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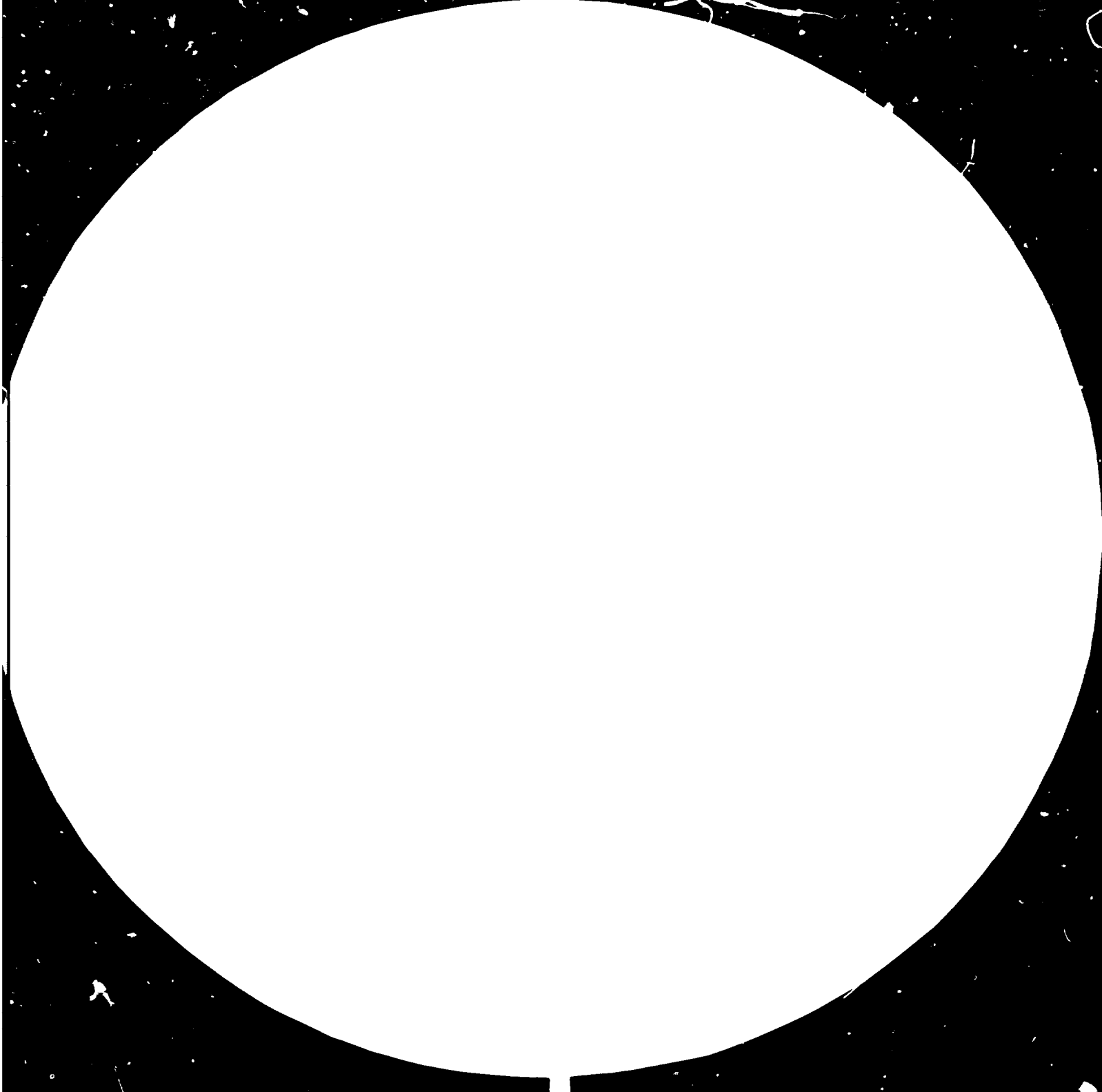

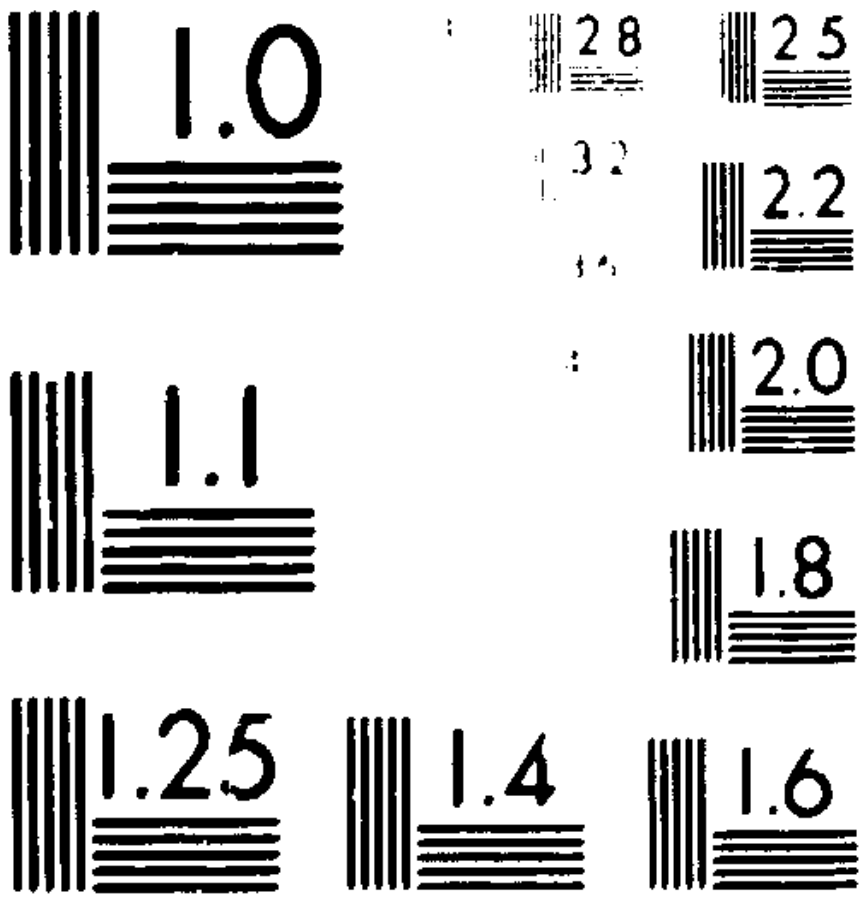
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United Nations Industrial Development Organization

Preparatory Meeting for the First Consultation
on the Pharmaceutical Industry

Cancun, Mexico, 24-27 April 1980

ISSUES THAT MIGHT BE CONSIDERED AT THE FIRST CONSULTATION*/

Prepared by the UNIDO Secretariat

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TABLES

INTRODUCTION

1. The Second General Conference of the United Nations Industrial Development Organization (UNIDO), held at Lima, Peru, in March 1975, recommended that UNIDO should include among its activities a system of continuing consultations between developing and developed countries with the objective of raising the developing countries' share in world industrial output through increased international co-operation. That recommendation was endorsed by the General Assembly at its seventh special session in September 1975. It is being implemented under the guidance of the Industrial Development Board, the policy-making organ of UNIDO.

