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ECONOMIC AND TECHNOLOGICAL CO-OPERATION IN THE PHARMACEUTICAL INDUSTRY *

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* The views expressed in this paper are the author's and do not necessarily reflect the views of the Secretariat of UNIDO. This document has not been edited.

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Table of contents

EXECUTIVE SUMMARY

Economic disparity among the nations has been always the cause of major conflicts since time immemorial. In modern time, some significant factors accounting for economic disparity are technology and trade gaps among the nations. The pharmaceutical industry, which is techno.ogy intensive industry and also a completely international industry has all the characteristics to cause conflicts among nations. It is therefore a very important area for economic and technological cooperation and there is no much time to spare.

The gap is really formidable. In 1976 more than three-quarters of the drugs produced were consumed by 27 percent of the world's population living in developed countries. In 1985, this gap had increased further, 75 percent of the world population living in developing countries consumed only 21 percent of the world's drugs consumption. An estimate postulates that 2.5 billion of world's population have little or no access to modern medicines and depend on local traditional medicines of unproven efficacy.

The uneven distribution of drug consumption is due mainly to uneven distribution of drug production, which is still concentrated in a few developed countries. Only seven developed countries consumed 62.3 percent of the total global sale in 1985. Whatever the developing countries consumed in 1985, 64 percent was consumed by eight developing countries in the same year. The disparity was not only between developed and developing countries, it was also between countries in the same group. The production scenario in both the developed and developing world was the same, with production highly concentrated in a few countries. In 1980, more than 90 percent production took place in seven developed countries and about 67 percent of the total production in developing countries was in only six of them. In their Lima Declaration, UNIDO established the main objective of achieving at least 25 percent production in developing countries. This objective can only be achieved if economic and technological cooperation at international level is established.

Being a technology intensive industry, technology is a barrier for new entrants. Particularly, in the manufacture of active ingredients (i.e, bulk drugs) may not be that much to manufacture the dosage forms (i.e, formulations). Technology transfer from developed countries to developing countries is very vital aspect of cooperation. The management of trade in pharmaceuticals is very sophisticated, cooperation in the development of export/import potential would also be essential.

Ninety-four percent of exports come from developed countries and they import 64 percent of all pharmaceutical products. Developing countries export is only 6 percent and import 36 percent. Exports depend on quality and price, both the aspects are technology dependent and hence developing countries are at disadvantage, import is also dependent on the availability of finance, not strong point for most of the developing countries. Even then 41 percent of the total consumption in developing countries is imported. Europe is a dominant group -- trade. Traditional links between European and developing countries also helped Europe to achieve predominance, but now time has come for further development of the relation to help developing countries to be self-reliant whenever possible.

It also needs to be remembered that the developed countries achieved their strong position through imaginative investment and hard labor both in innovation of new drugs and marketing. It is therefore important in any mutually satisfactory regime that in cooperation they also should gain.

Various inter-related factors influence production decisions of therapeutical substances, it is therefore necessary to take into consideration of all such factors and also the guidelines advocated by UNIDO for establishing pharmaceutical industry in developing countries. On cooperation basis, a multitude of hurdles in establishing pharmaceuticals manufacturing facilities both international and intranational can be solved. There are certain bulk drugs, particularly antibiotics and vitamins, higher scale of production, reduces cost of production. In achieving the same participation of foreign capital and technology need to be arranged as envisaged by the first Prime Minister of independent India. Substantial increase in production in a short time in developing countries can only be achieved through joint endeavor between developed and developing countries.

There are many barriers both physical and/or tariff that hinder the free and useful movement of drugs around the world. All the controls, however, are not unnecessary, but the aim should be to ensure the easy availability of pharmaceutical products for the health needs of the people. Registration requirements are necessary but not hindrance to drug innovation. A system, satisfactory both ends need to be evolved by mutual discussion between industry and regulatory agencies. Effluent treatment, GMP implementation and patent protection are all important and related problems can only be solved through understanding and respect for the strength of the other side. It should be remembered that in a market economy, no investment would be forthcoming without assured return. In a high risk field like drug innovation, adequate return is not normal return.

It can be expected that brand loyalty will continue, whatever be the questions raised about its ethics. On a concensus basis, actions are taken to divulge all the side (ill) effects of a particular drug (brand or trade mark) it would move towards more understanding. Generic products should be encouraged in an atmosphere of cooperation and scientific evaluation.

Pricing of pharmaceuticals is another area of controversy. It has been alleged that drug prices had been kept very high because of patent protection and consequent lack of competition in market economies. The explanation is that in a very high risk innovation investment, the successful product of innovation naturally would carry the cost of R and D of unsuccessful projects. Both sides may be partially true, but the reality many be in between. In a cost-based pricing system on the basis of government control, inefficiency may also be perpetuated.

