Perspective on Developing Nations

Problems and obstacles of pharmaceutical sector transferring technology to developing countries

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While representing the pharmaceutical research-based industry located in countries with a free-market system and speaking therefore from the point of view of private ownership of these enterprises and technology development by them, we do fully see and recognize the numerous problems and difficulties in the field of drug supply in the developing countries.

In view of the magnitude of the problem and also of the necessity to find a solution, we shall try to be as objective as possible in the statements which will follow, but shall, at the same time, not hesitate to draw the attention of the participants of this conference to problems, difficulties and obstacles which were created and do exist in a number of developing countries, thus hindering the flow of technology and a fruitful cooperation with those who create this technology.

I want to emphasize that these frank remarks should not be considered as a criticism, but as a constructive contribution for a discussion.

This short presentation will be divided into the following chapters:

1. Pharmaceutical innovations, technologies and sources thereof.
2. Economic aspects of pharmaceutical innovations.
3. Protection of investments in pharmaceutical research and development.
4. Availability of pharmaceutical innovations and technology for developing countries.
5. Efforts undertaken by United Nations organizations to promote technology transfer.
6. Obstacles and problems in the transfer of technology.
7. Fruitful cooperation between innovators and developing countries in the field of pharmaceuticals.

PHARMACEUTICAL INNOVATIONS, TECHNOLOGIES AND SOURCES THEREOF

Technology is considered to be one of the most important instruments in the process of industrialization and economic development. Pharmaceutical technology is a term which includes basic research and development, leading to new active chemical substances which can be used for human therapy, and developing new forms for the applicaton of the aforementioned active substances in human therapy or new processes for their manufacture.

Without denying a certain importance to the last two activities, we do consider a genuine innovative activity leading to the discovery of new and novel drugs much more important in the process of industrial and economic growth and shall therefore concentrate on this kind of activity.

The two decades after World War II were characterized by an unprecedented growth of research in the pharmaceutical field. As a result, many novel classes of drugs have been introduced into therapy during this period, of which the following can be mentioned: psychotropic drugs, salidiuretic drugs, oral antidiabetics, antihypertensive drugs, antihistaminics, antitussives, muscle relaxants/antiparkinson drugs, corticosteroids, anti-TB drugs, antibiotics, tranquilizers.

The rate of introduction of new drugs into medical practice, for example, in the U.S.A., is well known. If we exclude relatively minor products and new specialty dosage forms and combinations of previously available drugs and focus only upon the new therapeutic agents *most significant to medicine*, then there were introduced in the U.S.A.: (average per year!) 19 new entities from 1946-1950; 31 new entities from 1951-1955; and 39 new entities from 1956-1960.

In the late 1950s and early 1960s, the well-known Kefauver Hearings were held in the U.S.A. and the Kefauver-Harris Amendment implemented. The consequence was a very tough scrutiny of novel active agents by the Food and Drug Administration and, as a result of the new conditions, there were only 20 important new entities introduced into therapy in the U.S.A. in the years 1961-1965.

Since then, this figure has diminished: 12 entities in the years 1966-1970, and similar figures up to now. While, in the early 1960s, out of 2,000 novel chemical compounds synthesized and studied in pharmaceutical research, one could be introduced into therapy, the corresponding figure today is only one out of 10,000 such compounds.

Discovery Origins

When analyzing objectively the sources of important novel pharmaceutical agents, we come to the conclusion that practically all these substances were discovered by private pharmaceutical enterprises of the United States, the Federal Republic of Germany, Switzerland, France, Great Britain, Japan and some of the Nordic countries.

