undertaken in the near future. A preliminary layout for the preparation of an industrial profile is detailed below.

SCHEME FOR THE PREPARATION OF AN INDUSTRIAL PROFILE

PRODUCT

PRODUCTION CAPACITY

SCHEDULED PRODUCTION

INVESTMENT (Fixed)

- Land and preliminary ground work
- Construction
- Equipment and machinery
- Others

WORKING CAPITAL

- Inventory
- Receivables
- Cash and bank

RAW MATERIAL REQUIREMENTS

Description	Origin	Unit	Price	Quantity	Domestic Imported	Total Value
Other requirements						
Water						
Energy						
Fuel						
Containers						
Packaging						

Labour requirements	Skilled		Half-skilled		Non-skilled		
	No. of employees	Wages	No. of employees	Wages	No. of employees	Wages	Total value
Labour fixed							
Labour variable							

Total cost	Cost Fixed	Variable
Salaries, Wages, Social Charges		
Director's Fees		
Raw materials and other materials		
Other		
Rent		
Insurance		
Depreciation		
Selling Expenses		
Interest		
Taxes		
Others (Royalties, etc.)		
Total		

Production	Unit	Quantity
Break even point		
Return on investment		
Project is sensitive to		
- increase in cost of raw materials		
- increase in cost of utilities		
- increase in cost of labour		

Total Value

Value Income Total

d) Availability terms and conditions for transfer of technology; restrictive clauses in licencing agreements

Availability of technology is the main constraint that developing countries have to overcome when they establish a pharmaceutical industry to cope with their essential drug needs.

Technology has been defined as the science of the application of knowledge to practical purposes in particular fields. This definition is shallow and of general nature and probably does not identify precisely the true meaning of what technology represents with respect to the pharmaceutical industry. When considering the problems arisen around technology and its transfer at equitable terms several other conceptual matters which will be analyzed in this chapter will have to be taken into account, otherwise the precise thought of the importance of technology would not be clearly exposed.

Many attempts have been made to expedite the transfer of technology from industrialized countries to developing countries. The negotiation is under study of an International Code of Conduct on the Transfer of Technology which was submitted by Algeria on behalf of state members of the Group of 77. The proposal which is known as the "Pugwash Code" refers to an applicable law on technology transfer and settlement of disputes. So far, developing countries have failed in counting with a legal instrument providing technologies on equitable terms and conditions.

Transfer of technology is closely linked to licensing agreements which will be discussed further on in this study. The latter, however, include a number of concepts such as know-how, "franchise", proprietor, copyright, public domain and the like, all of which are frequently mentioned in the international law of industrial property system which defines the rights to establish patents and trademarks. It could be stated, therefore, that developing countries must become acquainted with the hindrances that each and every concept might present, when said countries give thought to start negotiations to acquire pharmaceutical technology.

As it has been stated in this chapter, agreements to amend the system of industrial property and move towards the adoption of an international code for the transfer of technology have not been reached.

Developing countries must exercise pressure on their government policy-makers and national institutions to obtain the abolishment of a system which endangers the establishment of a pharmaceutical industry in said countries. The legal environment in which technology transfer takes place should be weighed. The governments in developing countries should assist in the establishment of integrated policies for strengthening technological capacities. Industrialized countries must learn that there is a progressive technological transformation in the Third World.

Until now, the issues involved in the transfer and development of pharmaceutical technology have been a prerogative of transnational pharmaceutical corporations based in the industrialized countries. According to the developing countries, the persistent attitude of the large pharmaceutical houses hampered the growth of the pharmaceutical industry in the developing world.

Developing countries have always held a weak position in their attempts to negotiate modern pharmaceutical technologies. Developing countries are almost entirely buyers of pharmaceutical technologies and very rarely sellers. Furthermore, they are more dependent on external sources of new technical knowledge than developed countries. Pharmaceutical technology existing in developing countries was the same used in developed countries when subsidiaries were set up by firms based in industrialized countries.

The transfer of technology and the development of domestic technological capabilities are complementary phases of a sole process. The effective transfer of technology and its further absorption into the socio-economic system requires that developing countries create and develop their technological capabilities.

It has been stated elsewhere in this chapter that developing countries must learn to distinguish the terminology commonly used in licencing agreements for the use of patents and the transfer of technology, such as public domain, non-propietary, know-how or trade secrets.

Know-how licensing is the most common form of technology transfer. It is usually combined with patent rights but it differs in some significant aspects. Know-how and trade secrets are commonly used interchangeably. Know-how has been defined as the practical knowledge of how to do something

with smoothness and efficiency and with practical skill and expertise. Know-how is, therefore, the knowledge of a company to make, market, distribute or sell the company's products.

Briefly, secret know-how could be viewed as a type of exclusive property, like a patent, and its owner should be encouraged to share the knowledge with others. Know-how, unlike a patent, confers upon the one who enjoys it, a universal power to exclude others and its value is gone when the technology it encompasses is gained by the experience of others. However, it confers upon its possessor the exclusive, although perhaps temporary, right to utilize it.

A trade secret consists of any formula, pattern, devise or compilation of information which is used in one business, and which gives the opportunity to obtain an advantage over competitors who do not know or use it. A trade secret is said to be in the public domain only when it is generally known to the trade.

When intellectual property is within public domain it is free to be used. The patent rights on several essential drugs have expired and it is said that they are in public domain. It should be clarified, nevertheless, that public domain has different connotations within the context of patents, trademark, copyright and trade secret law. Patent laws function to keep things out of the public domain temporarily. Whether or not things are in or out of public domain and free or not free to be reproduced depends on a variety of legal concepts which include the patent law and other legislation existing in industrialized countries such as antimonopoly policy and statutes, the law of trademarks and the like.

The concepts"propietary"and"franchise"are often used in licencing agreements related to the pharmaceutical industry. The latter is a constitutional or statutory right or privilege, that is to say, the right granted to an individual or group to market a company's goods or services in a particular territory, whereas the former is one who has exclusive title to a thing or one who posseses the ownership of a thing in his own right. A licensee is an entity which seeks to acquire all the information on a process of a product, irrespective of the distinctions between trade secrets and non-propietary know-how.

Pharmaceutical technology has reached developing countries lately through:

- Foreign subsidiaries
- Joint ventures
- Payment of a lump sum

The best arrangement, so far, is thrcugh joint ventures.

The general scheme which includes restrictive clauses in the transfer of technology are described as follows:

1. Grant-back provisions	Requiring the acquiring party to transfer or grant back to the supplying party all improvements arising from the acquired technology on an exclusive basis without off-setting obligations from the supplying party.
2. Challenges to validity	Requiring recipient to refrain from challenging the validity of patents and other types of protection for inventions involved in the transfer of validity of other such grants claimed or obtained by the supplying party.
3. Exclusive dealing	Restriction on the freedom of the acquiring party to either sales, representation or manufacturing agreements relating to similar or competing technologies.
4. Restrictions on research	Restricting the acquiring party in undertaking R + D directed to absorbing and adapting the transferred technology.
5. Restrictions on use of personnel	Requiring the recipient to use personnel designated by the supplying party.
6. Price fixing	Clauses whereby the supplier of technology reserves the right to fix the prices of imported raw materials.

7.	Restrictions on adaptations	Prevent the recipient from adaptation of the imported technology to local conditions, or introducing innovations.
8.	Exclusive sales or representation agreements	Requiring the recipient to grant exclusive sales or representation rights to the supplying party.
9.	Tying arrangements	Requiring acceptance of additional technology not wanted by the acquiring party.
10.	Export restrictions	Restrictions which prevent or hinder export by means of territorial or quantitative limitations or prior approval for export prices of exportable products resulting from technology suppliers.
11.	Restrictions on publicity	
12.	Payment and other obligations after expiration of industrial rights	
13.	Restrictions after expiration of the agreements	
14.	Limitations on volume, scope and capacity of production	
15.	Use of quality control systems not needed or not wanted by the acquiring party	
16.	Requirements to provide equity or participate in management	
17.	Unlimited or unduly long duration of arrangements	
18.	Limitation upon use of technology already acquired	

Licence agreements acceptable to developing countries should omit any unequitable clauses which directly or indirectly might represent an obstacle to the growth of the pharmaceutical industry. Furthermore, they should not include limitations on the policy or activities of developing countries with respect to R + D efforts.

With respect to the strength in the position of the sellers of pharmaceutical technology, transnational corporations derive their strength from a combine of access to technology and managerial and logistical skills, i.e. their aptitude to conceive new products although said products do not always harmonize with the needs of developing countries. Unlike industrialized countries, the developing countries as technology buyers have often to confront the following constraints:

- Lack of ability to decide what to produce
- Lack of financial resources
- Lack of management ability
- Unavailability of some kinds of skilled personnel
- Lack of knowledge to purchase imported raw materials and other inputs
- Lack of domestic R + D

In negotiating agreements for technology transfer, the above stated constraints weaken the bargaining power of developing countries which is considerably diminished. Technology transfer envisaged by developing countries should contain a number of mutually acceptable contractual obligations, including those relative to monetary obligations, access to improvements, confidentiality, dispute settlement arrangements and applicable law, description of technology, quality standards and completeness of information.

The above stated explanations define the outstanding topics governing technology transfer as a whole, likewise they are applicable in many ways to the pharmaceutical industry. Nevertheless, the pharmaceutical industry being science intensive, a number of various components have to be taken into account when the search for technology in under consideration.

The establishment of a primary stage in pharmaceutical production in developing countries, that is, the formulation of finished dosage forms, exhibit a small number of constraints with respect of the acquisition of technology. This is true for countries of developing Asia and for Latin American countries. As regards other regions like least developed Africa, the situation is just the opposite. There exists a technology in some developing regions to produce compressed tablets. Nevertheless, if the granulation stage is not adequately undertaken, the final product would be

unsuitable for human consumption. If injectable solutions are not prepared by using the appropriate technology, the finished dosage forms could not be satisfactory for further medicinal use. Similar occurrances are applicable to other pharmaceutical forms.

A sophisticated pharmaceutical formulation technology needs the support of an adequate infrastructure such as control of quality, analytical chemistry and elements for bio-chemical assay and control of production and acceptable product shelf life. These components need specialized equipment ranging from spectrophotometry to laminar flow systems, as well as skilled manpower. A majority of these components and technology with respect of most of these constraints is available in developing regions of Asia and Latin America from national wholly-owned formulators. They were also made available to some developing countries through UNIDO.

The obstacles related to acquisition of modern technology for basic production of bulk drugs in developing countries are of a greater dimension. It has taken considerable efforts to tionals in developing countries in terms of time and financial resources to become engaged in basic production. Technology to produce a number of essential drugs, mainly ampicillin, in the Latin American region has been acquired from industrialized countries like Italy. These technologies have been acquired at equitable prices and terms by national pharmaceutical companies due to the strong negotiating power of the Latin American entrepeneurs. Said technologies have been improved by innovation and, therefore, at least three producers of ampicillin in the Latin American region are open to discuss transfer of technology to developing countries under fair terms and conditions. Acetyl salicylic acid is produced by nationals in two countries of this region and it could be assumed that technology to produce this drug is also suitable for transfer.

As regards the region of developing Asia it is of public domain that India produces most of the UNIDO essential drugs although some of them in quantities below the domestic requirements. This fact, nevertheless, is insignificant, because it is not the dimension of the production, but the ownership of technologies what interests developing countries and the possibilities of transfer.

Other constituents, nevertheless, have to be taken into account when transfer of technology is negotiated, i.e. whether or not the technology is modern so that the output of the production of synthetics is adequate and, therefore, the level of its production cost allows the establishment of a competitive price for the bulk drug.

It should be mentioned in this study that the yield of a strain in the fermentation industry is crucial. A developing country in Asia cannot produce antibiotics at competitive prices because the yield of strain is below standard and, therefore, its production cost is higher than its selling price. A productive strain could be purchased from a multinational company, however, but at an exceeding high price.

It cannot be assured that a developing country possesses technology to produce an essential drug by the simple reason that there is domestic production of said drug. What makes a technology feasible for transfer depends on who is the owner of a technology. Bangladesh produces all the domestic requirements of chloroquine phosphate through a multinational subsidiary. Therefore, neither Bangladesh owns a technology to produce chloroquine phosphate nor the country is in a position to transfer it to another developing country.

e) Patents

The industrial property system - patents and trade marks - is one of the main constituents of a strategy of domination used by the industrialized countries to deter the scarce resources of the developing world.

Developing countries strive to abolish or at least to revise the international system of industrial property with dim success so far. Nevertheless, Brazil and India have abolished the patent protection governing processes in the production of bulk drugs. Other developing countries may like to follow the same path. Trademarks, likewise, represent a big constraint on the growth of the pharmaceutical industry. Besides representing a financial burden, they are at present a key obstacle to the preparation of national drug lists and constitute an element of distortion which contributes to the stagnation of the pharmaceutical industry in developing countries.

A number of developing countries have endevoured to amend their legislation on patents and trademarks. According to developing countries, this was unfeasible because it has been impeded by a strong opposition guided by interests supported by transnational pharmaceutical corporations.

Developing countries believe that patent legislation is a unilateral contrivance which provides full protection to the holder and represents to the patentee a means to exploit the developing countries with no consideration to the public interest. Patents provide the patent holder with prerogatives such as the monopoly over the production, import and sale of the patented commodity. Developing countries should consider the implementation of policies restricting the excessive privileges granted to the patent holders, which in most instances are detrimental to the patentee, such as the duration of the patent and the numerous obligations of the patentee.

The large pharmaceutical houses have publicly expressed that the lack of patent protection would discourage industrialized countries to establish or to expand production facilities in the developing world. No one could prove, however, that said assumption is correct: transnational pharmaceutical corporations expanded their production facilities in Brazil after the abolishment of the process patents on pharmaceuticals in that country.

The present international system of industrial property as it is now applied by transnational pharmaceutical companies solely endeavours to maximize the private interest of the patent holder; furthermore, it does not contribute to create an environment where the domestic technological capabilities of developing countries could be developed.