Registration for marketing pharmaceutical products should be based on mutually recognisable systems under the guidance of WHO. This will help rapid diffusion of new products.

Cooperation in licensing, managing units would help more production in developing countries. Buying/selling technology in mutually satisfactory terms would be an important item of cooperation. Research and

development in pharmaceutical industry should get back its pride of place as one industry whose innovative activities saved more number of people than were killed in all the wars in the world. Time has come to ponder over the declining in the introduction of new chemical entities during the last decade.

Traditional medicines only those which had stood the test of time should be encouraged and as most of these are being confined to the country of origin, they need to be dispersed to other countries.

The cooperation, depending on the particular issue, may be bilateral or multilateral. The aim should be to achieve results in the direction of making pharmaceutical products available to all the people of the world. The present target is to achieve 25 percent production in developing countries, slogans and patronising both will be harmful and will not achieve the necessary results.

1. Introduction

During the World War II, man recognised very badly the need of International Economic Co-operation, as a necessity to maintain peace. The policy makers, therefore, started looking for means to achieve such cooperation in both Economic and Technological fields and also in Trade. The Pharmaceutical Industry, which is a technology intensive industry is inherently a completely International Industry. The need for economic and technological co-operation between countries and manufacturing units is, therefore, paramount to maintain and improve health of the people.

As in the case of consumption of food, the North-South gap is very wide in the case of pharmaceuticals. The grossly unequal distribution of drugs between developed and developing countries has not changed much in the past decade. In 1985, 75% of the world's population still accounted for less than 25% of total drug consumption, and about 1.3 to 2.5 billion people had little or no regular access to the most essential drugs. The uneven distribution of the drug consumption is due mainly to uneven distribution of drug production, which is still concentrated in a few developed countries. Large multinational companies play a

key role in production and trade and pharmaceutical innovation continues to make an important contribution to health. The situation in developing countries is different. There are diseases for which treatment is inadequate as these diseases are not the problem for the developed countries. Well coordinated global cooperation only can improve the situation not by the slogans of the South or patronising approach of the North.

The aim of cooperation is not only for the innovation of desired newer medicines, but should also be directed to improve management of production and distribution and better health care system. Technology is an important barrier for the development of this industry in the South. Technology transfer on mutually satisfactory term is very vital aspect of cooperation. Another important item of co-operation is the development of export/import potential, i.e. expanding foreign trade.

According to Lima Declaration, 25% of the total pharmaceuticals production, should come from the Third World Countries, by the end of the century. The situation today is far from encouraging. At the beginning of the last decade of the century, the actual achievement is about 12 to 13% only, when it was 10.5% in 1973. At the same rate, we can hardly touch 15% at the end of this century.

The North-South gap, however, does not reveal the whole picture. In both the developed and developing world, production capacity is highly concentrated in few countries. In 1980, more than 90% production of developed countries took place in seven developed countries i.e.. The United States (30%), Japan (24%), The Federal Republic of Germany (13%), France (9%), the U.K. (6.4%), Italy (6%) and Switzerland (4%). Argentina, Brazil, Egypt, India, Mexico and the Republic of Korea produce two third of the output of developing countries. The cooperation, therefore, not only to be between North and South but North-North and South-South also.

Pharmaceuticals have an inelastic demand since the level of consumption is determined by the incidence of diseases and not by commercial demand. Further, the industry differs from most other industries in that the ultimate consumer (i.e. the patient) has no choice as to the product selected for his treatment.

These aspects require the drug manufacturers to meet certain criteria such as the establishment of an economy of scale, a high level of research and development activities,

and the sustaining of an intense marketing effort to achieve a viable market share and to retain or overcome strong brand loyalties.

The main commercial risks in the industry include product obsolescence, the unpredictability of research in its ability to produce a profitable product, and the intense competition within the industry on an international scale. These are, however, offset by the fact that the industry is less subject to short term fluctuations in the world economy than are most industries, and the relatively high profit ratios for successful new products.

These are several factors that influence the performance of the industry, including the patent and trade mark situation, extent of promotion, modes of distribution, availability of finance, pricing stratigies and profit levels.

2. Co-operation in trade and other economic aspects

2.1 Trade

There has traditionally been a strong international trade in therapeutic products because of the concentration of production in a few countries only. The main producing countries are showing increasing amounts of exports. Almost all drug exports (94%) come from

developed countries, and 64% of all imports are also in developed countries. Developing countries play only a marginal role in exports (6%) and imports (36%).

The extent of import into a country of a specific drug is dependent on such factors as an acceptable registration and a price that is usually in line with that prevailing in the country of origin. The extent of local production may also influence acceptance, even protective tariff barriers may be erected to protect local industry.

The availability of suitable finance for the purchase of the materials concerned is obviously of importance as is the degree of medical sophistication in the area. It is not, therefore, surprising to find the strongest balances of trade in pharmaceutical products amongst the more important developed countries.