2. Consultations are held among member countries. Participants may include officials of Governments as well as representatives of industry, labour, consumer groups etc., as deemed appropriate by each Government. Relevant international organizations are also invited to participate. In the past, attendance has been 150-250 participants from 50-70 countries.

3. The Industrial Development Board authorized the secretariat to undertake preparations for a consultation on the pharmaceutical industry including preparatory activities at the regional level.

4. The purpose of this Global Preparatory Meeting is to determine what issues should be discussed at the First Consultation.

Previous preparatory activities

5. Two panels of experts from developing and developed countries were convened in June 1977 and February 1978 and a number of issues suitable for consultations were identified in a preliminary way.

6. The Interregional Meeting to Prepare for Consultations on the Pharmaceutical Industry was held in January 1979 at Cairo, Egypt. The Meeting was attended by participants from 12 countries and from 9 regional organizations. The purpose of the Meeting was to identify priority issues that the developing countries wished to discuss with developed countries at the First Consultation.

WHO/UNIDO agreement

7. Recognizing the importance of implementing the health programmes required to attain the target of "Health for all by the year 2000" and with a view to mobilizing the industrial capacity of developing countries for the production of essential drugs including medicinal plants, the Executive Heads of WHO and UNIDO entered into an agreement in August 1979 to co-ordinate the efforts of the two organizations:

> "WHO's contribution would focus on the identification of health needs and on the definition and implementation of health and drug policies, UNIDO, on its part, would focus on the definition and implementation of industrial production policies, including pharmaceutical production and utilization of natural resources".

The need to establish a pharmaceutical industry

8. To make an effective contribution to health care in developing countries, a local pharmaceutical industry needs to be established. Many developing countries have no pharmaceutical manufacturing facilities; some have only facilities to formulate a limited range of drugs, that is, convert imported bulk drugs to ready-to-use dosage forms; a few countries have facilities for the basic manufacture of some drugs, that is, the manufacture of the active ingredients from local and imported intermediates and raw materials.

9. Consequently the availability of drugs in most developing countries still depends at present on imports. The growing cost of such imports, which doubled to almost $US 2 billion in the period 1972 to 1977, makes it imperative for developing countries to establish facilities for the local formulation or basic manufacture of as wide a range of bulk drugs as possible.

10. The main constraints to the establishment of the pharmaceutical industry in developing countries have been lack of access to technology on suitable terms, limited development of national technological capability when technology was transferred, lack of qualified and trained personnel, the

limited availability and high cost of imported bulk drugs and intermediates, and absence of well-defined national policies to promote the growth of the industry.

11. With a view to assisting the developing countries in the establishment of pharmaceutical industry, UNIDO has evolved strategies and elaborated a range of policies such as drug policy, production policy, basic principles for transfer of technology and strategy on replacement of chemical raw materials by natural raw materials.

Issues that might be considered at the First Consultation

12. UNIDO has, therefore, selected the following issues to present to the First Consultation Meeting:

(a) The pricing and availability of intermediates and bulk drugs.

(b) Guidelines for licensing arrangements for the transfer of technology for the basic manufacture of the active ingredients of essential drugs and formulations.

(c) The availability, terms and conditions for the transfer of technology for the manufacture of 25 essential drugs.

13. This document explains why UNIDO has selected these three important issues.

14. The Meeting is invited to examine these three issues and advise the UNIDO Secretariat what type of specific measures to increase international co-operation in these three areas might be agreed at the First Consultation.

15. The Meeting is invited to suggest, if it so desires, other issues that might be considered by the First Consultation, bearing in mind, however, that (a) the number of issues must be limited in order to obtain agreement on specific measures and (b) there will be an opportunity to consider other issues at subsequent Consultations on this industry.

THE DEVELOPMENT OF A PHARMACEUTICAL INDUSTRY IN DEVELOPING COUNTRIES AND THE NEED FOR A NEW FRAMEWORK OF INTERNATIONAL CO-OPERATION TO ACHIEVE THIS GOAL

The Alma Ata Declaration

16. There is an ever-increasing and widespread recognition of the importance of pharmaceuticals in promoting the health and well-being of people in the developing countries. 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." 1/

The Conference called for a new approach to health and health care and stated that:

> ..."A main social target of governments, international organizations and the whole world community in the coming decades should be the attainment by all peoples of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life." 2/

17. Recognizing that Primary Health Care requires a continuous supply of essential drugs, that the provision of drugs accounts for a significant proportion of expenditures in the health sector and that the progressive extension of primary health care to ensure eventual coverage entails a large increase in the provision of drugs, the Conference recommended that:

> ..."Governments formulate national policies and regulations with respect to the import, local production, sale and distribution of drugs and biologicals so as to ensure that essential drugs are available at the various levels of primary health care at the lowest feasible cost .... and that effective administrative and supply systems be established."

1/ Paragraph 13 of Report of the International Conference on Primary Health Care Alma Ata, USSR, 6-12 September 1978, WHO, Geneva 1978.

2/ Op. cit. Declaration paragraph V.

18. However, large segments of the world's population 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 in adequate quantities.

Per capita consumption of drugs

19. Although nearly half of the health budget of developing countries, which accounts for nearly 2 per cent of the Gross National Product of these countries, is spent on pharmaceuticals, the present level of consumption in the developing countries remains inadequate. The per capita consumption of drugs in several developing countries is around $US 1 as compared to about $US 50 in some developed countries.

The developing countries' share of world production

20. The value of pharmaceuticals produced in the world in 1977 has been estimated at $US 64.5 billion. The developing world, excluding China, contributed only 11 per cent of this production, out of which one half was accounted for by three countries, namely Brazil, India and Mexico.[3/] Furthermore, a major part of this so-called production in developing countries consisted of the formulation and packaging of imported bulk drugs.

The need for the establishment of a local pharmaceutical industry

21. Most of the developing countries do not have adequate foreign exchange resources to increase their imports year after year. A more rational way of supplying pharmaceuticals is an integrated development of the entire system of procurement, production and distribution of pharmaceuticals at the national level based on a national list of essential drugs which health care requires.

3/ Pharmaceuticals in the Developing World, Policies on Drugs, Trade and Production, Vol. I, United Nations 1979.

22. In addition to contributing to the industrialization process as a whole, the establishment of a pharmaceutical industry brings significant social benefits because it supplies products which are essential for the immediate medical needs of the population. In addition a national pharmaceutical industry will give each developing country more freedom to formulate its own health care policies.

Stage of development of the pharmaceutical industry in developing countries

23. Developing countries are at various stages of development of the pharmaceutical industry ranging from no industry at all to simple formulation and packaging based on imported bulk drugs (active ingredients) and manufacture of bulk drugs based on local raw materials and the principal groups are as follows:[4/]

(a) Developing countries with no manufacturing activity. In this category there are nearly 45 countries which have no pharmaceutical industry and are, therefore, dependent on imported pharmaceuticals in their finished form.