Trademarks "per se" constitute a serious constraint on the growth of the pharmaceutical industry in developing countries. The consensus of developing countries is that trademarks should be abolished since they conflict with the establishment of a system of generic medicaments. However, in the event that the present system of trademarks continues to exist, developing countries should establish a ceiling on royalty payments for the use of foreign-owned trademarks. Payments between foreign affiliates and parent companies should not be allowed.

f) Infrastructure

The implmentation of a domestic pharmaceutical industry in developing countries requires a broad number of elements of infrastructure. A majority of the requirements of industrial components are also common to the chemical and allied industries.

The energy requirements of the industry of formulations are lower than the same constituents required for basic production of bulk drugs. Steam,

cooling systems and extremely low temperatures are common elements in many processes in basic production of bulk drugs; air filtration is common to most pharmaceutical production operations whereas room temperature and humidity control are commonplace to the production of finished dosage forms. Substantial amounts of water and heavy wastage take place more often in basic production of bulk drugs and requires adequate systems of sewage disposal.

Besides the essential industrial infrastructure components outlined above, developing countries should take into consideration that many bulk drugs production processes are continuous and therefore uninterrupted supply of water and energy are indispensable. Lacking any of said elements will create a major constraint on the establishment of pharmaceutical production in developing countries.

With respect to manpower, lack of skilled, semi-skilled , technical and managerial personnel likewise could put a serious constraint in setting a domestic pharmaceutical industry in the developing world.

g) Trained personnel

Domestic pharmaceutical production in developing countries cannot be conceived unless the availability of a reservoir of trained personnel could be ascertained. Requirements for trained personnel comprise from skilled and semi-skilled personnel to engineering, biochemical and bacteriological analysts, and a broad range of technicians with capabilities to absorb and to transmit pharmaceutical technology.

In developed countries 1-3 per cent of the entire population is qualified. In the larger developing countries the proportion is 0.4 per cent whereas in the smaller developing countries the proportion is below 0.1 per cent.

Data on the number graduating in particular disciplines in developing countries is unpublished. It could be assumed, nevertheless, that 50-60 per cent of graduates in science are chemists, biochemists or biological scientists, and 10-15 per cent of the graduates in engineering are chemical engineers. Thus qualified manpower appropriate to the needs of the pharmaceutical industry is available in larger developing countries. Lack of trained personnel is a major problem in the small developing countries where the pool of science graduates could be insignificant.

In most countries a small minority of qualified scientists is engaged in research and development. In industrialized countries the proportion is 5-10 per cent, whereas in some developing countries it is 1 per cent or even less.

The pharmaceutical industry requires large numbers of educated personnel. For the manufacture of bulk drugs a number of chemists and engineers, technicians and artisans is required. For formulation and packaging a smaller proportion of professionals is needed. The bulk of the labour force is semi-skilled workers. The activity of research and development requires a type of personnel that is hardly available in the smaller developing countries.

The constraint of lack of qualified personnel could be alleviated when the projected UNIDO Pharmaceutical Centres are established.

h) National policies

The Alma Ata Conference on Primary Health Care proclaimed that the health status of hundreds of millions of people in the developing world is unadmissible. Over one half of the world population does not receive adequate health care. In view of the unequal distribution of health resources among developing countries, the Conference called for a new approach in order to close the gap between the elites which have all the elements for health care and the large segments of marginal population with little or no access to primary health care.

The Conference appraised primary health care to be based on socially acceptable methods and technology made universally attained to individuals at a cost that the countries can afford to maintain.

The installment of a system of primary health care requires the adaptation of appropriate health technology that people can use and afford. This implies the availability of low-priced, high-quality essential drugs.

In order to lessen the situation in developing countries where large sectors of the world's population cannot reach the indispensable elements to provide minimum health care, an urgent international action might be required. By the turn of the century the systems of primary health care in developing countries will demand a concurrent development of the systems of pharmaceutical supply, including domestic pharmaceutical production adjusted to the requirements of the population.

When taking into account the main constituents of a system for supply of pharmaceuticals, it is evident that the issuance of national policies becomes imperative. The lack of national policies constitutes by itself a big constraint on the growth of the pharmaceutical industry in the developing world.

The outlay of drugs is much lower in absolute terms in developing countries than in developed countries, but is higher with respect to the total health budget. Therefore it is crucial to optimize the expenditures in drugs in developing countries. A wealth of resources is wasted in the acquisition of some expensive drugs which have no justification whatsoever in coping with the basic health needs of the population. This could only be avoided by developing a national policy to safeguard the interest of the population.

There is a need to ensure that essential drugs are available to developing countries at equitable prices and developing countries should encourage research and development to produce drugs adapted to the requirements of said countries. Until now most developing countries have not issued a national drug policy identifying all the components regarding domestic pharmaceutical production. National drug policies should include furthermore, criteria on topics like therapeutic equivalence of two or more drugs. This could assist in reducing the number of finished dosage forms in developing countries. National drug policies should regulate the development of drug production through incentives for the development of domestic production, regulation of foreign investment in the pharmaceutical sector and moderation of patent and adaptation of generic names.

i/ **Regional co-operation**

The lack of a scheme of regional co-operation has been identified as one of the main constraints that contributed to the stagnation of the pharmaceutical industry in developing countries.

Efforts have been made in regions of the developing world to create an efficient system of regional co-operation. Said tentatives could be exemplified by the creation of the Economic Commission for Latin America (ECLA) and the Economic and Social Commission for Asia and the Pacific (ESCAP), which have promoted projects of regional co-operation in that region. The Economic Community of West Africa (ECOWAS) is another body entitled to promote industrial co-operation in a region of Africa.

The most outstanding effort of industrial co-operation in the developing world, nevertheless, is exemplified by the Andean Group Countries (Bolivia, Colombia, Ecuador, Peru and Venezuela). The Andean Group aims at the establishment of a system of economic co-operation with emphasis on industrial development. Among the sectoral projects under study by the Andean Group, an ambitious pharmaceutical one is under consideration.

The establishment of regional co-operation would assist to remove some of the obstacles to the growth of the pharmaceutical industry as part of an overall scheme of co-ordinated industrial co-operation which has not been accomplished so far. If the developing countries are going to attain the 25 per cent share in pharmaceutical production output by the turn of the century the cost of imported technology would be huge to the extent that the developing economies could not stand the load. Furthermore, technological dependence would be augmented. Thus, the lack of regional co-operation illustrates a prim constraint to the development of a domestic pharmaceutical industry in the Third World.

Regional co-operation would assist developing countries in many ways to obtain better terms and conditions in the procurement of technology as well as to adopt or create technologies suitable to their domestic requirements. Channels of regional co-operation could be set among countries of similar levels of development. Lack of regional co-operation is also a serious obstacle to the growth of the industry when production schemes or economies of scale are envisaged.

Pooled purchasing of raw materials and free circulation of bulk drugs and finished dosage forms within co-operative regions will improve the viability of regional domestic production and offset a constraint to the growth of the pharmaceutical industry.

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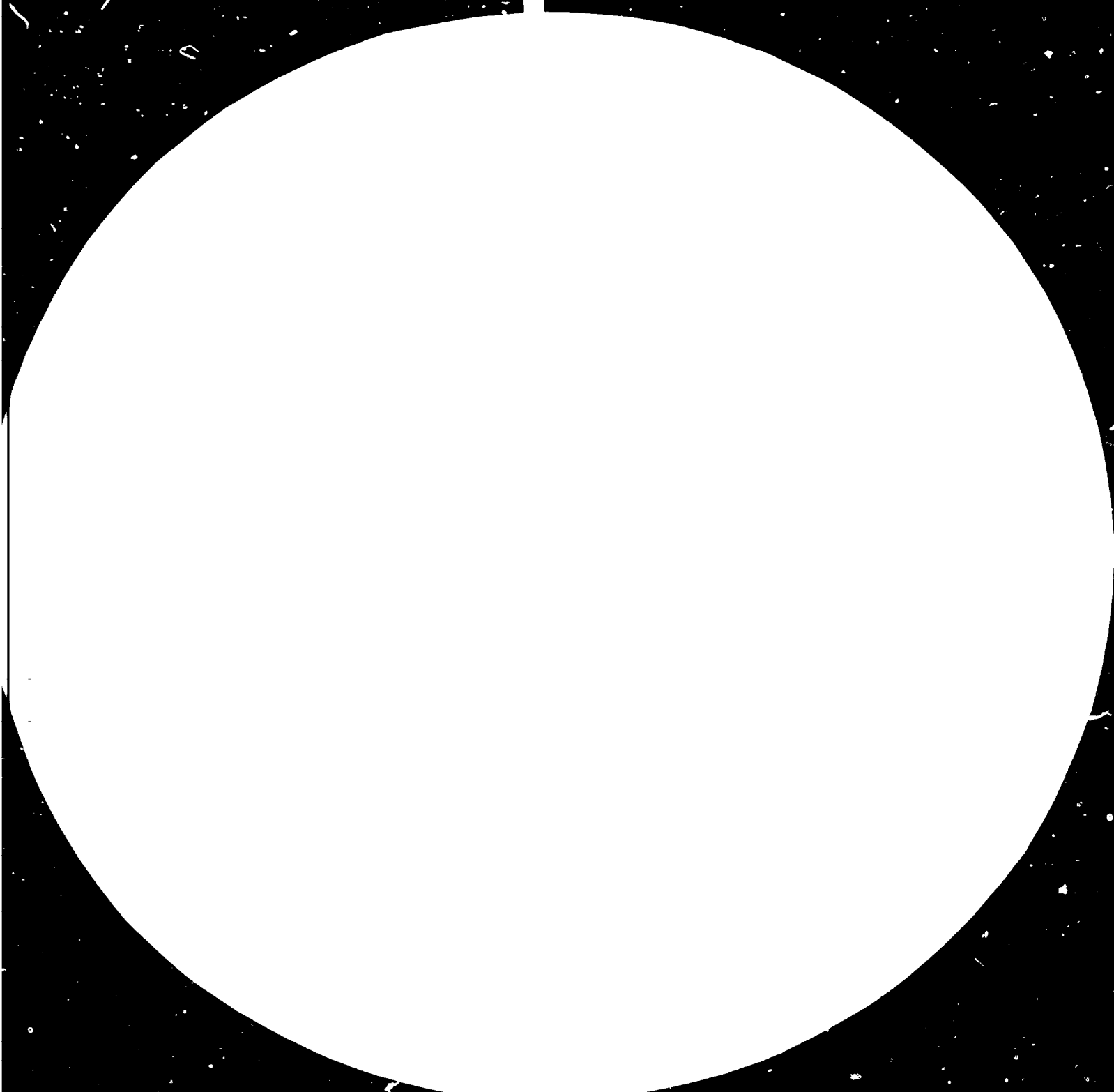

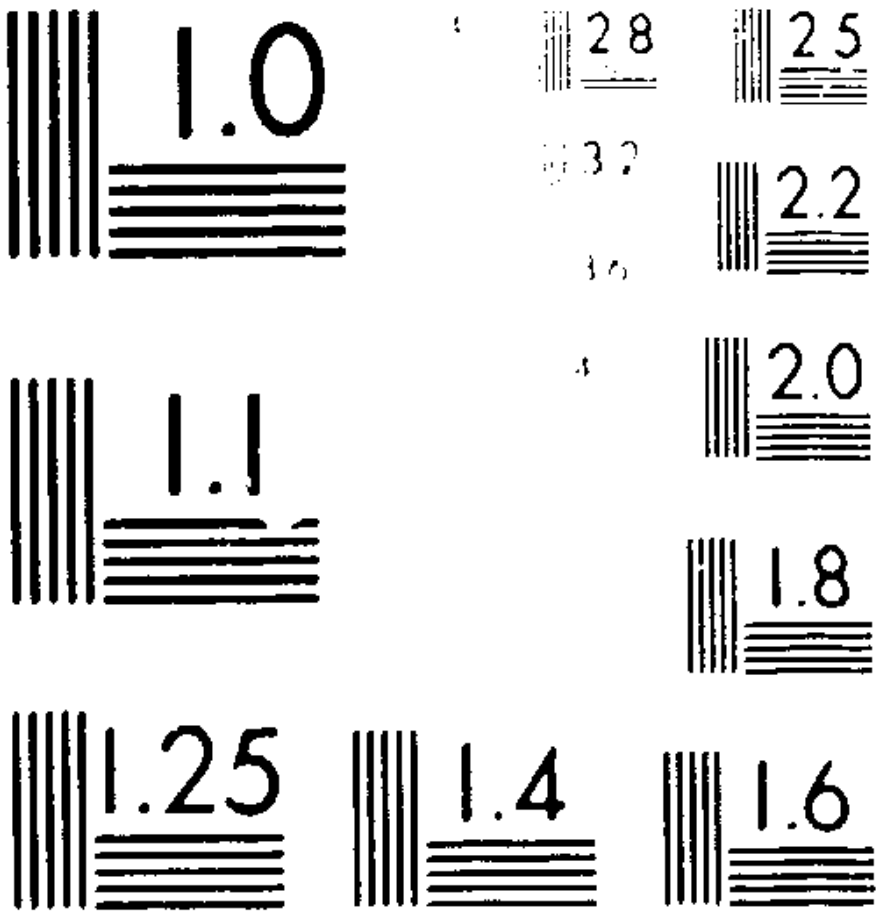
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VII. ROLE OF RESEARCH AND DEVELOPMENT IN THE DEVELOPMENT OF THE PHARMACEUTICAL INDUSTRY

Prontosil, the first so-called wonder drug, was discovered in 1935. Its chemotherapeutic efficacy and its essential component, the relatively non-toxic sulfanilamide, led to the realization of the goal of a specific chemotherapy, that is, the selective elimination of a parasite from a diseased animal without major damage to the host. Prontosil was effective in treating staphylococcal, streptococcal and other infections. Although the miracle drug Penicillin was discovered by Fleming in 1929, its germ-killing potentials were not recognized until Florey and Chain used it in humans. The development and efficacy of this antibiotic opened new avenues for the discovery of other therapeutic agents produced by micro-organisms such as streptomycin in 1946, chlortetracycline in 1948, chloramphenical in 1949 and oxytetracycline in 1950. Initially, the anti-bacterial action was the basis for the detection of an antibiotic and the selectivity of its toxicity was investigated subsequently. These investigations also produced important new substances and synthetic modifications of antibiotics to improve stability, distribution and antibacterial spectrum. The discovery of antibiotics has been of enormous impact on the progress of therapy and in preventive medicine. Besides, it has demonstrated the clear structural and metabolic differences existing between antibiotic-sensitive organisms and their mammaliar hosts.