Though international trade in pharmaceuticals with developing countries is marginal, imports of drugs are an essential element of the drug supply of these countries, 41% of the total consumption in the developing countries are imported, underlining heavy dependence of these countries on foreign supplies of drugs.

Imports of drugs and pharmaceuticals and drug consumption in developed and developing countries in 1984 (billion US $)

	Total	Developing Countries	Developed Countries
Drug Consumption	74.2	15.1	59.1
Imports of Medicaments	8.9(12.0%)	3.2(21.2%)	5.7(9.6%)
Imports of Pharmaceuticals	15.3(20.6%)	6.2(41.0%)	9.1(15.4%)

Source : International Trade Statistics Yearbook, 1984, New York, United Nations, 1986.

Note: Figures in parantheses give percentage of total consumption.

It would be seen from the above table that a substantial part of the drug consumption in developing countries is made from imports. The concentration of

pharmaceutical activity in developed countries will further be evident from the following table on regionwise distribution of drug imports and exports in 1970 and 1984.

	Imports (%)		Exports (%)	
	1970	1984	1970	1984
Africa	14.2	10.2	0.2	0.2
Latin America	8.5	6.5	2.0	1.7
Asia	16.6	18.9	3.2	3.6
Developing Countries	39.3	35.6	5.4	5.5
European Countries	44.1	42.4	79.1	77.5
North America	2.2	10.9	12.2	14.0
Japan	8.7	7.5	1.9	0.9

Other developed Countries	5.7	3.6	1.4	2.1
Developed Countries	50.7	64.4	94.6	94.5

Source : International Trade Statistics Yearbook, 1984. New York, United Nations, 1986.

Table above snows predominance of Europe both in imports and exports, which may partly be explained by the large amount of drugs exchanged within Europe. Besides, due to past colonial linkages, there exists formal links between several European Countries and developing countries, 50.9% of European exports are within Europe only 12.7% to Africa and 19.6% to Asia.

The concentration of imports originating mainly from Europe is an important issue for developing countries. Most of the drugs imported into Africa came from Europe (96%) as well as 58,4% of these imported into Asia. This concentration increases dependence on limited source of supply and creates trade flows that are often difficult to

change. The table below would furnish the sources of drugs imports to African, Asian and Latin American countries in 1984.

Percentage

	North America	Europe	Africa	Latin America	Asia	Others
Africa	2.4	96.0	0.7	0.1	0.5	0.3
Latin America	13.0	49.3	-	31.6	1.0	5.1
Asia	22.6	58.4	-	0.2	16.6	2.2

It would be seen from the above that amongst the developing countries, Latin America only have some trade between developing countries (31.6%). Asia is very poor second. All these discussions only lead to the paramount need of co-operation between the countries. Developing

countries range from these with total dependence on imported finished products to those that manufacture medicinal chemicals and active ingredients.

The Developed Market Economics are net exporters of Pharmaceuticals. Their trade surplus increased from 1.64 billion US $ in 1976 to 2.28 billion US $ in 1979. This was further increased to 3.74 billion US $ in 1984. Of the seven most important pharmaceutical countries, USA, UK, West Germany, France and Switzerland showed very favourable balance in pharmaceutical trade, Japan had showed negative balance (1976-78 period), Italy also showed negative balance in 1977 and 1978. These favourable trade balances are likely to continue into the future, unless equitable international co-operation both economic and technological became more a reality than good wishes.

It should, therefore, be remembered that the developed countries have achieved advantageous positions through imaginative labour both in innovations of new drugs and marketing. The figures discussed in earlier paragraphs would clearly show that the wherewithal for R & D came mostly from local or developed countries sales. Therefore, the claim that the multinational companies earned their money by charging more than the developing countries and

hence they should atone their sins by free transferring technology and give economic, managerial help, would be an impractical proposition. The priorities of international drug administration are to make drug available to the half of the world population, who do not have access to this vital life saving items. This can only be achieved by twofold increase in production. This is possible if the world pharmaceutical industry acts as a whole entity. We have already seen that the requirement of drugs depend on the incidence of diseases, prevailing in a country. For developing countries, anti-biotics, anti-bacterials, anti-protozols, analgesics, cough and cold medicaments are more required because of under nutrition and bad sanitary conditions. National Governments should streamline the health care system and the procurement agencies through rationalisation of the whole system. Single point incidence of various union duties should be established. Even duplicity in existing distribution channels can be turned into a sales network with deep in roads in even remotest spots all over the least developed countries.

2.2 Production

There are several inter-related factors that affect the production of therapeutical substances, all of which must be taken into account when considering the desirability to manufacture. The four most important requirements relate to the availability of:

i) Adequate finance,

ii) Appropriate technology,

iii) Suitable product range,

iv) Availability of inputs

A further requirement is the availability of an adequate number of trained personnel.