(b) Developing countries with facilities to formulate a range of drugs. These countries import bulk drugs which are converted into dosage forms such as tablets, capsules, ointments, liquids, powders, granules, infusions and injectables. There are about 43 countries which fall into this category. Latin America accounts for nearly half of the formulation plants followed by Asia with about 40 per cent of the formulation plants available in the developing countries.

(c) Developing countries with facilities to manufacture some of the bulk drugs as well as formulate drugs. The bulk drugs include synthetic drugs and antibiotics. The manufacture of synthetic drugs may be carried out from different stages, that is, from late intermediates, early intermediates or raw materials depending on the availability of intermediates

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4/ Interregional Meeting to prepare for consultations on the Pharmaceutical Industry, UNIDO, IL/WG.292/3, 1979.

and raw materials and status of chemical industry in the country. The manufacture of antibiotics involves fermentation technology using special types of microbial cultures in most of the cases. There are just about seven countries which are in this category and which have some kind of base for industrial scale production of some of the bulk drugs.

Production of formulations

24. Many of the developing countries with little or no manufacturing activity and those with facilities to formulate a range of drugs need to concentrate on formulating the essential drugs selected by WHO Expert Committee.[5/] The selected drugs are of the utmost importance and are basic, indispensable and necessary for the health needs of the population. Simple formulation and packaging based on imported bulk drugs would require less complicated technology, which is available in many developing countries. Apart from saving a considerable amount of foreign exchange in terms of the cost of imported pharmaceutical products, this would serve as the basis for the creation of an infrastructure for a more developed pharmaceutical industry.

Essential drugs for local production

25. The Second Panel of Industrial Experts convened by UNIDO recommended that each country should draw up a national list of drugs covering its major requirements to suit its particular health needs and its policy in the field of health, the model list of essential drugs drawn up by the World Health Organization Expert Committee serving as a reference in this connexion. The Panel suggested criteria for selecting drugs for local production as follows.[6/]

5/ The Selection of Essential Drugs, WHO Technical Report Series 615, 1977.

6/ Second Panel Meeting of Industrial Experts on the Pharmaceutical Industry, UNIDO, ID/WG.267/4/Rev.1978.

(a) The drug is widely used and/or required by the health authorities to treat diseases prevalent in developing countries;

(b) Its efficacy and safety in the treatment of diseases has been demonstrated and WHO has endorsed its use:

(c) The cost per treatment is low enough for the population to afford;

(d) There are other special advantages of local manufacture as opposed to imports (cost of transport, stability during transport, availability of raw materials, saving of foreign exchange etc.);

(e) Feasibility study of the project indicates that economic production could be ultimately attained including the meeting of regional and inter-regional demands;

(f) The manufacturing process is appropriate to conditions prevailing in the country:

(g) The know-how for manufacture is available for production whether patented or not.

26. The Interregional Preparatory Meeting recommended that the integrated production of bulk drugs from intermediates or local raw materials might concentrate on some of the essential drugs. The Pharmaceutical Meeting on the Production of Essential Drugs held in Hungary in September 1979[7/] reviewed the essentiality of the illustrative list of drugs identified by the Interregional Preparatory Meeting and recommended the production as a first priority of 25 drugs indicated in the Annex. The selection of the above drugs is in conformity with the criteria laid down by the UNIDO panel of industrial experts for the production of drugs in developing countries. Further, these drugs cover therapeutic groups of utmost importance based on disease patterns most common to developing countries and are needed in large quantities. For many of these drugs the main part of the world market is in developing countries. The technologies involved are more sophisticated and are available with the transnational corporations as well as in some of the developing countries.

7/ Pharmaceutical Meeting on the Production of Essential Drugs in Developing Countries, UNIDO/IOD.336, 1980.

Production levels of drugs in selected countries

27. The production status of the 25 essential drugs identified by UNIDO in selected countries in Africa, Asia and Latin America based on UNIDO country studies is summarized in Table 1 to serve as an illustration. Four levels of production are considered:

(1) Formulated locally, that is, bulk drugs are converted into ready-to-use dosage forms.

(2) Manufactured from late intermediates, that is, bulk synthetic drugs are manufactured from late intermediate chemicals involving in many cases the last step or the last step and the penultimate step of the process for the manufacture of the synthetic drugs concerned.

(3) Manufactured from early intermediates, that is, bulk synthetic drugs are manufactured from early intermediate chemicals involving the last few steps of the process for the manufacture of the synthetic drugs concerned.

(4) Manufactured from local raw materials, that is, bulk synthetic drugs or fermentation products such as antibiotics are manufactured from basic chemicals, agricultural products, medicinal plants etc.

(5) Research and development availability, that is, availability of facilities for carrying out research and development mostly applied research and pilot plants.

Table I. Production level of 25 essential drugs in developing countries

DRUGS	COUNTRIES Africa									
	Chad[a/]	Egypt	Ethiopia[a/]	Ghana	Guinea	Rwanda	Tanzania	Upper Volta[a/]
Acetylsalicylic acid	-	4	-	1	-	1	1	-
Ampicillin	-	-	-	1	-	-	-	-
Bephenium	-	-	-	-	-	-	-	-
Blood fractioning	-	-	-	-	-	-	-	-
Chloroquine phosphate	-	-	-	-	1	-	1	-
Dapsone	-	-	-	-	-	-	-	-
Diethylcarbamazine	-	-	-	1	-	-	-	-
Ethambutol	-	-	-	-	-	-	-	-
Ethinylestradiol	-	-	-	-	-	-	-	-
Erythromycin	-	-	-	-	-	-	-	-
Furosemide	-	-	-	-	-	-	-	-
Isoniazid	-	-	-	1	-	-	-	-
Methyldopa	-	-	-	-	-	-	-	-
Paracetamol	-	4	-	1	-	-	1	-
Penicillin Benzyl-	-	2	-	-	-	1	1	-
Piperazine	-	-	-	-	1	-	-	-
Primaquine	-	-	-	-	-	-	-	-
Reserpine	-	1	-	-	-	-	-	-
Streptomycin	-	-	-	-	-	-	-	-
Sulphadimidine	-	4	-	1	-	1	-	-
Tetracycline	-	2	-	1	-	1	1	-
Tolbutamide	-	4	-	1	-	-	-	-
Vitamin A	-	-	-	-	-	-	-	-
Vitamin B_{12}	-	-	-	-	-	-	-	-
Vitamin C	-	-	-	-	-	-	-	-
x	-	x	-	-	-	-	-	-

Explanation of table:

1. Formulated locally
2. Manufactured from late intermediates
3. Manufactured from early intermediates
4. Manufactured from local raw materials
x. Research and development availability