**Director, Sandoz Ltd., Basle, Switzerland; paper presented at the International Conference "Transfer and Development of Technology . . . in the Pharmaceutical Industry" in Belgrade, Yugoslavia in June 1979.*

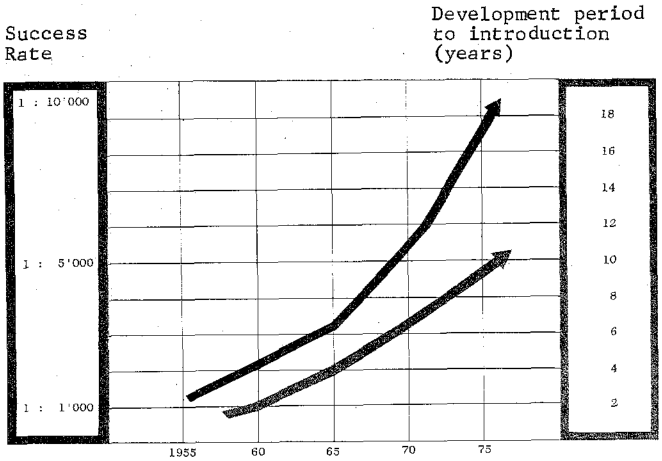
The costs involved in the discovery of these new drugs, borne by the private pharmaceutical enterprises of the aforementioned countries, amount to 10-15% of their turnover and were estimated to be now about $3 billion per year, or even more than that. Statistical studies indicate that the costs for research and development of one new therapeutic agent is somewhere around 100 Mio Swiss Francs.

Of importance in the context of our presentation is the time lag between the discovery of a new pharmaceutical agent and its introduction into therapy, It has been shown and proved that this time lag today is around 10 and more years. This figure is of great importance, since it has to be correlated with the duration of patent protection which, on the average, is 15 - 20 years, but not in developing countries where we are faced with patent terms as short as five years or even no patent protection at all. We shall revert to this problem later on.

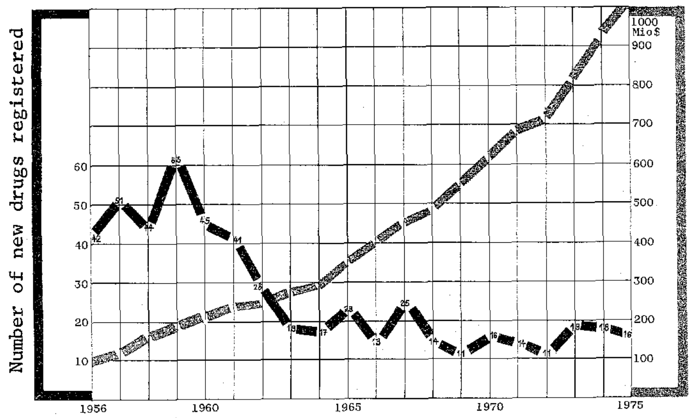
ECONOMIC ASPECTS OF PHARMACEUTICAL INNOVATIONS

We have already indicated that the major part of pharmaceutical research in the Western countries is carried out in private pharmaceutical enterprises, and that statistics prove that research and development cost these companies up to 15% of their turnover or roughly 100 Mio Swiss Francs per single new therapeutic agent.

Research costs are very rapidly increasing, but the success rate is rapidly declining, as illustrated in the following two tables:

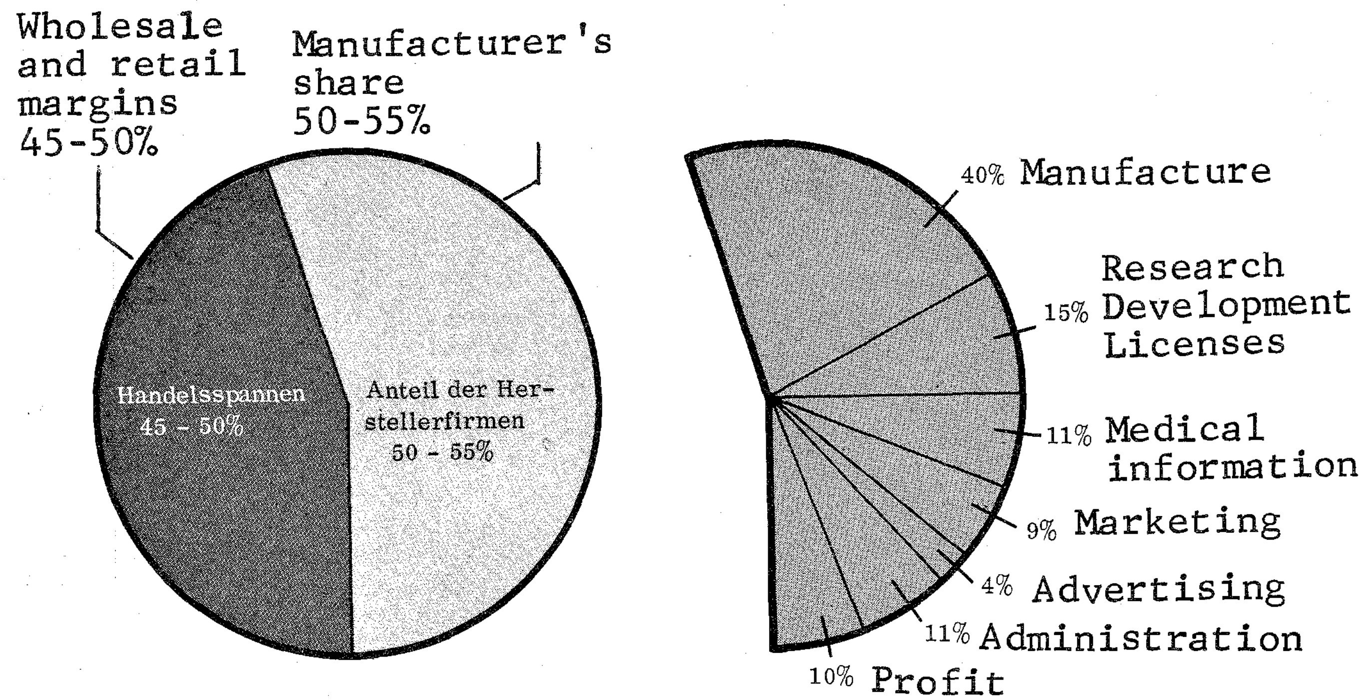


Pharmaceutical research: decreasing success rate, increasing product development period.



Research grows costlier but not more productive. R & D expenditure in the U.S. pharmaceutical industry and the number of new active substances registered in the U.S.A.

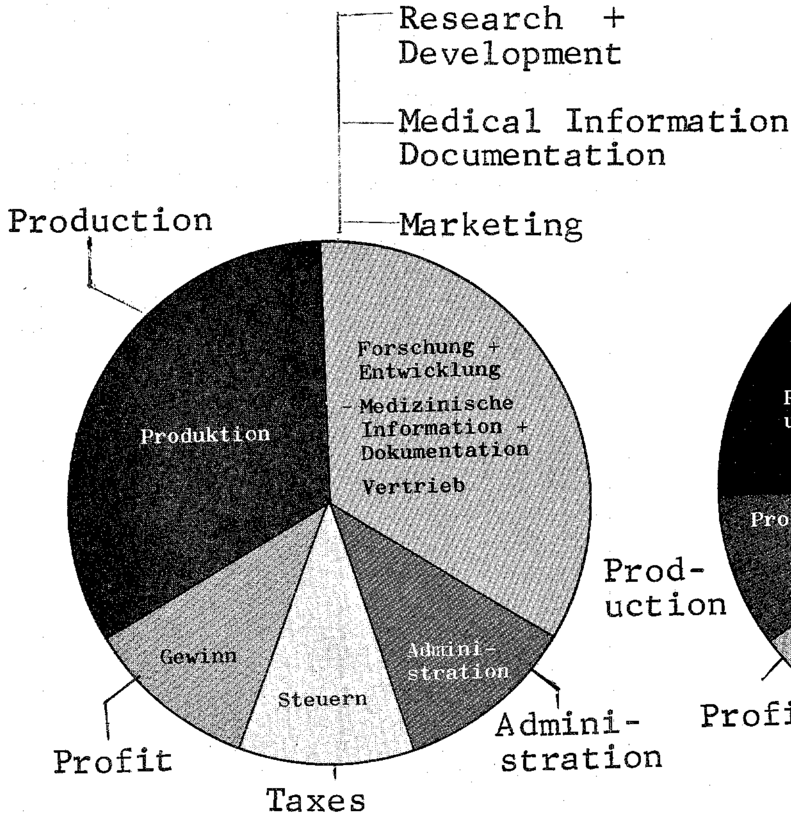
Investment in drug research must therefore be considered to be extremely risky. Enterprises which carry out such research activity find themselves confronted with growing difficulties with respect to recouping