The product range is determined primarily by market demand, and the scale of production. Economies of scale in the pharmaceutical industry are usually small and hence do not deter entry into the industry. Production of most types of drugs are carried out in multipurpose equipment following batch process based on unit processes and operations. Consequently, the production can be increased by allocating more equipment hours and if needed increasing the number, rather than the capacity o reaction vessels. Economies of

scale is not that important in the manufacture of bulk drugs. Even though the output of a particular drug may be small, even very small companies can economically produce several diverse products using the same equipment and personnel.

However, there is one constraint relating to the scale of production that can cause problems for small firms. This pertains to adequate quality control, the costs of which may be so high as to prevent the smaller manufacturers providing an adequate acceptable assurance of efficiency and safety. This problem can be solved by joint ventures. Several small manufacturing units can establish a combined quality control facilities, thereby sharing the fixed cost of a quality control laboratory amongst themselves.

There are, however, some items of bulk drugs (active ingredients) which when produced on a large scale, reduce the cost of production. In these cases, investment on global co-operation basis would be very fruitful. As far back as in 1948, the then Prime Minister of India, Mr. Jawaharlal Nehru, reiterated the need for foreign capital in the following words:

"Indian Capital needs to be supplemented by foreign capital not only because our national savings will not be enough for the rapid development of the country on the scale we wish, but also because in many cases scientific, technical and industrial knowledge and capital equipment can best be secured alongwith foreign capital."

The above statement is still very much applicable under today's context, particularly in the case of drugs and pharmaceuticals, manufacture and distribution. Apart from finances, scientific, technological and industrial knowledge, managerial skill is also very vital in the manufacture and sales of pharmaceuticals. We have already observed that a major part of the consumption of pharmaceuticals in developing and most of the developed countries came from seven sisters (USA, UK, FRG, France, Switzerland, Japan and Italy). Even the local production of other than these countries is by the Multinational Corporations belonging to seven sisters. Their share of market, range from 30% (in Egypt), 50% (in Argentina), 70% (in India), 78% (in Brazil), 90% (in Ecuador), or nearly 100% in many African Countries (PHN Technical note 86-31, World Bank, 1986).

To increase local ownership, many developing countries, have been promoting joint ventures between foreign and national companies. A bilateral cooperation agreement usually includes a commitment by the new industry in the developing country to buy active ingredients, excipients, packing materials or technology from its international partner. The international partner is committed to investing capital, transferring technology, training personnel, and selling raw materials to the new industry. Most developing countries in recent decades have developed an interest in the local production of drugs., as a way of improving their economy and decreasing their dependence. Lima declaration also emphasises that production in developing countries should increase substantially, so that availability of drugs would be ensured.

Substantial increase in production in this technology intensive industry can only be achieved in a short period only through joint endeavour between developed and developing countries. In an industry, where obsolescence is very rapid, the developed countries also stand to gain by such joint ventures. If joint ventures in capital intensive Hi-Tech manufacturing facilities are

undertaken on co-operative basis, this will minimise under utilisation/operational cost achieving higher level of "economies of scales"

2.3 Non-Tariff barriers:

Controls on the drug industry are many, and vary a great deal from country to country and many regulations hinder the free and useful movement of drugs around the world. All the controls are, however, not unnecessary. Some of them are vital to health care systems. Almost all countries have registration requirements, the most stringent being those of the USA and Canada, and some countries (West Germany & UK), in Western Europe. Unless a product is approved in the country of origin, it can not be imported by another country. This, however, is a very understandable regulation. Registration requirements vary widely between countries. Some countries do not admit foreign data (USA, Japan, India etc.) on one side and the other extremes are the countries, who accept foreign data as presented, provided it conforms with requirements of local regulations. International co-operation could help simplify the registration procedure. This will help free movement of drugs and reduce cost avoiding duplication.

Developed countries have their own national regulations, whereas till late seventies, many developing countries did not have any such regulations. The scenario have changed under the guidance of WHO. The main impetus being to ensure that available pharmaceutical products serve the health needs.

The need for international cooperation and understanding was realised by WHO, when they introduced "certification Scheme on the Quality of Pharmaceutical Product, moving in international commerce, and the associated Good Manufacturing practices and Quality Control of Drugs."

Manufacture of drugs (particularly active ingredients), produce many toxic effluents, which is hazard to environment. Environment protection has assumed a very important aspect while planning for any new production activity. The cost of treatment of effluent is also getting higher over the years. Cooperation between the nearby manufacturing units to establish joint effluent treatment facilities, would certainly reduce the cost.