Blank: Data not available
Source: Country studies

a/ No local production

Table I (cont'd). Production level of 25 essential drugs in developing countries

COUNTRIES / DRUGS	Acetylsalicylic acid	Ampicillin	Bephenium	Blood fractioning	Chloroquine phosphate	Dapsone	Diethylcarbamazine	Ethambutol	Ethinylestradiol	Erythromycin	Furosemide	Isoniazid	Methyldopa	Paracetamol	Penicillin Benzyl-	Piperazine	Primaquine	Reserpine	Streptomycin	Sulphadimidine	Tetracycline	Tolbutamide	Vitamin A	Vitamin B_{12}	Vitamin C	x
Latin America																										
Argentina	4	4	2	-	2	2	2	2	-	-	-	2	-	2	4	2	2	2	4	2	4	2	-	-	-	x
Brazil	3	4	2	-	1	1	1	2	-	-	2	1	-	2	4	2	1	1	4	1	4	2	-	-	-	x
Colombia	2	1	-	-	-	-	-	-	-	1	-	1	1	-	1	1	-	-	1	-	1	1	-	-	1	-
Mexico	4	4	1	4	1	1	1	4	4	4	-	1	-	2	4	2	1	1	1	1	'	2	1	2	1	x
Peru	1	3	1	-	1	1	1	1	-	1	-	1	1	1	1	1	1	1	1	1	1	1	-	-	1	-
Uruguay	1	1	1	-	1	1	1	1	-	-	-	1	-	1	1	1	1	1	1	1	1	1	-	-	-	-
Venezuela	1	1	1	-	1	1	1	2	-	1	-	1	1	1	1	1	1	1	1	1	1	1	-	-	1	x

Explanation of table:

1. Formulated locally
2. Manufactured from late intermediates
3. Manufactured from early intermediates
4. Manufactured from local raw materials
x. Research and development availability

Blank: Data not available
Source: Country studies

Table I (cont'd). Production level of 25 essential drugs in developing countries

DRUGS	Afghanistan[a]	Bangladesh	India	Indonesia	Nepal	Pakistan	Thailand
Acetylsalicylic acid	-	2	4	1	1	2[b]	1
Ampicillin	-	1	4	1	1	1	-
Bephenium	-	1	4	1	-	-	-
Blood fractioning	-	-	4	-	-	-	-
Chloroquine phosphate	-	2	4	1	1	2[b]	-
Dapsone	-	1	4	1	-	-	-
Diethylcarbamazine	-	1	4	1	-	-	-
Ethambutol	-	1	4	1	-	1	-
Ethinylestradiol	-	-	4	-	-	-	-
Erythromycin	-	-	4	-	-	1	-
Furosemide	-	1	4	-	-	1	-
Isoniazid	-	1	4	1	1	2[b]	1
Methyldopa	-	-	-	-	-	1	-
Paracetamol	-	1	4	-	1	1	-
Penicillin Benzyl-	-	1	4	1	-	4	1
Piperazine	-	2	4	-	1	-	-
Primaquine	-	1	4	1	-	-	-
Reserpine	-	1	4	1	-	1	-
Streptomycin	-	1	4	1	1	1	1
Sulphadimidine	-	1	4	1	1	2[b]	1
Tetracycline	-	1	4	1	1	1	1
Tolbutamide	-	-	4	-	-	-	-
Vitamin A	-	1	4	-	-	2[c]	-
Vitamin B_{12}	-	-	4	-	-	2[c]	-
Vitamin C	-	1	4	-	-	1	-
x	-	x	x	-	-	x	-

Explanation of table:

1. Formulated locally
2. Manufactured from late intermediates
3. Manufactured from early intermediates
4. Manufactured from local raw materials
x. Research and development availability

Blank: Data not available
Source: Country studies

a/ No local production
b/ Plant idle due to high cost and restricted availability of intermediates
c/ Limited production

28. It can be seen from Table 1 that only few developing countries have facilities for the manufacture of some of the 25 essential drugs in varying degrees. The activities in the case of most of the countries are confined to the formulation of drugs. Further there is no local production in some of the countries studied and their entire requirement of pharmaceuticals is met through the imports of dosage forms. This is also the case to a large extent even in the case of comparatively more advanced regions of the developing world in this sector. For example, the consumption of antibiotics in the Latin American and the Caribbean regions has been estimated at $US 524 million in 1976 and the countries in the region depend heavily on the importation of antibiotics.8/

Investigation of constraints by UNIDO

29. A review of the present status of the development of the pharmaceutical industry in developing countries thus reveals that there are some key factors responsible for hindering the growth and development of this industry. In view of this UNIDO carried out a quick investigation of the key elements hampering the development of this industry in developing countries by sending consultants to selected countries in Africa, Asia and Latin America during the second half of 1979. The consultants identified various constraints to the growth and development of the pharmaceutical industry in those countries. These include the wide disparity in prices at which formulations, bulk drugs and intermediates were supplied to different countries and the unfavourable terms and conditions for the transfer of technology.

The high cost and disparity in prices and restricted availability of imported bulk drugs, formulations and intermediates

30. Some comments pertinent to the consideration of the issue on pricing and availability of imported bulk drugs, intermediates and formulations are set out in the following paragraphs.

8/ Regional Seminar on the Industrial Application of Microbiology in the Pharmaceutical Industry, UNIDO, ID/WG.300/13, 1979.

Disparity in prices of imported bulk drugs

30.1 The experts observed that there was a wide disparity in prices at which a bulk drug was supplied to different countries. Such a variation in prices was found to exist even within the same country depending on the source of supply and licence tie-ups as can be seen from the following table: (Table II)

Sources and processing of information concerning data indicated in the table

The information sources were the governmental agencies concerned with the import of drugs, intermediates and raw materials; public sector central procurement agencies; Drugs Administration; Pharmaceutical Manufacturers Federation: National Census and Statistics Office and the local manufacturing units actually utilizing the intermediates and raw materials to produce bulk drugs. The information was either collected on the spot by UNIDO consultants or communicated by the concerned authorities.

Except where otherwise stated, the prices quoted are those which were operative during the year 1979. For comparison, all prices quoted in national currencies have been converted into US dollars on the basis of the average value of the dollar during April to September 1979.

The f.o.b. price at the port of despatch has been adopted as the basis for evaluation. Where only a c.i.f. price was quoted, it was assumed that the c.i.f. price was 2.5 per cent higher than the f.o.b. price.

The information collected does not provide a fully representative sample of bulk drugs and intermediate prices but does provide enough data for some general tendencies to be discerned.

It can be seen from the table that there is considerable disparity in import prices of bulk drugs offered by different suppliers to different countries ranging up to 11 times in some cases.

High prices of intermediates

30.2 The study revealed that even in the case of intermediates required for the manufacture of certain essential drugs, the price is often higher than the imported bulk drug concerned with the result that local production of the bulk drug becomes uneconomic as can be seen from the following table: (Table III).

Table II. Import prices of bulk drugs

(In US dollars per kg)

Bulk drug	Argentina	Bangladesh	Brazil	Colombia	Egypt	Iran	Peru	Philippines	Thailand
1. Acetyl Salicylic Acid		1.80 to 2 91	1.63[a]		3.63			0.83 to 3.52	1.99[b] to 3.03
2. Ampicillin Trihydrate	85.0	85.9 to 158.8	126.7[a]	95.0[d]	80.0 to 87.2			90.0 to 143.0 [b]	
3. Ethambutol		87.9	41.5[a]		44.0	100.0		60.5[b]	41.5
4. Gentamicin	1385.0				1650.0 to 4380.0 [e]				
5. Reserpine			1297.5[a]		119.0				180.5[b]
6. Streptomycin		45.6 to 49.8	18.0[a]	42.0[d]	61.6 to 63.6	30.0 to 34.2	24.4 to 86.3	48.0[b]	
7. Tetracycline		30.2 to 87.8	66.0[e]	30.0[d]		66.4 to 240.0	31.2 to 144.2	37.6[b]	32.1[b] to 37.6

a/ Average yearly price (1978).

b/ 1978 price.

c/ Average yearly export price (1978).

d/ September 1978 price.

e/ Licence.

f/ 1977/1978 prices.