The global investment in research and development relating to private industry and public sector institutions is estimated at US$ 150,000 million and involves 3 million scientists and engineers. Out of this, the total world expenditure on health research is estimated at 7 percent of the global total for research and development. The geographical distribution in both the cases reflects the world's distribution of economic power and research and development capability. In financial terms, 95 percent of all health research takes place in the economically developed countries, and is mainly geared to the

problems of these countries. However, the outcome of such research continues to have direct and practical implications on the solution of many of the health problems facing the people of the Third World. Drug development today is a highly complex and convoluted process requiring many years of continued collaborative effort between chemists, biologists, physicians and other experts in an empiric fashion.

a) Contribution by transnational corporations

On account of the large scale of the scientific, technological and financial resources necessary for developing new drugs, the discovery and development process is limited to a very small number of developed countries, essentially Japan, Western Europe and the USA. Further, the investments, manpower, apparatus and material needed for the discovery of new drugs as well as compliance with all the requirements and regulations regarding their efficacy and safety are so immense that only strong industrial organizations in these developed countries can provide them. There are about 20-25 large industrial laboratories throughout the world which spend between 50 and 200 million US dollars a year for drugs research. It is estimated that world wide, the industry spends about US$ 4.5 billion annually in the search for new drugs. In addition to these, there are a large number of medium-sized companies engaged in limited developmental research rather than basic research work. The research laboratories of large international organizations often maintain laboratories in several countries.

It has been stated that the development of a new drug today costs between US$ 50 and 100 million, which has to be spent over a period of 6-10 years.

On the average R and D expenditures of the largest German and Swiss drug manufacturers are around 15 percent, while leading American drug companies spend around 10 percent as illustrated below: 10/

10/ Trends and Prospects in Drug Research and Development, CIOMS 1977

	Current Rand D (as percent of drug sales)
All research based drug firms	10% ± 5%
Leading research based drug firms	15% ± 5%
Leading drugs (= main contributors to R + D)	20% ± 5%

No return has been included on the invested fixed assets

The ethical pharmaceutical industry through its primary emphasis on innovative research has been highly successful in discovering new drugs. The new therapies made enormous contributions to the control of diseases and there has been a profound impact on the health care systems.

The new products introductions in the Ethical Pharmaceutical Industry during the period 1950-1974 are shown in Table 31. The innovations by country of origin are indicated in Tables 32 and 33. In the course of the past 35 years, the great majority of significant new chemical entities (NCEs) were discovered and introduced by the pharmaceutical industry as can be seen from Table 34.

An analysis of drugs registered in the USA or UK since 1940 is given in Tables 35 to 42 and these drugs are listed below in descending order:

1. Agents intended to affect CNS
2. Antiinfective drugs
3. Cardiovascular drugs
4. Respiratory drugs
5. Anticancer drugs
6. Gastrointestinal drugs

Research and development related to drugs has become increasingly complex. Spiralling costs of industrial drug R + D, coupled with mounting costs of compliance with proliferating regulatory requirements tended to serve as disincentives to innovative research. There has, therefore, been a perceptible decline in the new drug introductions in the USA since 1964 by roughly 50 percent, creating a "drug lag" as can be seen from Table 43. It is obvious from Table 44 that the rate of

innovation reached a peak in the last half of 1950's when the annual average of basic new agents reached almost 40. This rate was approximately halved during the period 1961-65 in comparison with the previous period. The rate further declined by almost half again reaching a low of 12 during the period 1966-70. Current decreased efforts and discoveries will only be evident after ten years.

b) Research and development of transnational corporations oriented towards diseases prevalent in developing countries

Parasitic and infective diseases remain the major causes of morbidity and mortality in most of the tropics. One billion people including the poorest in the world, are still affected or exposed to a variety of parasitic and other infections. Many new drugs have been introduced to treat tropical diseases but the rate of development lags much behind the actual needs. Further, the progress of R + D in this area is relatively slow compared with the progress made in relation to drug development in other areas. The major constraints on the development of new drugs for tropical diseases include financial and other resources, socio-economic factors, limited scientific approaches and geographical dissociation. Only about 3 percent of expenditure of biomedical research throughout the world is directed to diseases afflicting the tropical countries. However, the people from the Third World do benefit from the general R + D effort being undertaken by industry in developed countries, since diseases such as hypertension and measles are not exclusive to tropics.

The programmes of the American pharmaceutical industry related to the health problems of the developing countries are long-standing involving investment of many millions of US dollars, although they form only a small component of the overall R + D effort of the industry. Very common illnesses such as influenza, the common cold, rheumatism and bacterial infectious diseases are as frequent in the developing world as in developed countries. Drugs effective against these diseases are, therefore, as important in the developing countries. Effective medications already exist for each of these diseases although some have limitations. New products have been forthcoming over the past several decades. A recent survey carried out by the PMA showed that twenty-one companies of the US pharmaceutical industry have been engaged in research

in one or more areas of tropical medicine. Another survey carried out among 15 research-oriented European pharmaceutical sompanies has shown that seven are actively engaged in research covering with varying emphasis all six tropical diseases emphasized by the WHO as can be seen from Table 45. These companies allocated a budget of abour US$ 40 million to this field of research and there is a trend to allocate larger sums in the future.

c) Research and development of public sector

There is appreciable research and development effort in the public sector in the developed as well as some of the developing countries. For example, during the fiscal year 1978, the agencies of three United States Departments - Health, Education and Welfare (National Institute of Health, Centre for disease control, and Bureau of biologicals), Defense (Army and Navy), and State (Agency for International Development) - spent an estimated US$ 31.5 million for research and development related to seven major tropical diseases plus an estimated US$ 33.7 million for eleven other disease categories which are also important health problems in developing countries. For the tropical diseases, intramural and extramural investigators devoted about 32 percent of their budgets to studies of pharmaceutical agents; for the other diseases, 11 percent of expenditures were related to drugs for chemoprophylaxis and/or treatment. However, there are some constraints on involvement of the government and research community in develcped countries toward development of pharmaceuticals for primary use in other parts of the world and these include legislative constraints, inadequate resources; restrictive attitudes and a lack of investigators committed to this effort in either the developing or the develcped world.

d) Research and development in developing countries

The resources and requirements for finding new drugs for diseases of the Third World are in no way different from those of drug discovery in general.

The R + D effort in developing countries can be broadly classified into three categories:

(i) R + D undertaken by developing countries

(ii) R + D undertaken by transnational corporations in developing countries

(iii) R + D promoted by international organizations

(i) R + D undertaken by developing countries

Based on the stage of development of the developing country and the infrastructure available, there is appreciable R + D effort undertaken by some of the developing countries themselves. Due to the inherent constraints involved in basic research work as described earlier, major effort in developing countries in this area is limited to developmental research rather than basic research work. India has a chain of scientific and industrial research laboratories in the public sector in addition to several R + D laboratories maintained by the private industry. Other countries in which R + D facilities are available in this field include Argentina, Bangladesh, Brazil, Egypt, Iraq, Rep. of Korea, Mexico and Pakistan. R + D on drugs based on medicinal plants is carried out in some of these countries.

(ii) R + D undertaken by transnational corporations in developing countries

As indicated earlier, the research departments of large international organizations often maintain laboratories in several countries, including some developing countries, such as Ciba/Geigy Research Centre near Bombay, India. There are also joint projects undertaken by the transnational corporations and the governments of developing countries for proper use of existing drugs. A recent survey showed that 1976 nationals of Third World countries comprising their own staffs and government nominees have been trained by 15 European companies during the past two years.

As regards new medicines that might be derived from local botanical sources, especially for the Third World, there are companies for instance in the Federal Republic of Germany, which specialized in this area. However, they experienced difficulty in isolating the active principle and standardizing the drug to provide government regulatory agencies with the requisite data on comparative efficacy of such drugs.

(iii) R + D promoted by international organizations

WHO identified six diseases as prime targets for major efforts in the developing countries as indicated below:

Malaria
Schistosomiasis
Filariasis
Leishmaniasis
Trypanosomiasis
Leprosy

WHO initiated a Special Programme for Research and Training in Tropical and Parasitic Diseases in 1976, with special reference to the above diseases. Several companies are co-operating with WHO in this programme. The Special Programme aims at the development of improved tools needed to control tropical diseases and strengthening of biomedical research capability in tropical countries. The Special Programme involves a network of national research centres throughout the world and technical collaboration among scientists from affected and non-endemic countries. In the USA the agencies of three US Departments - Health, Education and Welfare, Defense and State - spent about US$ 31.5 million during 1978 on research and development related to seven major tropical diseases in addition to about US$ 33.7 million for eleven other disease categories which are also important health problems in the Third World.

e) Outlook to the future

Despite stupendous progress made in various fields of therapeutics during the past thirty years, numerous and widespread diseases still lack effective treatment and these include parasitoses, tropical diseases, systemic mycoses and malignancies, artherosclerosis, rheumatic disorders, degenerative and auto-immune diseases. Fortunately, the rapid progress of science is providing new tools to meet these therapeutic needs, such as improved chemical and physical processes giving easy access to complicated molecules, new biochemical and molecular approaches for the pharmacologists, sophisticated equipment for metabolic and pharmacokinetic studies, increasing knowledge of the pathogenesis of diseases, improved methods for the toxicological screening. Phenomenal progress has been

achieved in the fields of engineering and technology. There has also been an improvement in many countries of the quality and quantity of trained scientists. Issues such as patent rights, profits, compliance with regulations involving international transfer of new drugs and vaccines, according to the industry, are inhibiting innovative research. The identification of these positive and negative factors and influencing them in a favourable way is bound to overcome the present phase of stagnation in drug research and provide benefit not just to a few economically privileged countries but to all mankind.

One possible way to remedy the situation is the development of a collaborative effort between the pharmaceutical industry, academia, and national and international bodies to facilitate the rational development of promising drugs. The involvement of local scientists and institutions in developing countries through strenthening institutional support and training opportunities is essential to increase national competance to tackle health problems of high national priority.

VIII. POLICY OPTIONS FOR DEVELOPING COUNTRIES

The establishment of appropriate policies in developing countries must be viewed by taking into account the requirements of medicinals of the said countries. After a careful examination of all the components the alternative should be to determine what share of the requirements for drugs is met by imports and what portion is covered by domestic production. The imports bill of pharmaceuticals in developing countries is growing at such a rhythm that there will come a time whereby the scarce exchange reserves of many impoverished countries will be inadequate to secure their minimum of medicinals' needs utilized in primary health care. An illustrative example shows that the value of pharmaceuticals imported by eleven African countries amounted to US$ 106 million in 1975. Therefore it has become imperative that developing countries give serious consideration to establish policies ruling the domestic production of pharmaceuticals.

The successful outcome of a pharmaceutical industry in developing countries is mostly dependent on the selection of the policies governing the establishment of a domestic pharmaceutical industry. In order to optimize the use of the national capabilities and that of all national resources, developing countries must identify the prerequisites for an integrated pharmaceutical industry. This poses the dilemma of selecting the policies that will prepare the ground to enter the area of domestic pharmaceutical production.

Among the policy options to be considered by developing countries preventive medicine is a crucial issue. Therefore, developing countries are urged to expand the production of biologicals such as vaccines, antitoxins and sera since these medicaments are important components in the national health scheme.

It should be clearly stated, however, that one of the options of developing countries must be to ascertain national policies leading to an improvement of their bargaining power; otherwise, their dependence

from industrialized countries would continue to delay the growth of their pharmaceutical industry.

It is well known that the broad use of high quality pharmaceuticals in a number of developing countries has been mainly a privilege of an urban elite while the lowest strata of the population very seldom had access to essential drugs. It is not a secret that developing countries have been paying exceedingly high prices for their supply of essential drugs in detriment of their financial resources.

High quality drugs at reasonable prices manufactured under fair contractual conditions should be the aim of developing countries in the decade of the 80 s. Developing countries will have to consider policy options that are hereby outlined in this chapter.

a) Essential drug list

Developing countries believe that they have been exploited by the pharmaceutical corporations which have flooded the developing countries with an excessive number of branded products, mostly during the last fifty years. The strategy of the large pharmaceutical houses using a costly system of professional promotion created a generation of strong supporters among the medical profession, which nowadays is perhaps the strongest ally defending the brand-name medicinal preparations. The latter concept is to some extent a corollary of the patent and industrial property system which now constitutes one of the main obstacles that hampers the growth of the pharmaceutical industry in developing countries.

The adoption of an essential drug list is one of the pre-conditions for a fruitful pharmaceutical industry in the developing world. The doubtful therapeutic superiority of brand-name medicaments vis-à-vis generic preparations has been already overcome since some transnational pharmaceuticals corporations are promoting in industrialized countries a parallel line of generics, not with the aim of providing inexpensive drugs for those which cannot afford to pay a higher price for medicaments, but with the object of increasing their gains by controlling larger segments of the markets. Countries that adopt a policy of generics should set up sound quality control systems.

The preparation of an essential drug list constitutes the correct approach to create a free market drug supply environment whereby high quality drugs at appropriate cost are put at the reach of the population. Furthermore, the sizable expenditures incurred by the private sector in promoting branded drugs could be channelled to some other activity of higher social content like research and development of new drugs for prevalent conditions in developing countries.

National drugs lists, however, cannot be generalized for all developing countries. The criteria for the selection of drugs has to conform to the country's health pattern. The most suitable to the conditions of the country must be chosen under the guidelines established by WHO. The enforcement of an essential drug list would not only aim the object of avoiding or reducing imports, but also it would assist to promote the formulation and packaging activity. Likewise, it would set the grounds for basic manufacturing.