Good Manufacturing Practice (GMP) is universally accepted requirement for the manufacture of Pharmaceuticals. It is part of Quality Assurance aimed at ensuring that the

product is consistently manufactured to a quality appropriate to its intended use. It is thus concerned with both manufacturing and quality control procedures. While the primary purposes of GMP is protection of the consumer, the secondary benefits include aid to the manufacturer, improved efficiency and some common ground for discussions between the regulatory bodies and industry. It is, therefore, obvious that GMP should not be used as a barrier to entry. Instead cooperative approach between various regulatory agencies and the manufacturing units, would help a long way in achieving the target of making drugs available to the population.

One of the most controversial aspects of Industrial development in Third World Countries is the one relating to the patent system, which seeks to protect the intellectual rights of the original discoverer of a product for his innovation and the Research and Development effort that has gone into it. Once company has invested in the Research, Development and marketing Society acknowledges and promotes research by granting patents. There are two types of patent protection: Product Patent which covers the substance itself, and process Patent which covers only the method of manufacture. The latter does not provide very strong protection for the innovators. Until the 1950s most

countries relied only on Process Patents for Pharmaceuticals. However, since then most developed countries have introduced Product Patents.

In developing countries, patent protection for pharmaceuticals has two aspects. On the one hand it can provide a favourable atmosphere for foreign investment, protect domestic innovation, if any, foster foreign innovation and facilitate domestic licence. On the other hand, according to a UNIDO Report (The growth of Pharmaceutical Industry in Developing Countries: Problems and Prospects, Vienna, United Nations, Industrial Development Organisation, 1978), Patents have often been used to secure import monopolies (stopping the importations of cheaper products) and to protect local manufacturers from producing similar products.

In the 1970's many developing countries tried to abolish or at least revise the international patent system, but with little success. Research based pharmaceutical industry is mounting pressure on developing countries in favour of product protection and extension of the patent term to 20 years and more in developed countries. The reason attributed for increasing the life of patent is time consuming testing procedures. It takes years to prove that a drug can help prevent, say a second heart attack.

Regulators are also more demanding. In the early 1960's it took ICI 31 months to get registration for Inderal, a novel remedy for heart attack, through all regulatory process. In the later 1970's and early 1980's it took ICI 108 months to win approval for Tenormin, a chemically related drug, starting from the time it was first patented in 1977.

One, therefore, can see that two extreme positions are being taken in this controversy. Those who oppose any change for more patent protection argue that it is the restrictive provision in the Patent Act, due to which no product patent is granted and the process patent is also for a shorter period ensures faster growth of the national sector for developing countries. The argument on the other side, is that the purpose of a patent being to afford and support the intellectual rights of the inventor, the enormous human effort and cost involved in the discovery of a modern drug, would be worth the risk, only if the inventor is protected from duplication for a reasonable period of years in which he can hope to recoup his huge investment. The patent system being one of the key elements necessary for the promotion of a healthy and prosperous economy system in which innovation and wealth creation prevail.

In the worldwide controversy about the patent the people tend to forget a basic principle i.e. business, may it be pharmaceutical (life saving), or otherwise would always survive on reasonable return on the investment. Mr. Henry Grabowski, an economist from Duke University, North Carolina, has calculated the net present value of a new drug is 40% lower than it was a decade ago. Due to uncertain profit from new products, the number of new chemical entities (NCE) are falling over the years, when NCE was 92 in 1961, it was 42 in 1976. Future generation should not accuse us for killing the goose that yielded golden eggs. It is, therefore, necessary to ensure as a Patent system that will encourage innovation. Both sides should meet half way to satisfy all round needs.

It is true that the discovery of a new drug is comparatively a rare phenomenon and requires investment in the research of an order that developing countries can ill afford. On the other hand the developed market economies insist on products being protected by Patent Law. The developing countries, on the other hand, wish to restrict the same by adopting process patents only. It is not a question of morality; it is a question of practicability. It has already been observed that the number of new chemical entities (drugs) is coming down substantially over the

years. Unless a global stand is taken on this question on the basis of cooperation, 21st Century will have very less "Wonder Drugs".

2.4 Trade Marks

Increasingly the ethics of wide spread utilisation of brand names and trade marks will continue to be questioned and it is also unlikely that these will be specifically prohibited in the future. The main reason could be that it would not be advisable to single out the drug industry from other industries, where brand names and trade marks are continuously being used. Abolition of brand names (i.e. trade marks) is a means to accomplish cheaper prices for the drug. It is claimed that by adopting generic names instead of brand names the prices come down very substantially as observed even in the USA, the leading drug manufacturers in the world. The industry, however, argues that brand names are a means of achieving product differentiation particularly, when there is no patent. The consumer associations all over the world, however, argued that a brand name provides an opportunity to the manufacturers to attach to the product certain hidden and undisclosed properties which are in reality not possessed by it. The manufacturers do this through constant advertisements in medical journals for ethical products and