Table II. Import prices of bulk drugs (cont'd)

Bulk drug	Malaysia	Pakistan	India	Source of Supply
1. Acetyl Salicylic Acid	2.35 to 3.05	0.98 to 2.75	1.86	Delgium, Germany, Hong Kong, Japan, USA, Graesser Salicylate, UK; Ciech, Poland; LPS, England, Siemsgluss and Sohn, W. Germany, China, Soviet Union, and otner unidentified sources
2. Ampicillin Trihydrate		81.97 to 227.3 f/	78.2	IBI, Italy; Bayer, FRG; USA; Beecham, UK, and Singapore; Switzerland, Finland and other unidentified sources
3. Ethambutol		54.65 to 116.1 f/	6.65	ICI, IT, Cyanamide Swiss; Medimpex, Hungary and other unidentified sources
4. Gentamicin			1884	Schering, USA; Medimpex, Hungary and other unidentified sources
5. Reserpine	392.5		1537	Della Befa, Italy; Boehringer, Germany; and other unidentified sources
6. Streptomycin	59.3		44.5	Glaxo, UK; Rhône Poulenc, France, Shin Kee, Hong Kong
7. Tetracycline	30.98		31.7	Sefton, Italy; IBI, Italy; Marcel Quarre, France; and other unidentified sources

Table III. Import prices of intermediates in relation to bulk drugs

(In US dollars per kg)

Name of drug	Intermediated for manufacture	Price of imported intermediates	Cost of imported intermediates Per kg of drug	Price of drugs if imported
1	2	3	4	5
1. Chloroquine phosphate	4.7 Dichloroquinoline 2 Amino-5-Diethyl Amino pentane	42.90 27.3	20.28 12.23 Total: 32.51	23.10
2. Ampicillin Trihydrate	6- Amino Penicillanic acid (6-APA) Phenyl Glycine	84.00 a/ 23.00 a/	46.69 16.85 Total: 63.54 b/	80,00
3. Acetyl Salicylic Acid	Salicylic acid sublimed	1.80 to 3,10	1.584 Total: 1.584 c/	0.84
4. Piperazine Citrate	Piperazine anhydrous	4.83		3.23 to 3.54
5. Metronidazole	2 Methyl-5 nitro imidazole	14.76 a/		19.04 a/

a/ Average yearly price (1978) b/ Data from Mexican Plant (1979) c/ Data from Indian Plant (1978)

Restricted availability of bulk drugs and intermediates

30.3 The restricted availability of bulk drugs and intermediates required for the manufacture of bulk drugs is one of the key factors hindering the development of pharmaceutical industry in the developing countries. For example in one of the developing countries, there are 15 units having facilities for the manufacture of some of the essential drugs based on imported intermediates. However, most of the units are at present inoperative due to high cost as well as restricted availability of intermediates in the world market. Even in cases where some bulk drugs and intermediates became available, there was no assured availability on a continuous basis even for a short period to sustain production without interruption.

A perusal of the data given in the table shows that the cost element contributed by imported intermediates alone renders the local manufacture of certain essential drugs uneconomic. The present international commercial conditions in respect of intermediate prices lead us to the conclusion that it might be cheaper to import certain essential drugs than to manufacture the same from imported intermediates.

Disparity in prices of imported formulations

30.4 A survey has been conducted in 1976 under the auspices of the International Union against Tuberculosis with the co-operation of those of its constituent members who agreed to participate with a view to finding out whether the five essential anti-tuberculosis drugs as well as others which were widely used were obtainable "at a reasonable price".[9/] The results are illustrated in the following table: (Table IV).

9/ P, Chaulet, A. Benachenhou, J.P. Virot, A. Fekar and N. Ait Khaled: Bulletin of the International Union against Tuberculosis, volume 53, No. 4, December 1978.

Table IV. Imported prices of formulations
(in US Dollars per kg)

FORMULATION	ALGERIA	EL SALVADOR	HONGKONG	LIBYA	MADAGASCAR	MALAYSIA	PORTUGAL	SWITZERLAND	TAIWAN	URUGUAY	SOURCES OF SUPPLY
Ethambutol[1/] (1000 400mg tablets)		126.00	108.64	36.60		249.00		220.00		80.00	American Cyanamid, Italy; Lederle, UK, USA
Ethionamide[1/] (1000 250mg tablets)	5.00	33.21	18.94	22.33	30.70	56.44		144.00		25.00	Theraplix, France; G. Richter, Hungary; P.C.T. Tunisia; May + Baker, UK; Marsing, Denmark
Isoniazid[2/] (1000 150mg tablets)		2.18	1.28	1.01 2.24	2.22	1.41				0.50	Otsuka, Japan; Bayer, FRG; Hoffman La Roche, France; Carlo Erba, Italy; and other unidentified sources
Pyrazinamide[1/] (1000 500mg tablets)	31.24		43.68	36.77		241.36		100.00		143.00	Merck, Sharp + Dohme, UK; Bracco, Italy; Sankyo, Japan; Merck, Sharp + Dohme, USA; and other unidentified sources
Rifampicin[1/] (1000 300mg gelloids)	225.00	400.00		231.00	417.50	803.00	801.00		396.00	520.00	Lepetit, Italy; Ciba-Geigy, Switzerland; Lepetit, France
Streptomycin[1/] (100 1 gramm vials)	7.23	8.70	7.86	8.08	15.45	18.00				6.02	USSR; Glaxo, UK; Spécia, France; China; and other unidentified sources

1/ c.i.f. prices in 1976

2/ f.o.b. prices in 1976

Based on the international co-operation survey, the authors came to the following main conclusions:

- "The prices observed in 1976 are more often related to general market condit ons and to the commercial strategies of the numerous manufacturing firms than to the real production costs".

- "In order to choose the means of implementing a national chemo-therapy policy, and more generally, a policy with regard to drugs, each country should have pertinent and impartial economic information on the different prices charged for the same product of equal quality".

30.5 It is obvious from the foregoing that a common constraint to the growth and development of the pharmaceutical industry in developing countries was the high price and restricted availability of imported bulk drugs and intermediates. In view of this, the feasibility of evolving some kind of pricing scheme which could take care of all the elements could be discussed in the Global Preparatory Meeting.

Problems relating to transfer of technology

31. The survey confirmed that the transfer of technology was perhaps the largest single constraint to the development of indigenous production. The common problems encountered in the process of transferring technology are as follows:

- restrictive conditions such as export restriction, import tying, price control;
- excessive royalties and technical know-how fees;
- transfer pricing:
- adaptability of technology to local conditions in terms of scale, skills, capital intensity, formulation and packaging;
- horizontal transfer of technology to other local enterprises.