These objectives, nevertheless, could only be accomplished if developing countries adopt a production policy by considering a number of factors such as the selection of the most appropriate production technology. It might be the case, however, that a selected drug could be substituted until a better and more suitable drug is identified. UNIDO could help to establish a list of drugs feasible for local manufacturing. An essential drug list, however, should aim to curtail the proliferation of drugs.

The establishment of an essential drug list in developing countries besides its favourable economic impact on the consumer, is an important element in the reduction of the number of medicaments. In an area of the developing world, the ASEAN countries, over forty thousand medicaments are marketed in the five countries. The strong opposition to the national drug list displayed by transnational corporations proves, perhaps, the rightfulness of the national drug list.

Two of the most advanced developing countries, Brazil and India, have adopted a national drug list although the scheme in the former is only implemented in the poorest areas of the country. Five African countries, Algeria, Chad, Egypt, Ethiopia and Guinea, have adopted national lists.

b) Centralized procurement

The aim of the establishment of centralized procurement in developing countries is to guarantee an uninterrupted supply of high quality bulk drugs at the lowest world market prices. Likewise the system of centralized buying could be extended to intermediates and to other elements utilized in pharmaceutical manufacturing. Although the system was successfully started by one country in Asia and reproduced in Africa and in the Middle East by some twelve countries, a country in the developed world, Norway, has tried to establish a similar state monopoly system.

Centralized procurement is a system directed to provide developing countries with a scheme to secure most effective ways of purchasing bulk drugs. The most desirable option for developing countries under this scheme is to rationalize a centralized purchasing system on a national or perhaps regional basis. In developing countries where the government lacks an adequate infrastructure, another option could be to engage a central wholesaler as a contractor for purchasing on tender basis, the total country annual drug requirements. Large orders could, therefore, provide lower prices for bulk drugs. Another option aimed to reduce cost of bulk drugs is to contract a private procurement function. This option has been followed by the Republic of Zaire.

Likewise centralized procurement could be established to encompass the bulk drug demand on a national basis or to provide the needs of the public sector alone.

A system of central procurement constitutes a method of economizing foreign currency reserves. It is more effective when local production is well established in developing countries.

Furthermore, as it has already been proven, a well organized system of procurement with knowledgeable professional advise would increase the bargaining power of developing countries.

Essential preconditions for the establishment of a centralized procurement system are the preparation of an essential drug list and the use of generic nomenclature. A well-maintained inventory control system is crucial to avoid bulk drugs shortages or spoilage of outdated materials.

c) Domestic production

Production of medicaments as discussed briefly in the introduction of this study could be summarized in three main stages: formulations and packaging of finished dosage forms, basic production of bulk drugs based on intermediates or by fermentation , and production of intermediates. The four most advanced developing countries in pharmaceutical producers, Argentina, Brazil, India and Mexico, undertake the first two stages in pharmaceutical production. A large number of developing countries in Latin America and also in Asia undertake the first level in pharmaceutical manufacturing, meanwhile, a majority of countries in Africa depend on imports of finished dosage forms to meet their medicaments' requirements.

The establishment of domestic pharmaceutical production is a means to reduce the cost of drugs and to promote industrial development in developing countries. It must be emphasized, nevertheless, that domestic production will not make developing countries 100 percent self-sufficient in their bulk drug supply unless a backward integrated industry could be established. There is no doubt, however, that the expansion of domestic production in developing countries will attain two main objectives: adequate bulk drugs supply and cost reduction of the finished dosage forms to the population.

The entry of the least developed countries into the first level of pharmaceutical production, that is, formulation, will imply the development of an adequate infrastructure otherwise the attainment of this stage would be rather difficult to be accomplished. Likewise, said developing countries should have to acquire formulation technology which is available in advanced countries of the three developing regions.

One of the best choices towards self-reliance in drug supply would be to mobilize developing countries to increase their local production of essential drugs linked to their disease patterns. Nevertheless, no matter how good local production could be still it might be dependent, to some extent, on external supply. Local production, as it has been stated in this paper, would minimize said dependence and, therefore, it should emphasize the importance to urge developing countries to obtain the highest yields from local production otherwise domestic production could not meet competitive prices. Local pharmaceutical production, furthermore, opens a broad range of opportunities to developing countries,

such as the use of indigenous materials from vegetal origin. About 30 percent of the medicaments comprising the WHO essential drugs list are derived from medicinal plants.

The dependence of developing countries from industrialized countries in terms of pharmaceutical supply could be expressed by the formula "giving-taking". Until now developing countries have been only taking from industrialized countries. A fair balance in "taking-giving" must be established.

Economies of scale do not have value, in absolute terms, when taking into account that once a system of regional co-operation is firmly established sizable production of many essential drugs could be undertaken. On the other hand, the establishment of a system of quality control is crucial in all stages of pharmaceutical manufacturing. It should be observed, nevertheless, that the quality control concept has been distorted by the large pharmaceutical houses in such a way that it had been misinterpreted as a hamper to the growth of the pharmaceutical industry in the developing world. Local production of drugs in developing countries must be accomplished within a rigid system of quality control.

In order to absorb foreign pharmaceutical technology and to build up local capabilities, local production, either by the private or the public sector should be undertaken in developing countries. Private or public sector joint ventures should be welcome provided that they are well composed and that the equity of the investment is fair to both parties. Formulations and packaging as well as basic production by both sectors should be encouraged so that the supply of all inputs could be ascertained and that the transfer of the capabilities is undertaken.

Governments in developing countries should become engaged in production of at least the most urgently needed essential drugs because said drugs constitute a daily need of the population. Furthermore, the profit margin of a number of essential drugs is rather narrow and, therefore, their production is not attractive to the private sector.

The governments of developing countries should endeavour to enforce a legislation to protect the national pharmaceutical industry, to establish a system of prices monitoring, to promote price control, and to avoid prices manipulation together with other constructive legislations.

A policy of overpricing leads to a monopoly and therefore ruins the national pharmaceutical industry in developing countries and prepares the ground for drugs' importation as the only alternative to secure their drug supply.

Developing countries should also be urged to pass legislation banning the exports of non-processed drugs.

In centrally planned economies health care is the privilege of the public sector. Those countries have excellent pharmaceutical facilities and 100 percent of their health needs are provided only by the State.

Production of biologicals is insufficient in most developing countries and could be solely undertaken by the public sector. Technology for production of biologicals could be obtained from WHO.

Domestic production based on intermediates has to take into account other elements such as availability and cost of technology which not always is at reach of most developing countries. It is fortunate that a number of national wholly-owned companies based in the most advanced developing countries in pharmaceutical production are in a position to negotiate and to transfer technology and know-how production of a number of essential drugs, presumably at fair price and conditions.

Economies of scale take place in production of bulk drugs from intermediates or by fermentation, nevertheless, in bulk drugs obtained by synthesis this principle is not applicable at full extent if it is taken into account that an assortment of bulk drugs could be economically produced in moderate quantities by multipurpose plants.

Although economies of scale cannot be ignored, developing countries feel that they have been often promoted by transnational pharmaceutical companies with the aim of decelerating the growth of basic production operations in the developing world.

It cannot be anticipated the upsurge of basic production of bulk drugs in each developing country in ten years time. Nevertheless, it can be reasonably expected that developing countries like Indonesia, which are already engaged in small scale of basic production, will increase their production yield to the level of domestic self-sufficiency and that other developing countries with technical capabilities and adequate infrastructure will give thought to escalate to higher levels

in pharmaceuticals manufacturing.

d) Engagement of the public sector in the production of essential drugs

As already indicated, an illustrative list of essential drugs to be considered for basic domestic production in developing countries has been identified by UNIDO. Said list has been endorsed by most developing countries.

The implementation of health programmes in developing countries rely to a large extent on the availability of essential drugs at a fair price. If a close analysis of the urgent drug needs of a large number of the least developing countries is undertaken and the shortage of financial resources is taken into account, it could be concluded that a strategy for production of essential drugs on a non-profit scheme has to be studied. It is doubtful that the private sector would even give thought to produce a number of essential drugs under said conditions. Hence, the engagement of the public sector in the production of essential drugs is one of the options of developing countries endeavouring to provide higher quality drugs at low cost.

The public sector is now engaged in basic production in several developing countries. The best example is illustrated by Indonesia where Kimia-Farma, a state-owned pharmaceutical company, is engaged in production at different levels such as formulation of a broad assortment of finished dosage forms from imported bulk drugs; production of quinine salts from indigenous raw materials and production of rifampicin and chloramphenicol under licence agreements with foreign enterprises. Cost to the consumer of finished dosage forms produced by Kimia-Farma are among the lowest. Furthermore, this state-owned company is not only the largest supplier of drugs to the government of Indonesia, but in addition it has a large network of retail outlets throughout the country.

In India the State owned Indian Drugs and Pharmaceuticals Ltd and Hindustan Antibiotics Ltd play a very important role in manufacturing bulk drugs including antibiotics and synthetic drugs and formulations and thereby attaining self-sufficiency in the country.

The public sector is also deeply involved in basic production in Pakistan, where Antibiotics (Private) Ltd., a wholly-owned government

enterprise, produces about 50 percent of the country needs of benzyl penicillin. In 1977-78, the production of this company was 14.3 MMU. The Government of Pakistan also participates in joint ventures with a transnational subsidiary and owns interest in an extraction plant producing santonin.

The Government Pharmaceutical Organization in Thailand is a large scale producer of finished dosage forms from imported bulk drugs. This public sector enterprise also produces inorganic salts and it is studying to enter basic production with ampicillin and two analgesics.

Small scale production of finished dosage forms is now accomplished in Malaysia and Singapore by the public sector. The latter country is planning to establish the largest formulations facility in Southeast Asia.

The above examples should be considered by other developing countries. It has been proven, therefore, that the engagement of the public sector in the production of essential drugs is one of the best policy options for developing countries as regards the growth of the national pharmaceutical industry.

e) R + D development towards disease patterns

The role of research and development in the growth of the pharmaceutical industry has been discussed in detail in the preceding chapter, nevertheless, R + D oriented towards disease patterns in developing countries constitutes by itself an option of considerable significance for developing countries.

Disease patterns of developing countries have rarely been taken into account by the large pharmaceutical houses. Contrary, the minimal R + D effectuated by transnational pharmaceutical corporations in developing countries has been oriented by the disease patterns prevailing in industrialized countries.

Developing countries should, therefore, issue policies enforcing the pharmaceutical industry whether or not it is associated with the private or with the public sector and provide the guidelines for a consistent programme of R + D. With small variations the trends of the disease patterns in developing countries are very much alike.

Helminthiasis, gastro-intestinal disorders, malaria, tuberculosis and malnutrition constitute the largest group of diseases which are prevalent in many developing countries. It is obvious that the issuance of a policy on R + D must contain the elements clinging to the disease patterns and not otherwise.

f) Utilisation of medicinal plants based on modern technology

The world's largest reservoir of medicinal plants exists in the rich flora of the developing world. Many of the plants that grow in developing countries have a great demand in international markets such as Acacia senegal, Carica papaya, Ricinus communis and Eucalyptus species.

A broad variety of medicinal plants is used in the developing world particularly in Asia and Africa. Nevertheless, a majority of the constituents of the medicinal flora is utilized empirically in traditional systems of indigenous medicine. It could be observed, nevertheless, that utilization of medicinal plants or the extraction of their active substances in developing countries rarely conforms with the principles of modern technology.

The Meeting on Technical Consultation on Production of Drugs from Medicinal Plants in Developing Countries convened at Lucknow, India on 13-20 March 1978 by UNIDO classified developing countries into three groups: 11/

1. Those with no facilities for research and development, pilot plants or industrial production
2. Those with facilities only for the preparation of extracts of medicinal plants
3. Those with facilities for pilot plants for the industrial production of active principles from medicinal plants.

Developing countries should encourage the use of plant products used in modern medicine although the production of plants used in traditional systems of medicine should also be stimulated. A regular

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11/ Report of the Technical Consultation on Production of Drugs from Medicinal Plants in Developing Countries, UNIDO, ID/WG.271/6

supply of medicinal plants of uniform quality is indispensable for a plants processing industry as well as a number of solvents utilized in the process of extraction. These elements, therefore, should be weighed when studying the technology for the extraction from medicinal plants is under consideration.

There are technologies for the preparation of total extracts of medicinal plants and for the extraction of their active principles as well. These technologies are available and they could be transferred to developing countries.

IX. OUTLOOK TO THE YEAR 2000

The perspective of the pharmaceutical industry to the year 2000 has to be viewed vis-à-vis the panorama of the socio-economic and political issues that gravitate on the developing world. An analysis of the prospect for the beginning of the next century should endeavour to forecast what the gap between the rich and poor nations would be by the year 2000. A close examination of a number of factual constituents could provide, in all probabilities, the clue to the solution of many problems which have contributed to the stagnation of developing countries in many fields of industrial activity.

The technical dependence of the poor on rich countries has been aggravated by many components, among which the constant brain-drain has been identified. Technicians, scientists and high-level professionals have constantly emigrated from the poor to the rich countries where they can expect better remunerated employment and more suitable work environment.

Several factors at work within the industrialized countries reinforce the subordination of the developing to the developed countries such as the monopoly effect and the brain-drain effect described above. These factors aid to intensify the demand of the poor countries for resources and skills available mainly in industrialized countries, therefore contributing to the economic dependence. The monopolistic effect that serves to establish the economic dependence of the developing on the industrialized countries originates from the relationship between domestic and foreign private enterprises. In developing countries, foreign enterprises have distinct advantages opposite domestic enterprises, with respect to technology, know-how, etc. and it often occurs that their monopolistic control of some or all factors accounts for their interest in investing in poor countries.

Ranges of disparity in the levels of income of the industrialized and the poor nations are expected to be reduced; nevertheless, the prospect of closing the gap between the poor and the rich nations by 2000 on the basis of current trends is very dim.