aggressive high pressure sales techniques. Thus the sale of a product is not based on its inherent therapeutic properties but on promotion and advertisement. It is said that larger companies assail the doctors from all sides, often with attractive gifts and free samples which creates a psychological obligation to prescribe the drugs under their brand names. Once this campaign succeeds, the manufacturer has a monopolistic control over the market. As a result of the increased pressure from consumer movements and governments the International Federation of Pharmaceutical Manufacturers Association (IFPMA) developed a voluntary code of marketing practices in 1981 and W.H.O was asked to convene a meeting of experts in 1987, to develop ethical criteria for product promotion. In 1984, a new survey was undertaken which found that many of pharmaceutical firms were limiting their promotional claims in the third world to those supported by scientific evidence and were more willing to disclose side effects. This is very good beginning, although there is room for further improvement on the part of both multinational and domestic companies on mutual cooperation basis.

The uneven distribution of world drug consumption is associated with uneven distribution of drug production, which is concentrated in a few developed countries. The large companies oriented towards research and development

play a key role in production and continues to dominate the world market. However, the success of generic in the United States market is a new development and augur a better future, for drug consuming public.

2.5 Pricing policy

Pricing policies adopted in fixing the ex-factory prices of pharmaceuticals can broadly be divided into two categories. The first category is followed in free market economics, where the price is based on market acceptability in the presence of competition. If there is no competition, in the case of a new drug under patent, the price can be very high. The second category is followed in controlled economics, where price is on the cost plus basis taking into consideration the efficiencies. This category of pricing does not encourage innovation and make the country dependent on the outside technology.

In cost plus pricing if non-essential drugs are not covered by price control but essential drugs are strictly monitored and price controlled, the production and sales of non-essential drugs increases and availability of essential drugs diminishes. If the whole range of drugs are brought

under price control, then investment is diverted to other industries, where there is no such control. This was witnessed in India during 1980's.

Moreover, a differentiation should also be made between he cost and value of drug. There are many low dosage drugs where the actual material cost is low. For example, clonidine, ethinyl oestradiol, vitamin B12 etc., a pricing formula based on material cost and post manufacturing cost would be irrational. This compels the drug manufacturer to produce only high dosage high value drugs. A solution to such problems can be obtained through mutual understanding and cooperation between the manufacturers and regulatory agencies. International organisations can help to find a solution to avoid overcharging in some countries and adequate return through rational pricing in some others.

2.6 Mutual recognition of registration

It has been observed that registration of a product is one of the very important time consuming and costly part of pharmaceutical business. The cooperation between countries can help mutually recognise the registration. This will save time and money. Consequently availability will be quicker and cheaper.

3. Cooperation in technology-related areas

3.1 Management agreements/licensing

Through mutual licensing and/or managing units owned by different agencies cost reduction as well expansion of activities can be achieved. This is a strategy of major importance to the pharmaceutical industry and involves one company granting another the rights to manufacture, distribute and sell certain proprietary products in particular geographical areas. This mode of operation is frequently favoured by those unable and unwilling to make a direct investment in a major market and involves the supply of appropriate technical knowhow. The advantage to the licensor is not only the royalty payment but also the gaining of an experience in a new market. This way a multinational company can operate in a market where regulations prohibit the setting up of a foreign subsidiary. A further interesting aspect may also be, when any company develops an alternative to its own useful product and hence they dc not want to introduce the alternate product in the same market, the unused drug can be licensed to another firm and some developments cost recovered in the form of licence fee. It can also be exchanged for another product from the licensee company.

Marketing agreement differ from licensing, in that the associate is not given access to patented protection knowhow. Under this arrangement the associate company merely handles the sales of the product. Such arrangements can be extremely flexible and so are widely used throughout the industry on an international scale.

3.2 Buying/selling technology

Buying/selling technology would be taking place more and more in the future on national and international cooperation basis. This will increase the possibility of the reduction of development cost for basic research efforts when the cost could be divided between buyers and sellers with complimentary interest in the field. This was difficult to achieve in the past in a formal and voluntary way but because of increasing the cost of development of technology and reduction in the value of a new entity, R & D units, would be benefited by such long term arrangements with some units operating in areas not accessible to the units, who have developed the particular product.

3.3 Research and Development

Research and development is the principal mechanism through which society is supplied with new drugs to prevent, control and cure diseases. They are, therefore, very important for pharmaceutical companies in maintaining growth and competitive advantages. There is a continuing requirement for the development of new pharmaceutical product. The development of a new drug is a long term and continuing process that shows a high risk factor and which involves a considerable expenditure.