31.1 The position concerning royalties is illustrated in the following table: (Table V)

Table V. Royalties paid for technology transfer for formulation and packaging of bulk drugs

Ownership	Argentina	Andean Group of Countries	Colombia	Mexico[2]	Peru	Egypt	Asean Group of Countries
Private national producers	up to 5% of sales	5-10%	not exceeding 4% on net sales	not exceeding 1% of total sales	not exceeding 4%	0-5%[3]	5%
Subsidiaries of foreign company	3-5% of sales			not exceeding 3% of sales value (Licensor has less than 25% of shares)		5% decreasing to 2%[4]	
Use of brand-names without transfer of technology	not exceeding 1% of net value of sales[1]			not exceeding 2% of sales value (Licensor has less than 50% of shares)		0-5%[3]	
Other cases	not exceeding 10% of net value of of sales			0% of sales value (Licensor has more than 75% of shares)		not exceeding 5%	
Joint ventures						5% decreasing to 2%[4]	

1/ Argentina, Law No. 21617

2/ Programa de Fomento Para La Industria Farmaceutica en Mexico - Direccion General de Industrias, Mexico D.F. Abril 1979

3/ For a maximum period of five years

4/ For a period extending up to 20 years

It is obvious from Table V that the royalties paid by producers under licensing agreements to licensors regarding formulation and packaging based on bulk drugs vary widely from 0 to 10 per cent.

Analysis of licensing agreements

31.2 An analysis of 104 contracts relating to the pharmaceutical industry has been carried out with particular reference to the restrictive conditions contained therein. These contracts were executed during the period 1956 to 1978 and related to 21 licensee firms and 74 licensors with a country. Among the licensee firms, 12 had foreign participation in the capital, while 11 of the licensor firms entered into agreements with their subsidiaries in the country.

The sources of technology for the production of pharmaceutical products were:

- Federal Republic of Germany
- France
- Italy
- United States of America

The situation in respect of restrictive clauses included in the licensing arrangements for the transfer of technology for the manufacture of bulk drugs and formulations is summarized in Table VI.

31.3 It can be seen from paragraph 31.2 that in many of the licensing agreements already executed, there were restrictive clauses, which evidently were not in the interests of the developing countries. New forms of co-operation have, therefore, to be devised for which some main principles are indicated below as guidelines.

Table VI. Nature and frequency of the restrictive conditions

Restrictive Clauses	Number of Agreements		
	1956 to 1973	1973 to 1978	Total
1. Compulsory acquisition of active ingredients and raw materials from the transferor or from an entity designated by the transferor	59	11	70
2. Prohibition of manufacturing or commercializing competitive products	35	4	39
3. Restrictions to exports	60	18	78
4. Compulsory transmission of innovations	26	13	39
5. Post-expiry conditions:			
. Compulsory end of production	30	10	40
. Compulsory devolution of information	33	10	43

It can be seen from the above table that restrictive clauses were included in most of the licensing agreements - compulsory acquisition of raw materials and restrictions to exports predominating.

Some main principles for making licensing arrangements

31.4 Although licensing is a well established practice in the pharmaceutical industry, there appears to be no single accepted form for licensing agreements. Negotiations are usually based on texts presented by the licensor. Furthermore, existing practise which is reflected in the Licensing Guide for developing countries prepared by the World Intellectual Property Organization (WIPO) has been developed mainly on the basis of experience on the relationships between enterprises in the industrialized countries. This however, relates primarily to transactions invoking industrial property rights. The continuing discussions of the transfer of technology in UNCTAD are rather general as they relate to all industries and do not take account of the special features and social benefits of and implications of the pharmaceutical industry. In view of this, it is appropriate to highlight some of the main principles to be considered while working out licensing arrangements particular to the pharmaceutical industry between enterprises of developed and developing countries. The following are some of the main principles suggested to serve as guidelines for licensing arrangements for the transfer of technology for the manufacture of pharmaceutical formulations as well as bulk drugs. The order in which these principles are presented is neither a reflection of their importance nor does it represent the actual construction of a contract.

Further, an attempt was made to incorporate the main features deriving from policy decisions at the level of governments in developing countries aimed at streamlining licensing procedures for the acquisition of foreign technologies and investment in accordance with their economic and social objectives.

(a) Remuneration and payments for technology

It is recognized that the question of payments is primarily dependent on the technological know-how and expected contribution from the foreign enterprise or licensor (supplier). Taking into account the interest and expectations of the foreign enterprise, it is accepted that the licensor must receive a fair and reasonable compensation for the know-how and services offered.

On the other hand from the point of view of the recipient countries, emphasis is placed on ensuring the maximum benefit that is to be derived from a particular transaction both in the interest of the recipient enterprise as well as with regard to the sector of industry in general, and the socio-economic benefits that knowledge brings to the country.

To illustrate this, governments of developing countries have endeavoured to ensure that the terms of transfer ought not to be onerous but reasonable, with a bare minimum for the WHO list of essential drugs, a fair fee for speciality drugs already in use and a reasonable maximum for products which are the result of original research and development of the licensor.

Suggested range of royalties for formulations

(i)	based on essential drugs in WHO list	0 to 1 per cent
(ii)	based on speciality drugs (according to the level of technology transferred)	1 to 2 per cent
(iii)	in exceptional cases	up to 3 per cent

Suggested range of royalties/lump sum payment for the manufacture of bulk drugs

A basis of 2 per cent (in exceptional cases, it may be raised to 3 per cent according to the level of the technology provided and the drug produced) on sales for a period of five years maximum may be considered.

Royalties payment should be calculated on net ex factory sales price after deducting discounts, allowances, rebates, turnover taxes, value of basic drugs supplied by the licensor (supplier) or other sources indicated by him.

(b) Exclusivity

From the point of view of the recipient country and their enterprises a license contract for the manufacture of pharmaceuticals, particularly bulk drugs, would be to secure exclusive manufacturing rights at least for the domestic market, enabling the recipient company to build up the necessary capability and market in order to benefit as much as possible from the application of foreign know-how. In this connection the licensor shall provide the know-how etc. exclusively to the licensee (recipient) and to no other party in the licensee's country.

On the other hand the licensor's preference would be to grant non-exclusive rights for manufacturing retaining the right to transfer the same technology to other enterprises in a given country.

The issue of exclusivity is also related to sales and distribution of a product manufactured under a license. In this connection the licensor's preference as observed from past experience would be to ensure that he retains the right to sell directly in the domestic market.

(c) Duration of agreement

The duration of an agreement becomes an issue closely linked with the remuneration for technology. From the point of view of the recipient country the duration of the contract should never be shorter than the time required to fully absorb the know-how under consideration; in other words, the duration of the agreement is closely related to the type of process or technological know-how in question. In view of this, the duration of the agreement should be reasonably long enough to enable the licensee to fully assimilate the technology.

(d) Confidentiality

Issues pertaining to confidentiality in contractual agreements deserve to be considered at two different levels:

(i) the recipient enterprise in the developing country;
(ii) the overall interest of the developing country.

With respect to the licensee, the issue of confidentiality largely relates to specific provisions in the technology contract; whereas with respect to the recipient developing country the issues relate primarily to the question of sharing and disseminating information and experience with the objective of broadening the area of technological choice, know-how and expertise regarding the acquisition of foreign technologies in various production sectors.