Underdevelopment reinforces economic and social stratification and external dependency. Many developing countries suffer from stagnation, growing marginality and de-nationalization. For example, in twenty years, since World War II, the developing region of Latin America has gone through a slow and unstable process of development. In some areas, the process has deteriorated to the extent where the per capita income has grown only 50 percent over the entire period from US$ 280 to about US$ 430. If these trends are not changed the 600 million inhabitants estimated by 2000 will enjoy a per capita income of US$ 650. This slow rate of development suggest precarious material and cultural conditions for most people within the region. The above figure is only a fifth of current per capita income in the United States and more than half that of Western Europe and the USSR.

With respect to the outlook of the pharmaceutical industry, estimated world-wide consumption of medicaments at the turn of the century will be of the dimension of US$ 135 billion, assuming a cumulative rate of growth of the demand of about 4 percent per annum. Assuming a similar value for production, US$ 27 billion would correspond to the production value of bulk drugs and the balance or US$ 108 to finished dosage forms. The share of developing countries world-wide pharmaceutical production was 11.7 percent in 1978.

a) Demographic factors

The growth of the population in developing countries has been underanticipated in spite of the fact that a decline in mortality was expected. In 1949 it was projected that the growth of the world population at a rate of one percent per year would yield 3.5 billion by 1990 and a leading world demographer made an estimation in 1950 of a world population of 3.3 billion for the year 2000, which is about the number of people thought to be alive today.

Nearly 70 percent of the world's population resides in developing countries; four-fifths of this poor population lives in Asia and Africa. The total GNP of the latter is only around 10 percent of the combined world GNP. Demographically, for example, the combined population of Brazil and Mexico is more than half of the Latin American region. Of the 619 million inhabitants estimated for Latin America in 2000, about 317 million will live in the latter two countries perpetuating the current disproportion. Africa will share 13 percent of the world population when it reaches about 800 million by the turn of this century.

As regards developed countries, projections were also made before World War II forecasting in European countries the cessation of population growth within a generation. Similar projections were made for the United States and Canada. Results exceeded the projections.

The growth of the world's population between now and the turn of the century implies the expansion of the health systems and therefore, a sizable increase in production and consumption of essential medicaments with adequate standard of quality. Said drugs will have to be provided to conform with the programmes of primary health care. This will only be accomplished by the developing countries when the obstacles which interfered with the growth of the pharmaceutical industry hitherto could be removed.

b) Social and political factors

Uncertainty grows over the future of some countries in developing regions where the political climate becomes increasingly discouraging. Predicting how different forms of government will evolve by 2000 will be difficult. It could be visualized, nevertheless, that the future political order must ensure popular participation and the opportunity of communication and dialogue among all sectors.

In order to achieve economic development, a socially equitable political order is essential. The political environment exercises a strong influence over the ambience of the pharmaceutical industry. It would be desirable that a number of hindrances to the availability of essential drugs at a cost that people can afford to pay will be abolished by the year 2000. These obstacles have prevailed in many developing regions on account of adverse political environments which favoured the enforcement of legislation sometimes unfair to the interest of the people and to the development of the pharmaceutical industry.

c) Economic factors

The outlook to the year 2000 does not seem promising for developing countries in terms of estimated per capita income. In average, the Latin American region GNP per capita will be twice as much as the GNP per capita income in Africa or Asia (excluding Japan) and about one tenth that of the industrialized countries. The GNP rate of growth of the developing world has been estimated in 6.0 - 6.5 percent per annum. If developing countries cannot increase their purchasing power

to reasonable levels some action will have to be studied by the industrialized countries to prevent a socio-economic stagnation.

Large pockets of undernourished areas in the developing world reflect low income of the people rather than world scarcity of food. So, a wide variety of world's problems could be grouped under the umbrella of the economic imperative. Developing countries live under the pressure of economic dependence which also implies continued political subordination. An optional path to accelerate the growth of th economy in the developing world would be the establishment of an adequate system of integration.

(d) Analysis

A review of the demographic, social, economic and political factors shows that the prospects of attaining the goal of "Health for all by the year 2000" are very dim. Similarly based on the current rate of growth of the pharmaceutical industry, it is very unlikely that the industrial output of developing countries will reach 25 percent of total world industrial output by the turn of the century as stated in the Lima Declaration and Plan of Action on Industrial Development and Co-operation. Since it is universally accepted that all peoples of the world should attain by the year 2000 a level of health that will permit them to lead a socially and economically productive life, the only positive way to achieve this, as shown in the outlook to 2000,could be through a genuine co-operation between developed and developing countries at all levels, social, economic, political, industrial and health in order to achieve the objective of creating a healthy partnership and a more just world.

CONCLUSIONS

General:

There is an ever increasing and widespread recognition of the importance of pharmaceuticals in promoting the health and well-being of people. However, as the study shows, large segments of the population of the world in the developing countries do not have access to the most essential drugs that are indispensable to ensure even minimum health care. Effective prophylactic and therapeutic agents already exist for many diseases afflicting millions of people in these countries, but these are not available to them in adequate quantities. Although nearly half of the health budget of developing countries is spent on pharmaceuticals, the per capita consumption of drugs in these countries still remains at low levels. Most of the developing countries do not have adequate foreign exchange resources to increase their imports.

It should be noted that with the growing emphasis on health care in developing countries, the demand for pharmaceuticals is ever on the increase. As the national health programmes gain momentum and adequate funds are made available to support the same, the requirement of pharmaceuticals is bound to grow further. The immediate need is therefore for an integrated development of the entire system of procurement, production and distribution of pharmaceuticals at the national level to meet the requirements of preventive and curative health care. Although centralized procurement does contribute to some saving in foreign exchange expenditure, it has certain limitations. First the import bill is constantly going up due to increase in the domestic demand which in turn will require larger allocation of scarce foreign exchange resources. Second, the country continues to be dependent on outside sources in a vital area such as pharmaceuticals.

In view of the above, it is apparent from this report that the most rational way of supplying pharmaceuticals to ensure the success of health programmes is through the establishment of domestic production. This will give the developing countries relative independence to formulate their health care policies.

Processing of bulk drugs into dosage forms

As indicated in the study, many of the developing countries with little or no manufacturing activity and those with facilities to formulate a range of drugs should concentrate on formulating the essential drugs selected by WHO expert committee. The selected drugs are of the utmost importance based on prevalent diseases and are, therefore, indispensable and necessary for the health needs of the population.

Production of bulk drugs starting from intermediates/raw materials

It is obvious from the report that the establishment of pharmaceutical industry which has to start with formulation and packaging has to be integrated backwards into production of bulk drugs needed to treat the most common diseases. For this purpose, the UNIDO illustrative list of 26 essential drugs can serve as the basis for the integrated production of bulk drugs from intermediates or raw materials in the developing countries. These drugs cover therapeutic groups of utmost importance to the developing countries, based on the most common prevailing diseases and are needed by these countries in large quantities.

Constraints on the development of pharmaceutical industry

It is evident from the study that there are some key factors responsible for hindering the growth and development of the pharmaceutical industry in the developing countries. These include the non-availability of favourable contractual arrangements and suitable technology for the manufacture of bulk drugs and the wide disparity in prices and high prices at which formulations and bulk drugs and intermediates were supplied to different countries.

Many of the primary raw materials are available in the developing countries: for example, several of these countries have been the leading suppliers of medicinal plants used in the production of essential drugs. As can be seen from the report, some of the developing countries are in the process of establishing or expanding their petrochemical industry, which will make available many of the chemicals required by the drug industry.

Drugs from medicinal plants

It is seen from the study that the developing countries have been the sole producers and exporters of a number of medicinal plants that do not grow elsewhere. Nearly 80 percent of the population in these

countries have no access to modern medicine and depend on traditional medicine based on plant drugs. However due to the non-availability of suitable technology the plants are used by these countries as simple extracts of questionable purity and stability. The developed countries import these plants and process them whereby the export value of the items increases as much as ten fold. It is estimated that 25 percent of all the prescriptions issued in the U.S.A. every year contain one or more drugs from plants.

In view of the above, it is essential that technology for the production of bulk drugs based on local raw materials and medicinal plants is made available to them under equitable terms and conditions. The transfer of such a technology will facilitate the development in these countries of an integrated pharmaceutical industry, which produces pharmaceuticals needed by them. Thereby the developing countries instead of exporting the medicinal plants can derive benefit from the production of drugs based on medicinal plants. They can also introduce plant drugs in traditional medicine in place of unstable extracts.

Transfer of technology

One of the ways of transferring technology is through the establishment of joint ventures. Theoretically such joint ventures should bring about the transfer of suitable technology. However, as is evident from the study that no technology starting from basic raw materials as such has been transferred to the developing countries and no significant improvement has taken place in the industry. In view of this, a new form of co-operation between the developed and developing countries is needed to facilitate the transfer of such a technology.

Disparity in prices of bulk drugs

It is obvious from the study that the wide disparity in prices charged for bulk drugs used in the production of pharmaceutical formulations is another major constraint on the development of the pharmaceutical industry in the developing countries The prices of bulk drugs will have direct impact on the prices of pharmaceutical formulations and such disparities in bulk drug prices will limit the ability of these countries to make available pharmaceutical products at reasonable prices to the vast masses who at present have no access to the same. It is, therefore, necessary to evolve a mechanism whereby the bulk drugs are available to the developing countries at reasonable prices.

High cost of intermediates

Similarly the high cost of intermediates used in the production of bulk drugs often renders the manufacture of such drugs uneconomic. In view of this, it is essential to formulate a scheme whereby the intermediates are available at a reasonable price and the manufacture of bulk drugs in the developing countries becomes viable.

Research and development

The developed countries, the transnational corporations in particular, through their innovative research and development effort discovered several new drugs which made enormous contributions to the control of diseases and made a profound impact on the health care system. However, a small fraction of this research has so far been directed to tropical diseases research. Still numerous and widespread diseases prevalent in these countries lack effective economic treatment. It is therefore essential that the developed countries devote more of their research and development effort towards finding remedies for diseases afflicting the tropical countries.

There is a considerable amount of research and development effort in the public sector in developed countries with regard to pharmaceuticals. It is, therefore, desirable that the developing countries contact the respective governments directly for possible co-operation in this sector.

Some of the developing countries are relatively more "advanced" than others in the technological field and they would be in a position to assist other developing countries in this field. There are also other spheres such as technical training, valorization of raw materials - medicinal plants in particular - supply of basic chemicals and intermediates, pooling of production capacities and exchange of pharmaceutical products, establishment of regional pharmaceutical centres in which technical co-operation amongst developing countries will promote the development of pharmaceutical industry in these countries.

The developing countries need to strengthen their research and development base to develop their own technology, as for example in the field of medicinal plants. This process will, no doubt, take some time to materialize but the developing countries should become relatively more independent in the field of technology leading to their technological emancipation from the industrialized countries.

Actions to be taken by governments of developing countries

Some well defined national policies are vital for promoting the development of the pharmaceutical industry in developing countries. The governments of these countries may therefore take various measures including the creation of the necessary infrastructure, providing facilities for industrial training and enacting necessary legislation.

Government protection

The study has clearly shown how the local production of bulk drugs becomes uneconomic due to the high cost of imported intermediates and lack of suitable technology. In view of this, it would be unrealistic if the governments of developing countries decide on the relevance of establishing a domestic pharmaceutical industry based on the judgment of local bulk drug production costs compared to the corresponding prices prevailing on the international market. First, as can be seen from the study, the prices on the international market are not static and are subject to wide fluctuations. Second, on account of inherent difficulties such as the high cost of imported intermediates and poor technology, the local production costs are bound to be higher. Third, the prices also tend to be higher during the gestation period of the industry. Last but not least, the country continues to depend on imports of essential pharmaceuticals and will have to pay higher import bills when the prices go up and as the domestic consumption increases. In view of this, the governments of the developing countries have to take measures to protect the national industry which is of strategic value to the country.

Bargaining power

In addition to transnational corporations, small companies in the developed countries as well as companies in some of the developing countries also are involved in the pharmaceutical industry. In view of this, the developing countries should keep themselves well informed about these companies and the products and technology available with them to find out the possibility of obtaining more favourable prices and terms.

Resumé

If the universally accepted goal of "health for all by the year 2000" is to be achieved, conditions have to be created to promote the growth and development of the pharmaceutical industry in the developing countries. Based on the present distribution of world output of pharmaceuticals, the

pharmaceutical industry in the developing world would have to grow at a much faster rate bearing in mind that the developing countries (excluding China) will have nearly 75 percent of the world's population in the year 2000. In view of this, the relationship between the supplier of technology, bulk drugs, intermediates and raw materials and the recipient developing country has to be established from a new perspective. This naturally calls for a new framework in international co-operation.

Table 1. Population, rate of increase, birth and death rates, density, GNP per capita and medical team density for the world, continents and geographical regions (selected years)

Continents, geographical regions	Estimates of mid-year population (in millions) 1977	Birth rate (per 1000) 1965-77	Death rate (per 1000) 1965-77	Annual rate of population increase % 1970-77	Density (per km²) 1977	GNP per capita (US$) 1976	Medical team density per 100,000 1975
World total	4 124	31	13	1.9	30	1 650	394.6
Africa	424	46	20	2.7	14	440	101.2
Eastern Africa	121	48	21	2.8	19	210	59.0
Middle Africa	48	44	21	2.3	7	230	59.0
Northern Africa	104	43	15	2.8	12	650	137.6
Southern Africa	29	43	16	2.8	11	1 240	377.3
Western Africa	122	49	23	2.7	20	350	65.8
America	584	28	9	2.0	14	3 950	-
Latin America	342	37	9	2.8	17	1 100	-
Caribbean	28	32	9	2.0	119	1 060	237.3
Middle America	84	42	9	3.3	34	1 000	127.5
Temperate South America	40	24	9	1.4	11	1 400	304.2
Tropical South America	130	38	9	2.9	13	1 090	122.6
Northern America	242	17	9	0.9	11	7 850	853.3
Asia	2 355	34	13	2.2	85	-	231.2
East Asia	1 037	26	10	1.6	83	350	399.1
South Asia	1 318	41	16	2.6	83	-	-
Eastern South Africa	342	42	15	2.7	76	330	97.0
Middle South Asia	882	41	17	2.5	130	220	80.7
Western South Asia	93	43	15	2.9	21	1 730	157.3
Europe	478	16	10	0.6	97	4 420	575.7
Eastern Europe	108	17	10	0.6	109	2 820	635.5
Northern Europe	83	15	11	0.4	51	4 910	667.7
Southern Europe	134	18	9	0.7	102	2 620	438.2
Western Europe	154	15	11	0.5	155	6 900	604.6
Oceania	22.2	23	10	2.0	3	4 730	597.3
Australia and New Zealand	17.4	19	9	1.8	2	-	687.8
Melanesia	3.3	41	17	2.5	6	-	155.5
Polynesia and Micronesia	1.4	34	7	2.6	47	-	262.9
Union of Soviet Socialist Republics	260	18	8	1.0	12	2 760	1 116.5

Source: United Nations Demographic Yearbook, 1977/Sixth report on the world health situation, WHO, 1980.