The great majority of pharmaceutical research and development effort is in the hands of private industrial sectors, to such an extent that it is often considered that the pharmaceutical industry has a virtual monopoly as far as the development of new drugs is concerned. Industrial research and development has a definite commercial target whereas the academic and other institutions tend to direct their research efforts towards an increase in basic knowledge of biochemistry and related disciplines. The search for new drugs is essentially empirical, and hence is inherently capital intensive. The systematic research efforts rapids screening on a large scale and other operations are, therefore, better suited to more plentiful physical and human resources that are available in industrial environment. There are, however, complaints that because of concentration of R & D efforts in industry, who

have commercial aims as priority, many times wasteful expenditures are incurred to develop alternative generic products (i.e."me-too drugs") this allegation is something like asking the impossible. It is now appreciated that such "me-too drugs" are often essential if a pharmaceutical company is to maintain its market position and hence its profitability and ultimate usefulness to the society. It has been stated earlier, recently because of fall in profitability of a new chemical entity the number of drugs introduced in recent years are much less when compared against previous wonder drug period.

Research for the development of new molecular entities (drugs) may be divided into four groups, viz. through synthetic routes, phytochemicals, biologicals and fermentation.

Synthesis and screening are directed and speculative screening involves the rapid biological testing of potential therapeutic material. Other routes viz. botanical, animal and microbial routes involve the identification and isolation of therapeutic process and natural sources and is the traditional route of the new drug. Irrespective of the source of origin of a new type of drug there are a number of

sequential steps that must be followed before the product is commercially proven. The duration and cost of each stage may vary considerably.

New therapeutical products that appear on the market are generally classified into four distinct types namely :

- completely new chemical entities (NCEs) comprises products that are new single chemicals not previously known.

- duplicate products, that are virtually identical with materials already on the market.

- compounded products, comprising materials with more than one active ingredient.

- alternate dosage forms, which are materials previously offered in one form (tablets, capsules, liquid, aerosol etc.) and now available in another.

It will be readily realised that the first category only must be used as a measure of the rate of pharmaceutical innovation, although these represent only between 10% and 20% of new products becoming commercialised in any one year.

There is a steady overall decline in the number of new chemical entities appearing on the worldwide markets over the past several years. This can be attributed to several causes including the impact of increasing severe drug registration regulations in the more advanced countries, cutbacks in research expenditure due to world recession, and profit limitation that restricted the amount of finance available for further research and development. Some critics suggest that the efficiency of the industry has declined which has restricted new product development but this is an unfounded complaint. Of great importance in causing a decline in the rate of product innovation is the fact that there were very rapid advances in the biomedical sciences over the 1950's and 1960's, these being accompanied by the development of numerous significant new drugs. Future advances are becoming increasingly difficult as the output of basic biomedical knowledge has not kept pace with that of medical chemistry.

Most of the developments in the developing countries is on process improvement where there is no patent protection for product. This has helped many developing countries to become near self-sufficient in the production of certain groups of drugs. Formulation development is also very important as the consumer takes the formulation and various aspects like life of the formulation viability etc., and dependent on the formulation techniques. International cooperation in this field between the countries and the units is an essential requirement.

Substitution of imported materials can be achieved through developmental work. In this field also inter-units cooperation would help reduce the cost of development when there is a free exchange of data.

3.4 Traditional medicines

For thousands of years mankind has employed variety of ways of dealing with diseases. In all societies there are fast remedies and people advise on how to deal with disease and its consequences. Even today a vast number of people may be 2.5 billion depend on traditional medicines. Even in countries where modern health care is available people still depend on traditional treatment. Some of the traditional medicines are very effective, some are not ,

some are only mere witchcraft. Countries like India, China developed very strong traditional medicines. These schools however did not develop with times. International cooperation between the countries under the aegis of international agencies needed to bring these schools up to the modern level.

4. Other relevant important aspects

4.1 Depending on level, parties, issues and duration the specific form on cooperation can vary from limited aspect period i.e. bilateral understanding between two units (say for supply of raw materials), to all encompassing industry-wise consensus (say, adherence to a particular quality parameter). The diverse forms of cooperation being available, offer the very flexibility and uniqueness which may be desired by some participating members.

4.2 The areas available for cooperation have different potential. From most obvious and direct one-procurement, to rather uphill but yet possible formulary. Specific "coming together" will choose its own depth and form in meeting their own requirements.

4.3 Over last several decades, various Governments are clearly offering constructive policies for growth in cooperative activities. On the international scene the prospects are all the more encouraging, as is evident since last few years.

4.4 International organisations due to their intrinsic universal presence, and exposure to latest developments are uniquely positioned for extending the national level co-operative efforts to multinational fields. They have a vital role in harnessing the benefits of international cooperation to all the nations, including those developing ones.