One of the areas of conflict related to the question of confidentiality is that the foreign licensor introduces contractual obligations for the licensee that prevent the use of this information even after the termination of the agreement. A more reasonable provision will be the one requesting the licensee to keep during the life-time of the agreement on a confidential basis the technical information specifically indicated by the licensor as being of a confidential nature.

(e) Access to improvements and grant-back provisions

Through the examination of a large number of contracts executed in developing countries it has been found that grant-back provisions have been

introduced requiring the licensee to assign-back to the licensor any new patents, improvements or the result of technical developments, achieved by the licensee during the life of the agreement.

Grant-back provisions can be broadly divided into three parts:

1. Provisions in which the licensee is obliged to inform the licensor of all the knowledge and experience which licensee has acquired in connection with the goods and services covered by the contract.
2. Provisions that oblige licensee to assign the rights (patent rights or rights arising from application thereof) related to any improvement, invention or application of inventions which the licensee has made through his own efforts.
3. Provisions that oblige licensee to grant to licensor a licence on any improvement, invention, or application of invention which the licensee has made.

The basic criteria considered by many developing countries are that these provisions shall not work against the interest of the licensee. A further consideration is that the supplier of technology is placed under the same kind of obligations and the obligations of the licensor and the licensee are properly balanced in relation to:

- royalty payments;
- duration of said obligations;
- the territory in which improvements will be exploited by either party;
- the degree of exclusivity applied to either party.

On the basis of the above it might be considered that:

The licensor and the licensee shall communicate to each other free of charge any improvements/rationalization/economies/innovations in process know-how and all the other items agreed upon during the lifetime of the agreement.

(f) Indemnification for patent infringement

The licensor should indemnify the licensee from and against all actions by third parties regarding infringement or alleged infringement of patents involved in the manufacture, use and sale of the drugs.

(g) Restrictive clauses

- the licensor should not restrict the use of technology after the expiration of the agreement;

- impose prices or restrict the volume of production;
- designate or restrict the source of supply of intermediates and basic chemicals to be used by the licensee.

(h) Supply of drugs, intermediates and raw materials

The licensor should supply drugs, intermediates and raw materials during specified duration at prices no less favourable than the price usually charged by the licensor or other suppliers for such products in conformity with specifications agreed upon.

The licensee shall be free to buy such drugs, intermediates and raw materials conforming to agreed specifications from other sources.

(i) Export

The licensee should be free to export the products covered by such agreement with a view to avoiding duplication of manufacturing activity and eliminate avoidable investment of scarce resources.

(j) Training

The licensor should provide at the production facilities in licensor's country adequate training to licensee's personnel.

(k) Joint ventures

In the case of joint venture arrangements, the participation of the foreign company may not exceed 40 per cent of the total capital and the rate of royalty should be inversely proportional to the percentage of its equity in the capital and that a portion of its profits be spent on research and development in the host country.

(l) Laws governing the agreement

The licensing agreement shall be governed by the laws of the licensee's country. Conciliation by parties acceptable to both the parties and governments as the case may be or arbitration may be taken recourse to.

The availability and terms and conditions for the transfer of technology for the manufacture of 25 essential drugs

32. Since the developing countries are at different stages of development of the pharmaceutical industry, the level and sophistication of technology required in each case would naturally vary. For example the production operations involved in formulation and packaging do not necessarily involve sophisticated high-priced technology. It is therefore a matter of negotiation for a better arrangement based on royalty payment. However, there is a lack of information and knowledge concerning the facilities and infrastructure available in the recipient developing country. Many of the developing countries have a large under-employed man-power but scarce capital. So a sophisticated technology which tends to be capital-intensive aiming at the maximum output per man-hour will be unsuitable. Hence the choice of right technology to suit the environment of the developing countries on reasonable terms and prices is a prerequisite to produce a good quality product at a competitive price.

As regards those countries which are already involved in this industry and which would like to expand their activity in chemical-based drug production, the matter of acquisition of technology is very crucial since such technology is virtually not available or even if available is so expensive to render local production often uneconomic. In this case, too, the evaluation of technology and its appropriateness to the anticipated production programme have to be carried out with expert knowledge to suit the conditions, capacities, raw materials with a view to secure the economic and technical viability of such production. The UNIDO survey confirmed that there were difficulties in obtaining access to the technology suitable for the environment of developing countries at a reasonable price. Hence it is necessary to find ways and means to obtain suitable technology to promote the growth of this industry.

Conclusion

33. If the Alma Ata goal of "Health for all by the year 2000" is to be achieved, conditions have to be created conducive to facilitating the production of adequate quantities of pharmaceuticals 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 about twice the rate of that in the developed world over the entire period till the end of this century if it were to contribute a 25 per cent share of the total world production of pharmaceuticals in the year 2000. This must be considered a minimum requirement bearing in mind that the developing countries (excluding China) will have nearly 75 per cent of the world's population in the year 2000 and the need for the industrial output of developing countries in all sectors to reach 25 per cent of total world industrial output as stated in the Lima Declaration and Plan of Action on Industrial Development and Co-operation.[10/] However, the present state of the pharmaceutical industry in these countries already accounting for over two thirds of the population of the world is far from adequate to meet these commitments.

Many developing countries cannct be expected to continue to depend indefinitely on imports to meet their entire requirement of pharmaceuticals. Similarly, the developing countries where there are facilities for formulation and packaging are not expected to limit themselves to these activities and should be in a position to proceed towards backward integration into the manufacture of active ingredients from intermediates and raw materials. The overriding facts that a healthy population is the backbone for any development programme and that an indigenous pharmaceutical industry has other social benefits to confer should outweigh the oft repeated considerations such as the economy of scale and availability of large enough markets being the decisive factors for the establishment of a pharmaceutical industry in the developing countries. Similarly the relationship between the supplier of technology and bulk drugs, intermediates and raw materials and the recipient developing country has to be worked out from a new perspective. This naturally calls for a new framework in the international co-operation which could be worked out at the First Consultation.

10/ UNIDO, ID/CONF.3/31.

ANNEX

ILLUSTRATIVE LIST OF 25 ESSENTIAL DRUGS FOR WHICH FACILITIES FOR THE LOCAL MANUFACTURE OF ACTIVE INGREDIENTS SHOULD BE ESTABLISHED IN DEVELOPING COUNTRIES