Table 2. National expenditure on health as % of GNP

Country category	Total as % GNP
Low income	
India	1.0
Ethiopia	0.8
Kenya	1.7
Middle income	
Philippines	0.5
Iran	0.6
Brazil	0.5
Centrally planned economies	
Hungary	3.0
USSR	3.5
Industrialized	
Italy	8.0
W. Germany	8.0
U.S.A.	7.9

Source: Pharmaceuticals for Developing Countries, National Academy of Sciences, 1979.

Table 3. Major health problems of developing countries nominated by at least three WHO regions (1970)

Problems	Regions				
	African	American[a]	S.E. Asian	W. Pacific[b]	E. Mediterranean
Malaria	x	x	x	x	x
Diarrheal diseases	x	x	x	x	x
Malnutrition	x	x	x	x	
Tuberculosis	x		x		x
Leprosy	x		x	x	
Sexually transmitted diseases	x	x		x	

Source: Pharmaceuticals for Developing Countries, National Academy of Sciences, 1979

a/ Excluding North America.

b/ Excluding Australia, New Zealand, Japan.

Table 4. Leading causes of death in a more developed and a less developed group of countries (1975)

Age group	More developed countries	Less developed countries
All ages	Heart diseases Malignant neoplasms Accidents	Heart diseases Malignant neoplasms Accidents
Under 1 year	Causes of perinatal mortality Congenital anomalies Influenza and pneumonia	Causes of perinatal mortality Enteritis and other diarrheal diseases Influenza and pneumonia
1-4 years	Accidents Congenital anomalies Malignant neoplasms	Influenza and pneumonia Accidents Congenital anomalies
5-14 years	Accidents Malignant neoplasms Congenital anomalies	Accidents Malignant neoplasms Influenza and pneumonia
15-44 years	Accidents Malignant neoplasms Heart diseases	Accidents Heart diseases Malignant neoplasms
46-64 years	Heart diseases Malignant neoplasms Accidents	Heart diseases Malignant neoplasms Accidents
65 years	Heart diseases Malignant neoplasms Influenza and pneumonia	Heart diseases Malignant neoplasms Influenza and pneumonia

Source: Sixth report on the world health situation, WHO, 1980.

Table 5. Leading therapeutic classes by sales through retail pharmacies in selected developed and developing markets

Country/Class	Market share %	Country/Class	Market share %
BRAZIL		PHILIPPINES	
systemic antibiotics	14	systemic antibiotics	19
cough and cold preparations	6	cough and cold preparations	12
vitamins	6	vitamins	8
antispasmodics	4	analgesics	6
sex hormones	4	tuberculostatics	5
analgesics	3	nutrients	5
antirheumatics	3	antiasthmatics	3
psycholeptics	3	antidiarrheals	3
psychoanaleptics	3	topical steroids	2
cholagogues/hepatic protectors	3	antacids	2
PAKISTAN		VENEZUELA	
systemic antibiotics	25	systemic antibiotics	14
vitamins	13	vitamins	8
cough and cold preparations	5	cough and cold preparations	7
analgesics	5	analgesics	4
nutrients	3	sex hormones	4
antianemics	3	topical steroids	3
antidiarrheals	3	antianemics	3
antacids	3	psycholeptics	3
tuberculostatics	3	systemic steroids	3
antispasmodics	3	antirheumatics	3

Source: Pharmaceuticals for Developing Countries, National Academy of Sciences, 1979.

Table 6. Leading therapeutical classes by sales through retail pharmacies in selected developed and developing countries

Country/Class	Market Share %	Country/Class	Market Share %
Japan[a/]		Germany, Fed. Rep. of	
systemic antibiotics	26	cardiac therapy	11
vitamins	6	psycholeptics	6
antirheumatics	4	peripheral vasodilators	5
antacids	4	cough and cold preparations	5
hematologicals	4	analgesics	4
hospital solutions	4	vasoprotectives	4
cardiac therapy	3	systemic antibiotics	4
cytostatics (anti-cancer)	3	hypotensives	4
psycholeptics	3	sex normones	3
cholagogues and hepatic protectors	3	antidiabetics	3
USA			
psycholeptics (tranquilizers/sedatives)	9		
analgesics	8		
systemic antibiotics	7		
cough and cold preparations	6		
vitamins	5		
hypotensives	4		
diuretics	4		
sex hormones	4		
antirheumatics	3		
psychoanaleptics	3		

Source: Pharmaceuticals for Developing Countries, National Academy of Sciences, 1979.

a/ Measured by sales through wholesalers.

Table 7. Comparative rankings of the leading ten therapeutic classes in selected developed and developing countries

Therapeutic Class	Brazil	Pakistan	Philippines	Venezuela	Japan	USA	West Germany
systemic antibiotics	1	1	1	1	1	3	7
cough and cold preparations	2	3	2	3	-	4	4
vitamins	3	2	3	2	2	5	-
analgesics	6	4	4	4	-	2	5
psycholeptics	8	-	-	8	9	1	2
sex hormones	5	-	-	5	-	8	9
antirheumatics	7	-	-	10	3	9	-
antacids	-	8	10	-	4	-	-
hypotensives	-	-	-	-	-	6	8
cardiac therapy	-	-	-	-	7	-	1
psychoanaleptics	9	-	-	-	-	10	-
cholagogues	10	-	-	-	10	-	-
antispasmodics	4	10	-	-	-	-	-
nutrients	-	5	6	-	-	-	-
antianemics	-	6	-	7	-	-	-
antidiarrheals	-	7	8	-	-	-	-
tuberculostatics	-	9	5	-	-	-	-
topical steroids	-	-	9	6	-	-	-
diuretics	-	-	-	-	-	7	-
hematologicals	-	-	-	-	5	-	-
hospital solutions	-	-	-	-	6	-	-
cytostatics	-	-	-	-	8	-	-
peripheral vasodilators	-	-	-	-	-	-	3
vasoprotectives	-	-	-	-	-	-	6
antidiabetics	-	-	-	-	-	-	10
antiasthmatics	-	-	7	-	-	-	-
systemic steroids	-	-	-	9	-	-	-

Source: Pharmaceuticals for Developing Countries, National Academy of Sciences, 1979.

Table 8. Per Capita Drug Consumption of Selected Countries
(dollars of the period)

	Year	Per capita drug consumption (in US$)	Population (in millions)
Developing countries			
Algeria	1976	8.2	16.23
Afghanistan	1976	1.2	14.00
Argentina	1975	18.0	25.38
Bangladesh	1976	0.9	80.40
Brazil	1976	12.0	109.96
Chad	1977	0.8	4.2
China	1975		822.8
Egypt	1977	5.5	38.08
Ethiopia	1978	0.8	2.86
Guinea	1977	1.7	5.7
India	1977	1.6	620.44
Indonesia	1976	1.8	135.19
Iran	1977	14	34.3
Korea, Rep. of	1977	14	35.96
Libyan Arab Jamahriya	1975	9.9	2.44
Malaysia	1977	2.5	12.65
Mexico	1976	11.6	62.05
Nigeria	1977	2.75	77.05
Pakistan	1976	1.3	71.30
Peru	1975	9.6	15.38
Sudan	1977	5.6	15.8
Thailand	1976	5.75	42.96
Tanzania	1976	1.3	15.1
Turkey	1975	4.1	40.1
Developed countries			
Austria	1975	26	7.5
Belgium	1975	42	9.8
Canada	1976	28	23.18
Denmark	1976	28	5.07

(continued)

Table 8. (continued)

Country	Year	Per capita drug consumption (in US$)	Population (in millions)
Developed countries (continued)			
Finland	1976	36	4.73
France	1976	50	52.92
FR Germany	1976	52	62.00
Greece	1976	24	9.13
Ireland	1976	13	3.16
Italy	1976	34	56.19
Japan	1976	41	112.77
Netherlands	1976	26	13.77
Norway	1976	24	4.03
Spain	1976	36	35.70
Sweden	1975	36	8.22
Switzerland	1975	35	6.41
U.K.	1976	18	56.07
U.S.A.	1976	33	215.12
Centrally Planned			
Czechoslovakia	1975	27	14.80
Hungary	1975	28	10.54
Poland	1975	14	34.02
USSR	1975	9	254.39

Source: Population data from World Bank Atlas 1977
UNIDO case studies on developing countries and ACDIMA: "Arab Pharmaceutical Consumption and Industries".

Table 9. Production and trade in pharmaceutical products selected countries 1973
(millions of dollars)

Country	Output value	Exports value	Imports value	Trade balance value
Developed countries				
France	2,283	439	274	165
Germany, Fed. Rep. of	3,293	855	175	680
Italy	1,785	262	288	-26
Japan	5,050	100	361	-261
Switzerland	671	588	128	460
South European and developing countries				
Argentina	162	-	-	
Brazil	761	9	82	-73
India	422	13	29	-16
Mexico	237	45	60	-15
Portugal	160	-	60	-40
Spain	1,180	26	150	-124
Yugoslavia	254	39	52	-13

Source: The Transnational companies and the Pharmaceutical Industry ST/CTC/9

Table 10. Value of worldwide consumption of pharmaceuticals and share of developing countries (in millions of dollars)

Drugs	1975		1980		1985		2000	
	Value	%Share	Value	%Share	Value	%Share	Value	%Share
Antibiotics	1,970	19.5	2,259	20.05	4,358	21.0	13,561	18.0
Analgesics/Antipyretics	354	6.3	715	6.5	1,250	6.5	4,970	6.6
Hormones	276	4.9	530	4.8	915	4.7	3,470	4.6
Vitamins	690	2.3	1,320	12.0	2,450	11.8	8,440	11.2
Tuberculostatics	23	0.4	55	0.5	104	0.5	300	0.4

Source: TESCO.

Table 11. Percentage contribution to combined total sales of the five leading pharmaceutical companies in selected therapeutic categories in 1973

Drug	%	% On sales of the five top products
Antibiotics	76.3	33.7
Oralataractics	91.9	72.6
Oral Diuretics	83.9	76.3
Antiarthritics	97.2	93.0
Antihistamines	83.3	75.8
Analgesics (Ethical)	73.6	59.6
Psychostimulants	87.9	85.8
Oral Hypoglycemics	71.4	52.6

Source: The Transnational Corporations and the Pharmaceutical Industry. ST/CTC/9.

Table 12. Consumption of a selection of essential bulk drugs

Drug	Worldwide 1977 MT Weight	Worldwide 1977 10^6 Value	Worldwide 1980 a/ MT Weight	Worldwide 1980 a/ 10^6 Value	Worldwide 1985 a/ MT Weight	Worldwide 1985 a/ 10^6 Value	Share of developing countries 1977 MT Weight	Share of developing countries 1977 %	Share of developing countries 1985 a/ MT Weight
Acetylsalicyclic acid	33,000	79	34,500	104	40,000	176	9,250	28	11,200
Paracetamol	9,500	53	10,750	70	12,500	98	1,950	20	2,500
Ampicillin	2,600	180	2,840	215	3,300	280	1,024	40	1,320
Amoxicillin	510	92	715	93	1,050	158	190	37	388
Penicillin Benzyl	7,500	180	8,950	285	11,350	435	350	4.6	520
Chloroquine	1,050	34	1,200	42	1,500	63	1,045	99.5	1,500
Piperazine	14,000	54	17,000	68	24,000	130	150	1.07	256
Furosemide	135	11.4	170	13.6	220	25.3	30	22	48
Hydralazine	55	5.5	67	7.4	95	13.8	0	-	-
Reserpine	1.7	0.5	1.4	0.5	0.8	0.3	0,2	0,1	-
Hydroxcobalamine	5.5	33	6.5	49	9.5	52	1.75	3.2	3
Ascorbicacid	29,750	270	36,000	415	48,000	675	250	0.84	403

Source: Survey on Drugs Production/Consumption, Lisbon, Portugal.

a/ Estimated.

Table 13. World consumption of pharmaceuticals by region
1978

Region		10^6	% of World consumption
America:	North	11,929	20.9
	South	3,509	6.2
Europe:	West	17,574	30.9
	East	7,263	12.8
Africa[a]		1,620	2.8[b]
Asia:	East	11,399	20.0
	West	1,193	2.1
	Central	925	1.6
	South East	925	1.6
Oceania		554	1.0
Total		56,891	

Source: IMS World Publications Ltd.

a/ Including South Africa.

b/ 2.33 percent excluding South Africa.

Table 14. Consumption of pharmaceuticals
Ten largest market economies in 1978

Region	10^6	% of World consumption
Argentina	971	1.7
Belgium	782	1.4
Brazil	1,370	2.4
France	3,800	6.7
Germany, Fed. Rep. of	4,800	8.4
Italy	2,190	3.8
Japan	7,520	13.2
Spain	1,400	2.5
United Kingdom	1,660	2.9
United States	10,060	17.7

Source: IMS World Publications Ltd.