It is also essential to consider greater level of co-operation among Government and Industry (Japanese Style)

5. Conclusions and recommendations in summary

Summary

The costs of Pharmaceutical are going up over the years and the prices many times even do not reflect the cost. International Cooperation and understanding is needed

to avoid aggravating the situation. It has been felt since World War II that the cause of all wars is mainly unequal economic opportunities, therefore, economic disparities should be removed as much as practicable. The pharmaceutical industry being the life saving industry, the requirement of cooperation is all the more very important. The following paragraphs would summarise the discussions made above.

1. Definitions, aims

1.1 Improving Managements: The co-operation aimed at is expected to optimise/pool resources so as to enhance the efficiency of the Industry as a whole in meeting both domestic and international demands of pharmaceuticals at a competitive cost.

1.2 Technological Levels: The cooperative ambience is sought to usher in a quantum of the Pharmaceutical technology and related engineering applied in the industry. This will serve a multifold purpose, lower costs, superior and uniform quality, widely spread dissipation of latest techniques. Enhanced cooperation in raising technological levels will contribute towards greater safety standards.

1.3 Foreign Trade - reexport: An offer through industry level cooperation, is bound to result in more remunerative price. The increased co-operation at the industry and regulatory levels will permit pooling of crucial capacities thus enabling meeting export demands at short notice. This will go far in expanding the trade, resulting, in part from earning precious Foreign Exchange, reinforcement of the strengths of the Industry.

2. Cooperation in Trade and other economic aspects

2.1 Trade: The properties of Drug availability as per National Health Policy can be better responded if the Industry acts as a whole entity. Streamlining, rationalisation, single point incidence of various union duties can be easily approached. Even duplicity in existing distribution channels can be turned into a network with deep in-roads in even remotest spots all over the nation.

2.2 Production: Joint investment plans or venturing in capital intensive Hi-tech manufacturing facilities, if undertaken on co-operative basis will minimise under utilisation/operational cost achieving higher levels of "economies of scale".

2.3 Non-tariff barriers : Various commercial/statutory impediments can be over come through mutual accommodation and agreements. The differences now wedged due to trade marks, patents, pricing etc., will be nonexistent once a cooperative functionary is established.

2.4 On an international scene an uniform policy on registration, GMP, environmental protection, patents, trade marks etc. will improve availability of medicines substantially.

3. Co-operation in technology-related areas

3.1 Through mutual licensing and/or managing units owned by different agencies (dedicated capacity lending/borrowing), the technological strengths of a particular unit can be best exploited. The facility and skill available for a particular dosage form may not suit a product. In such cases, on a reciprocal or co-operative form, capacities can be "bartered".

3.2 The above can be extended to outright leasing out or procuring technological set-ups on long term basis towards mutual and joint benefits.

3.3 The research and Development offers the most fertile ground for implanting co-operative activity. Expensive facilities, common raw material requirements, development of rare skills through sustained training, extensive drug trials etc., are activities needing a very wide span and base. Cooperative efforts generated by the entire Industry can alone meet the requirements in the truest sense.

4. Other relevant important aspects

4.1 The quality of life differs from country to country, community to community so widely that sometimes one tends to think they belong to different planets. This disparity can be minimised through cooperation.

4.2 In pharmaceutical industry co-operatives can achieve worldwide rationalisation of formulary, exchange of information will avoid wasteful duplication of various activities, help procurement of technology and or various input materials. Manpower development is another important aspect of pharmaceutical industry. This can be achieved through cooperation between nations and in a country between units.

4.3 Government policies can be implemented in right directions when approached jointly on a cooperative basis.

4.4 International organisations like UNIDO, WHO can play vital role in achieving co-operation at various levels.

Conclusions and recommendations

The past decade has witnessed a major debate on pharmaceutical industry. Doubts were raised about the efficacy and potency of many drugs. Irrational combinations of the drugs and high pressure techniques adopted in promoting such combinations were under severe criticisms. The cost of treatment was felt to be very high. Both in developing and developed countries, consumer associations are on war footing to challenge the manufacturers.

The manufacturers also point out the delay in registration of new drugs, various barriers in achieving free movement of the drugs, increasing input costs, high cost of trained labour etc., are the impediments for better pharmaceutical availability. They also contend that drug cost is only 15 to 20% of the total cost of treatment. The

associations and Governments do not make any attempt to contain the cost of medical advice, nursing, laboratories (for diagonostic purposes), hospitals, nursing homes etc..

To improve health standard of the people these aspects need to be studied based on cooperation of various agencies at international and national levels. It is now high time to introduce prescription audit in all countries. Registration procedures to be streamlined and international agency (WHO) should monitor and issue certificates, which should be accepted by all countries. Patent system should offer enough protection to encourage innovation so that the age of "wonder drugs" can come back. The possibility of exploitation should be controlled and monitored by international agencies like UNIDO. An immediate meeting under the joint auspices of WHO and UNIDO should be held to decide about the various aspects of cooperation for the healthy growth of this industry.