ANALGETICS

1. Acetylsalicylic acid
2. Paracetamol

ANTI-INFECTIVE DRUGS

Anthelmintic drugs

3. Bephenium
4. Piperazine

Antibacterial drugs

5. Ampicillin
6. Penicillin-benzyl
7. Erythromycin
8. Streptomycin
9. Sulphadimidine
10. Tetracycline

Antifilarial drugs

11. Diethylcarbamazine

Antileprotic drugs

12. Dapsone

Antimalarial drugs

13. Chloroquine phosphate
14. Primaquine

Antituberculosis drugs

15. Ethambutol
16. Isoniazid

CARDIOVASCULAR DRUGS

Antihypertensive drugs

17. Methyldopa
18. Reserpine

DIURETICS

19. Furosemide

ANTI-DIABETICS

20. Tolbutamide

ORAL CONTRACEPTIVES

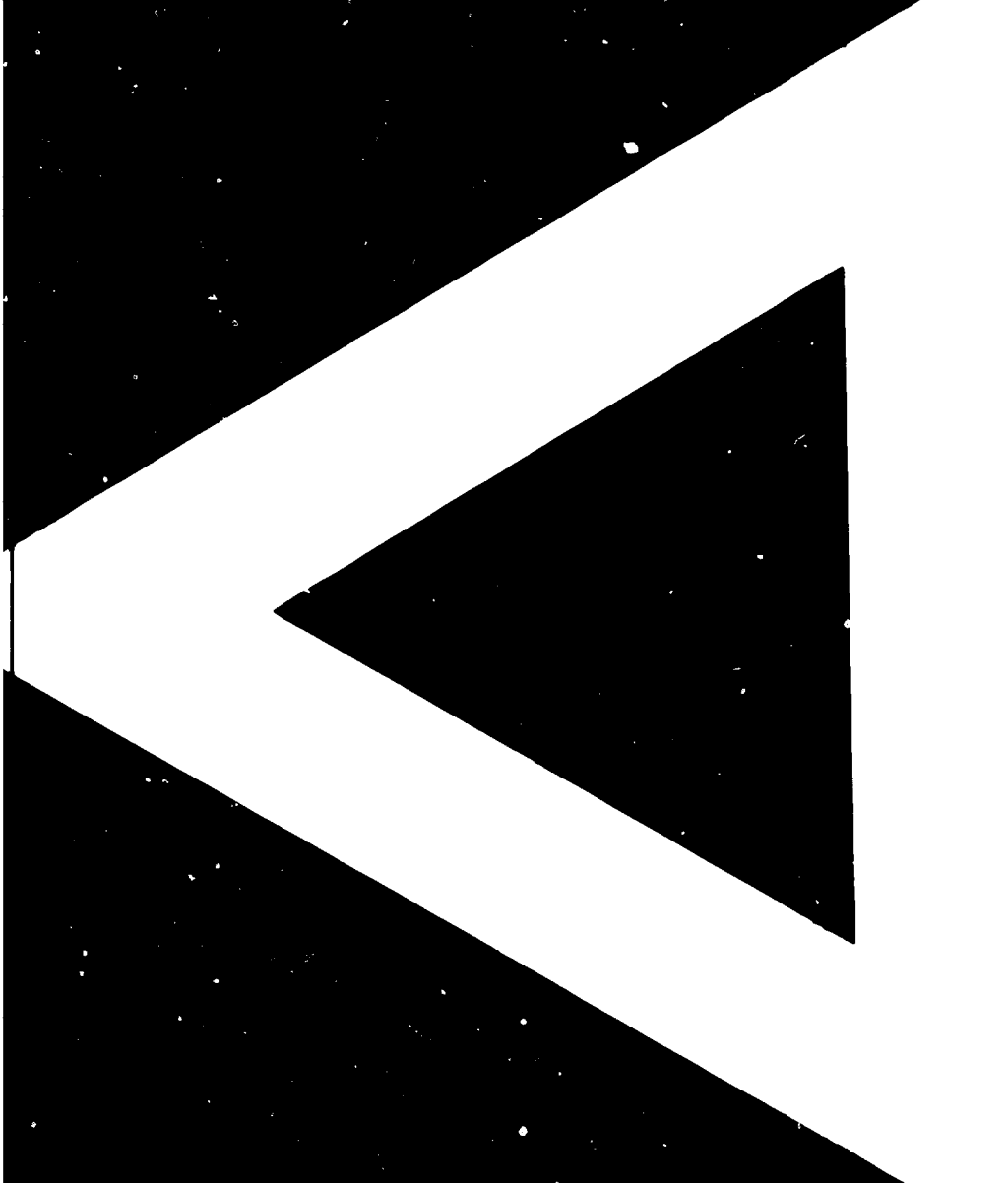
21. Ethinylestradiol

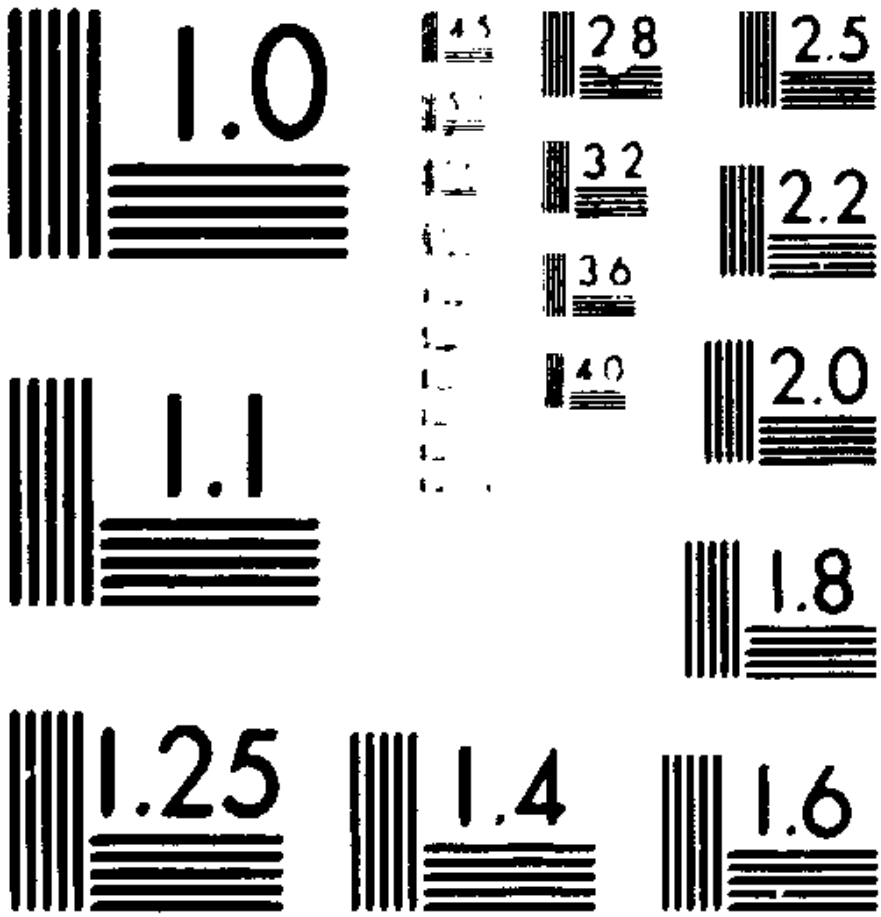
IMMUNOLOGICALS

22. Blood fractioning

VITAMINS

23. Vitamin A
24. Vitamin B_{12}
25. Vitamin C (Ascorbic acid)





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ISSUES THAT MIGHT BE CONSIDERED AT THE FIRST CONSULTATION

Prepared by the UNIDO secretariat

Corrigendum

Page 21, table IV

Entries for ethambutol:

for 249 read 100

for 220 read 130

Entries for streptomycin:

for 15.45 read 15.45 (in 1974)

for 6.02 read 6.02 (in 1974)

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