Table 15. Pharmaceutical consumption in the Americas

Region	1976	$ 10^6		Projection
		1977	1978	1979
North America				
Canada	672	662	687	748
Central America	135	169	199	238
Mexico	774	597	738	907
United States	7,900	9,240	10,060	11,360
Others	189	214	245	278
Total North America	9,670	10,882	11,929	13,531
South America				
Argentina	654	692	971	1,400
Brazil	1,210	1,310	1,370	1,890
Colombia	187	248	328	432
Venezuela	282	310	347	385
Others	447	442	493	600
Total South America	2,780	3,002	3,509	4,707

Source: IMS World Publications Ltd.

Table 16. Pharmaceutical consumption in Europe

Region	1976	$ 10^6$ 1977	1978	Projection 1979
Market economies				
Belgium	536	609	782	828
France	2,700	2,900	3,800	4,330
Germany, Fed. Rep. of	3,410	3,820	4,800	5,000
Italy	1,900	1,850	2,190	2,380
Netherlands	364	384	480	530
Spain	1,320	1,250	1,400	1,570
Sweden	400	428	480	547
Switzerland	330	350	492	506
United Kingdom	1,030	1,270	1,660	2,000
Others	1,121	1,232	1,490	1,701
Total market economies	13,111	14,093	17,574	19,392
Centrally planned economies				
oslovakia	445	500	550	605
German Democratic Republic	622	801	996	1,120
USSR	3,750	4,020	4,290	4,600
Others	1,380	1,591	1,427	1,609
Total central planned economies	6,197	6,912	7,263	7,934
Grand Total	19,308	21,005	24,837	27,326

Source: IMS World Publications Ltd.

Table 17. Pharmaceutical consumption in Asia

Region	$ 10^6$ 1976	1977	1978	Projection 1979
Western Asia				
Israel	78	76	65	87
Saudi Arabia	71	105	163	245
Turkey	252	277	360	468
Others	514	596	605	637
Sub Total	915	1,094	1,193	1,437
Central Asia				
India	508	570	660	720
Pakistan	99	119	143	170
Others	111	120	122	129
Sub Total	718	809	925	1,019
South East Asia				
Indonesia	230	260	300	345
Philippines	190	215	264	310
Thailand	130	145	164	180
Others	154	174	197	231
Sub Total	704	794	925	1,066
East Asia				
China	2,600	2,800	3,000	3,200
Japan	4,020	4,910	7,520	8,790
South Korea	400	495	650	850
Others	183	206	229	251
Sub Total	7,203	8,411	11,399	13,091
Grand Total	9,540	11,108	14,442	16,613

Source: IMS World Publications Ltd.

Table 18. Pharmaceutical consumption in Africa

Region	1976	$ 10^6 1977	$ 10^6 1978	Projection 1979
Algeria	115	133	155	180
Egypt	140	160	220	255
Nigeria	270	325	350	375
South Africa	260	267	294	317
Others	483	539	601	663
Total Africa	1,268	1,424	1,620	1,790

Pharmaceutical consumption in Oceania

Region	1976	$ 10^6 1977	$ 10^6 1978	Projection 1979
Australia	411	413	458	494
New Zealand	64	75	89	104
Others	5	6	7	8
Total Oceania	480	494	554	606

Source: IMS World Publications Ltd.

Table 19. Consumption of essential bulk drugs India 1978-1979 (IN MT)

Drug	Quatity
Acetylsalicylic Acid	1,640.45
Paracetamol	134.04
Tetracycline	211.84
Ampicillin	105.27
Erythromycin	40.26
Penicillin	337.37[a]
Streptomycin	296.86
Sulphadimidine	375.18
Chloroquine	346.51
Isoniazide	105.54
Dapsone	24.76
Diethylcarbamazine	24.25
Piperazine	194.33
Furosemide	4.22
Hydroxocobalamine	352.20
Ascorbic Acid	798.68
Insulin	287.93[b]

Source: Indian Drugs Statistics, Ministry of Petroleum, Chemicals and Fertilizers. Government of India 1979-1980.

a/ In MMU.

b/ In MU.

Table 20. Average share of consumption of main therapeutic groups at retail level
1975 - 1977

Therapeutic group	% Range of market share			
	Developed countries		Developing countries	
Anti-infectives	9.0	15.0	20.0	24.0
Central Nervous System	18.0	29.0	4.0	9.0
Analgesics/Antipyretics	4.0	5.5	5.0	9.0
Cardiovasculars	8.0	12.0	4.0	6.0
Vitamins and Tonics	3.0	8.5	5.0	12.0
Hormones	3.5	7.0	3.0	6.0
Neoplams and Endocrines	10.0	13.0	6.0	10.0
Digestives and Genitourinary	9.0	11.5	9.0	12.0
Respiratory System	6.0	10.0	3.5	7.0
Dermatologicals	2.5	6.0	3.0	6.0
Blood and Blood Forming	2.5	4.0	2.5	4.5

Source: UNIDO/ICIS.

Table 21. Direction of pharmaceutical exports of large producer countries in 1973

Exporting country	Latin America	Western Asia	Other Asia	Africa
Germany, Federal Republic of	22	22	25	13
United States	35	14	27	5
Switzerland	13	18	15	8
United Kingdom	9	21	14	20
France	6	11	7	47
Netherlands	8	5	4	3
Italy	7	9	8	4
Total	100	100	100	100
Total value US $ 10^6)	359.5	201.5	459.1	379.5

Source: Transnational Corporations and the Pharmaceutical Industry STC/CTC/9.

Table 22. Trend of pharmaceutical exports of major producers

1973

Exporting countries	Exports to (%)			
	Latin America	Africa	Western Asia	Other Asian
Germany, Federal Rep. of	22	13	22	25
United States	35	5	14	27
Switzerland	13	8	18	15
United Kingdom	9	20	21	14
France	6	47	11	7
Netherlands	8	3	5	4
Italy	7	4	9	8
Total	100	100	100	100
Total value (US$ 10^6)	359.5	379.5	201.5	459.1

Source: Transnational Corporations and the Pharmaceutical Industry, STC/CTC/9.

Table 23. Imports of essential bulk drugs in five Asian developing countries

(in mt)

	Bangladesh 1978	Pakistan 1977-78	Thailand 1977	Indonesia 1978	Philippines 1978
Bulk drugs					
Acetylsalicylic Acid	13.0	176.6	17.0	144.7	71.9
Ampicillin	3.9	7.2	-	34.9	-
Benzyl Penicillin	19.7	a/	-	-	-
Tetracycline	16.2	15.4	83.1	126.5	60.6
Sulphadimidine	15.0	38.5	-	40.5	-
Chloroquine	2.2 b/	29.9	-	44.8	-
Primaquine	0.2	-	-	0.06	-
Ethambutol	0.6	6.6	-	25.8	-
Isoniazid	3.8	5.5	10.3	41.0	-
Streptonycin	6.2	43.2	21.6	30.0	21.2
Dapsone	-	-	-	2.1	-

Source: UNIDO Pharmaceutical Project Reports.

a/ 50% of comsumption is fulfilled with local production.

b/ Most countries' requirements are met with local production.

Table 24. Imports of pharmaceutical products in selected African countries (US$ 10^6) in 1975

Country	Imports
Burundi	3.4
Ethiopia	10.8
Kenya	17.8
Madagascar	11.9
Malawi	2.4
Mozambique	9.7
Rwanda	1.5
Somalia	4.0
Uganda	5.7
Tanzania	27.4
Zambia	11.8
Total	106.4

Source: UN Yearbook of International Trade Statistics 1977, Vol. 1.

Table 25. Imports and exports of pharmaceuticals 1975 - 1977 (in US$ 10^6) a/

	1975		1976		1977	
	Imports	Exports	Imports	Exports	Imports	Exports
Developed regions						
Market economies						
North America	410	936	445	1,071	558	1,185
Western Europe	3,180	4,889	3,511	5,242	3,985	6,120
Other	708	253	823	298	918	353
Centrally planned economies						
Eastern Europe	768	834	956	792	1,101	874
Total developed countries	5,188	6,912	5,735	7,403	6,562	8,532
Developing countries						
Africa	575	n.a.	661	25	731	35
Asia (excluding China)	368	133	436	148	550	165
Latin America	527	135	522	141	587	140
Total developing countries	1,470	268	1,619	314	1,868	340
World total	6,658	7,180	7,354	7,717	8,430	8,872

Sources: UNIDO, UN International Trade Statistics, UN Annual Review of the Chemical Industry, IFPMA and miscellaneous sources.

a/ Imports at current CIF prices - Exports at current FOB prices.

Table 26. Estimated value of world production of pharmaceuticals for 1980, 1985, 1990

(in US$10^9)

	1980 (est)[1]	1985 (est)[2]	1990 (est)[3]
Developed Regions			
Market economies			
North America	18.60	29.95	
Western Europe	27.44	44.19	
Other	11.97	19.27	
Centrally planned economies			
Eastern Europe	15.96	25.70	
Total Developed Countries	73.97	119.11	175.01
% Share on World Total	88	87	84
Developing Countries			
Africa	0.47	0.82	
Asia (excluding China)	4.69	8.26	
Latin America	4.40	7.75	
Total Developing Countries	9.56	16.83	33.85
World Total	83.53	135.94	208.85
% Share on World Total	12	13	16

[1] Estimated annual growth for all regions 9 per cent over 1977

[2] Estimated annual growth: 10 per cent for developed regions, 12 per cent for developing regions

[3] Estimated annual growth: 8 per cent for developed regions, 15 per cent for developing regions.

Table 27. Production of pharmaceuticals and share by regions

(1977)

	US$10^6	% Share of Production
Developed Countries		
Market Economies		
North America	14 369	25.14
Western Europe	21 196	37.09
Others	9 247	16.18
Centrally Planned Economies		
Eastern Europe	12 331	21.58
Total Developed Countries	57 143	88.55
Developing Countries		
Africa	364	0.56
Asia (excluding China)	3 621	5.61
Latin America	3 397	5.26
Total Developing Countries	7 382	11.43
World Total	64 525	

Source: UNIDO

Table 28. Production of a selection of essential bulk drugs

(1977)

	World production		Share of developing countries			
	MT Weight	US10^6 Value	MT Weight	%	US10^6 Value	%
Acetylsalicylic acid	33 250	262.67	4 750	14.72	37.52	14.28
Paracetamol	10 250	59.45	575	5.60	3.33	5.60
Ampicillin	2 600	180	280	10.76	19.60	10.88
Amoxicillin	595	110	100	16.80	18.00	16.36
Penicillin Benzyl	7 600	75	350	4.60	8.22	10.81
Chloroquine	1 050	33.6	125	11.90	4.00	11.90
Piperazine	14 000	54	150	1.07	0.57	1.06
Furosemide	160	11.4	30	18.75	2.25	19.73
Hydralazine	55	5.5	0	-	-	-
Reserpine	3.1	0.77	0	-	-	-
Hydroxocobalamine	5.7	33	0.175	3.00	1.80	0.30
Ascorbic Acid	29 750	270	250	0.84	2.25	8.33

Source: Alves Survey

Table 29. Imports and exports of pharmaceuticals (in US$10^6)*

Country	1975 Imports	1975 Exports	1976 Imports	1976 Exports	1977 Imports	1977 Exports
Developed Regions						
Market economies						
North America	410	936	445	1 071	556	1 185
Western Europe	3 180	4 889	3 511	5 242	3 985	6 120
Other	708	253	823	298	918	353
Centrally Planned Economie						
Eastern Europe	768	835	956	792	1 101	874
Total Developed Countries	5 188	6 912	5 735	7 403	6 562	8 532
Developing Countries						
Africa	575	NA	661	25	731	35
Asia (excluding China)	368	133	436	148	550	165
Latin America	527	135	522	141	587	140
Total Developing Countries	1 470	268	1 619	314	1 868	340
World Total	6 658	7 180	7 354	7 717	8 430	8 872

Source: UNIDO, UN International Trade Statistics, UN Annual Review of the Chemical Industry IFPMA and Miscellaneous sources.

* Import at current CIF prices
Export at current FOB prices

Table 30. Value of production for bulk drugs and formulations
(millions of dollars)

India

Sector	Bulk drugs		Formulations	
	1977-78	1978-79	1977-78	1978-79
Public sector	54.8	61.2	60.9	75.0
Foreign sector	120.6	70.0	801.1	1,000.0
Indian organised private sector		93.7		
Small scale sector	13.8	25.0	172.4	237.5
Total	189.2	249.9	1,034.4	1,312.5

Source: Indian Drugs Statistics, Ministry of Petroleum, Chemicals and Fertilizers, Government of India 1979-80.

Table 31. New product introduction in the Ethical Pharmaceutical Industry 1950-1974

Year	Total New Products	New Single Chemicals	Duplicate Products	Compounded Products	New Dosage Forms
1950	326	28	100	198	118
1951	321	35	74	212	120
1952	314	35	77	202	170
1953	353	48	79	226	97
1954	380	38	87	255	108
1955	403	31	90	282	96
1956	401	42	79	280	66
1957	400	51	88	261	96
1958	370	44	73	253	109
1959	315	63	49	203	104
1960	306	45	62	199	98
1961	260	39	32	189	106
1962	250	27	43	180	84
1963	199	16	34	149	52
1964	157	17	29	111	41
1965	112	23	18	71	22
1966	80	12	15	53	26
1967	82	25	25	32	14
1968	87	11	26	50	21
1969	62	9	22	31	12
1970	105	16	50	39	23
1971	83	14	40	29	30
1972	64	11	35	18	30
1973	74	19	37	18	17
1974	83	18	42	23	26
Total	5587	717	1306	3564	1686

Source: Paul de Haen, Ten Year New Product Survey, 1950-1960; Non-Proprietary Name Index, Vol. VI (New York: Paul de Haen, Inc., 1967); New Products Parade, 1973-1974 (New York: Paul de Haen, Inc., 1975)

Table 32. Innovations by country of origin

Country	Proportion of innovations		
	1935-49 (N=25)	1950-62 (N=43)	1963-70 (N=87)
France	—	9.3%	2.2%
Germany, Federal Rep. of	18.0%	2.3	7.3
Sweden	4.0	2.3	1.1
Switzerland	4.0	7.0	2.2
United Kingdom	4.0	9.3	10.0
United States of America	70.0	67.5	70.6
Other countries	--	2.3	6.6
	100.0%	100.0%	100.0%

Source: Jerome Schnee, "The Changing Pattern of Pharmaceutical Innovation and Discovery" (Graduate School of Business, Columbia University, 1973). (Mimeographed)

Table 33. New chemical entities introduced in the United States
1940-1975

Country of origin	Proportion of innovations (N=971)
Belgium	1.2%
Denmark	1.5
France	2.9
Germany, Federal Republic of	4.9
Japan	1.0
Mexico	1.0
Netherlands	1.0
Sweden	1.2
Switzerland	7.0
United Kingdom	5.4
United States of America	64.0
Other countries	8.9
	100.0%

Source: Paul de Haen, "Compilation of new drugs: 1940 thru 1975", Pharmacy Times (March, 1976), p. 41

Table 34. Percentage of new chemical entities (NCE) discovered and introduced in the USA by the pharmaceutical industry

Source	Period in which drugs were introduced	
	1950-1959	1960-1969
Total	100%	100%
Industry	86%	91%
Other	14%	9%

Source: Pharmaceuticals for developing countries, National Academy of Sciences, 1979

Table 35. CNS drugs approved for marketing in US or UK
(1940-1976)

Major Tranquillisers	32
Minor Tranquillisers	29
Antidepressants	30
Pyschostimulants and Anorectics	18
CNS Stimulants	6
Hypnotics	24
Anti-emetics, anti-migraine, and anti-Meniere's	18
Anticonvulsant	20
Muscle relaxants	1
Antiparkinsonians	17
General anesthetics	14
Neuroleptanalgesics	4
Local anesthetics	20
Neuromuscular blockers	10
Non-steroidal anti-inflammatory analgesics	22
Narcotic and Narcotic Antagonist analgesics	23
Total	306

Source: Trends and prospects in Drug Research and Development, CIOMS, 1977.

Table 36. Anti-infective drugs approved for marketing in US or UK (1940-1976)

Penicillins	20
Cephalosporins	8
Aminoglycosides	7
Anti-tubercular	16
Anti-leprotic	6
Tetracyclines	11
Macrolides	4
Sulfonamides	24
General Antibiotics	21
Antifungal	26
Antiviral	7
Antimalarial	8
Antiprotozoal	6
Antitrypanosomal	3
Antischistosomal	5
Anthelmintic	13
Antiamebic	16
Topical Antibacterial	29
Urinary Antiseptics	4
Total	233

Source: Trends and prospects in Drug Research and Development, CIOMS, 1977.

Table 37. Cardiovascular drugs approved for marketing in US or UK
(1940-1976)

Antihypertensive	17
Beta-blockers	10
Anti-arrhythmics	8
Hypolipidemics	5
Diuretics	23
Miscellaneous	27
Total	90

Table 38. Respiratory drugs approved for marketing in US or UK
(1940-1976)

Mucolytics	5
Bronchodilators	18
Anti-allergic	3
Antitussives	14
Nasal decongestants	10
Total	50

Source: Trends and prospects in Drug Research and Development, CIOMS, 1977.

Table 39. Anticancer drugs approved for marketing in the US or UK (1940-1976)

Alkylating agents	13
Vinca alkaloids	2
Antibiotics	8
Antimetabolites	10
Hormones	4
Miscellaneous	4
Total	41

Table 40. Gastrointestinal drugs approved for marketing in the US or UK (1940-1976)

Peptic Ulcer	12
General	24
Diagnostic	3
Total	39

Source: Trends and prospects in Drug Research and Development, CIOMS, 1977.

Table 41. FDA data on active INDs and pending NDAs
(As of April 1, 1977)

Division	Active INDs [a]	Pending NDAs [b]
Cardio-Renal	590	22
Neuropharmacological	1,172	20
Metabolism and Endocrine	872	15
Oncology and Radio-pharmaceutical (including anti-arthritics)	915	28
Surgical-dental	380	29
Anti-infective	835	35
Total	4,764	149

Source: Trends and prospects in drug research and development, CIOMS, 1977

a/ New drugs under investigation

b/ New drugs for which registration has been requested

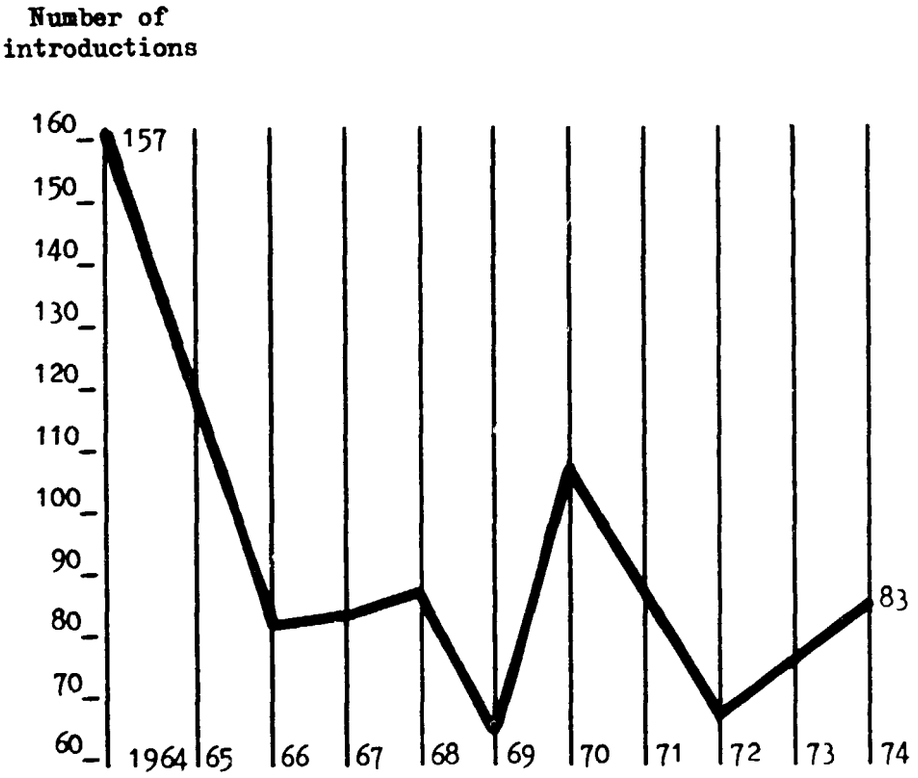
Table 42. New single chemical entities by product category

	Five-year periods		
	1958-62	1963-67	1970-74
	(Number of NCE's)		
Antihistamines	8	0	0
Cough remedies/nasal decongestants	6	1	0
Antispasmodics	7	2	1
Muscle relaxants/anti-tremor drugs	7	1	1
Thiazide-type diuretics	10	1	1
Antinauseants	3	1	1

Source: Barry M. Bloom, "Socially Optimal Results from Drug Research", Impact of Public Policy on Drug Innovation and Pricing: Proceedings of the Third Seminar on Pharmaceutical Public Policy Issues, eds. Samuel A. Mitchell and Emery A. Link (Washington, D.C.: The American University, 1976), p. 359

Table 43. New drug introductions in the US
1964 - 1974

(New single chemicals, duplicate products, and compounded)



Decrease 1964/1974
Total: 74
Percentage: -47.1

Source: De Haen, New York, 1978

Table 44. Basic new pharmaceutical agents

Five-year periods	Average number of basic new agents introduced per year
1941-45	10
1946-50	18
1951-55	31
1956-60	39
1961-65	20
1966-70 (through August)	12

Source: Barry M. Bloom, "The Rate of Contemporary Drug Discovery", Lex et Scientia, Vol. 8, No. 1 (January-March, 1971)

Table 45. Numbers of European companies with major activities in tropical diseases and family planning

Malaria	4
Schistosomiasis (Bilharziasis)	4
Filariasis	4
Trypanosomiasis	3
Leishmaniasis	2
Leprosy	2
Hookworm	2
Family planning	2

Source: Pharmaceuticals for developing countries, National Academy of Sciences, 1979

ACETYL SALICYLIC ACID

1. Production

Name of country, producer and quantity produced are given in Table 1.

Consumption

Name of the region and country and consumption are given in Table 2.

Forecast of world consumption

Year	1980	1985
Quantity in metric tons	34,500	40,000

based on estimated average annual growth of 3%.

Patent

Ger. Pat. 236,196 (1908 to Boehringer). Patent expired. However, Dow Chemical has recently patented a process which is reported to increase operating efficiency and produce finer crystals.

Price

Price in the international market (average) in May 1980 - US$ 2.1/kg.

2. Industrial profile

Based on the data received from a developing country for the manufacture of Acetyl Salicylic Acid from Salicylic Acid and Acetic Anhydride in 1979.

a) Outline of the manufacturing process

Acetyl Salicylic Acid is prepared by acetylation of Salicylic Acid with Acetic Anhydride and a small quantity of Sulphuric Acid 98 percent. About 100 percent excess of Acetic Anydride over the theroretical amount is added to get hard tabular crystals (it is important because Acetyl Salicylic Acid is directly compressed into

tablets without granulation) as well as stable product. Economic operations require the recovery of Acetic Acid and excess of Acetic Anhydride.

Preparation of Salicylic Acid sublimed - Salicylic Acid technical grade is produced by reacting Pehnol with Caustic Soda to produce Sodium Phenate. Carbondioxide is introduced under pressure to react with Sodium Phenate at 170°C to 190°C and converted to Sodium Salicylate.

b) Availability of intermediates and raw materials

The two important intermediates are Salicylic Acid and Acetic Anhydride; in addition to the developed countries some of the advanced developing countries also produce these materials. No problem in the availability of these intermediates has been reported.

c) Plant capacity

Based on the experience of a developing country, the plant capacity recommended in 1979 is 1,200 M/T per year.

d) Investment

Based on the experience of a developing country in 1979, the investment for a capacity of 1,200 M/T is US$ 4.0 million.

e) Requirement of different intermediates and other raw materials per kg of the finished product (F.P.)

Raw material	Requirement per kg of the F.P. in kg	Price per kg in US$	Cost in US$ per kg of F.P.
Acetic Anhydride	0.78	1.3	1.0
Salicylic Acid	0.88	1.68	1.48
Caustic Soda (lye)	0.051	0.426	0.023
Other raw materials	-	-	0.09
			2.59

f) Cost breakdown for the bulk drug

Item	Cost for 1,200 M/T in thousand US$	As percentage of total cost
Raw material	3,100.0	77.5
Wages	127.5	3.19
Utilities	100.0	2.5
Depreciation	400.0	10.0
Maintenance	127.5	3.19
Overhead	145.0	3.62
	4,000.0	100.00

Cost per ton: US$ 3,333.33

g) Cost of intermediates and other raw materials as percentage of the total cost

Total cost of raw materials	US$ 2.59	(A)
Total cost of production	US$ 3.33	(B)
A as percentage of B	77.77	

h) Cost breakdown of Acetylsalicylic Acid formulation

Dosage form - Tablet
Strength - 300 mg per tablet
Pack size - 1,500 tablets in a tin container

Item	Cost per pack in US$	As percentage of cost
Acetylsalicylic Acid	1.725	63.44
Other raw materials	0.094	3.46
Conversion cost a/	0.56	20.6
Packaging cost a/	0.1	3.68
Packaging materials	0.24	8.82
Ex factory cost	2.719	100.10

a/ includes direct wages, utilities, depreciation, maintenance and general overhead.

Table 1. Production of Acetyl Salicylic Acid during 1977

Country	Producers	Production in metric tons
Argentina	Quim. Farm. Platense	1,000
Australia	Monsanto	500
Brazil	Sydney Ross	600
Colombia	Industria Quimica Andina, Sydney Ross	400
Czechoslovakia	SPOFA	100
France	Rhone-Poulenc	3,800
German Democratic Republic	VEB Chem. Pharm. Werk	200
Germany, Federal Republic of	Bayer, Hoechst	2,000
India	Alta Laboratories, Southern Medico	1,000
Mexico	Lepetit, Salicylates de Mexico	1,750
Poland	POLFA	750
Romania	Uzina de Medicamente	1,000
South Africa	Fine Chemicals Epping Industria	500
Spain	Quim. Farm. Bayer	500
Turkey	Bayer Türk Kimya Sanayi	400
United Kingdom	Graeser Salicylates, Monsanto	4,200
United States of America	Dow Chemical, Monsanto, Norwich Pharmaceutical, Sterling Drug	14,000
Yugoslavia	Bayer Pharma Jugoslavia	100
	Total world production	33,250 tons

(continued)

Table 1. (continued) Production of Acetyl Salicylic Acid in developing countries during 1979

Country	Producers	Production in metric tons
Argentina	Quimica Farmaceutica	
	Platense	
	Sudamfos	
Brazil	The Sydney Ross Co.	
Colombia	Industria Quimica Andina	
	The Sydney Ross	
Egypt	Nasar Co.	reported to be 500 tons
India	Alta Laboratories	1,321
Mexico	Dow Quimica Mexicana	
	Saliclatos de Mexico	

Table 2. Consumption of Acetylsalicylic Acid during 1977

Region and country	Consumption in metric tons
North America	
Canada	750
United States	12,750
Subtotal	13,500
Latin America	
Argentina	1,100
Brazil	850
Chile	175
Colombia	325
Mexico	400
All others	650
Subtotal	3,500
Western Europe	
France	1,250
Italy	1,500
Germany, Federal Republic of	1,750
Scandinavian countries	250
Spain	750
United Kingdom	3,000
All others	1,000
Subtotal	9,500
Asia	
India	1,250
Indonesia	250
Japan	400
Pakistan	250
Philippines	250
Republic of Korea	100
Thailand	300
Turkey	400
All others	800
Subtotal	4,000
Africa	1,750
Oceania	750
Total	33,000