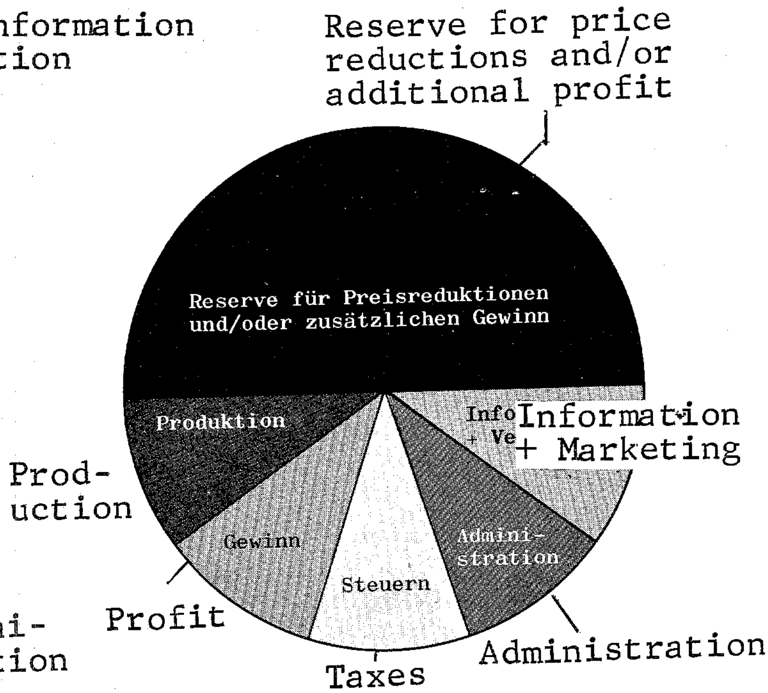
Price structure of drugs from research-based companies.

their research and development costs mentioned above. These difficulties stem from various sources. To be mentioned are governmental regulations concerning the safety of drugs, the prices of drugs, freezing of prices despite inflation, and the complicated bureaucratic procedures. Not to be neglected is the growing competitive, imitative activity of smaller or even medium companies all over the world, which themselves carry out no or little research and simply profit from innovative companies.

The next chart shows the price structure of drugs from research-based companies, the price and cost structure of imitators as compared to innovators:



Cost structure of research-based pharmaceutical companies



Cost structure of imitative pharmaceutical companies

The conclusion is clear and simple: Imitating companies bear little risk and have the possibility of much higher profit margins than innovating companies.

PROTECTION OF INVESTMENTS IN PHARMACEUTICAL RESEARCH AND DEVELOPMENT

In view of what we have said above with respect to the high costs of research and development, the high risk associated with corresponding investments, and the reduced chances of success, it should be clear that the rare positive results achieved in the pharmaceutical field by a smaller number of private pharmaceutical enterprises deserve to be, and must be, properly and adequately protected.

When speaking of results achieved, we must differentiate between results which can be — and if possible are — patented, and results of research and development which fall into the category of know-how. As far as know-how is concerned, we must be aware of the fact that, in the majority of countries, there are no specific laws to protect know-how and, therefore, the common practice of the owners of know-how is to keep it secret.

As far as patentable inventions are concerned, it is usual to apply for patent protection. If the application is successful, the innovator is rewarded with a patent. The latter represents a negative right in that it does not automatically allow the patentee to do anything, but only prevents third, not involved, parties from doing what the patentee has protected in his patent.

In the field of pharmaceuticals, we have today a clear situation in that, worldwide, there are only about a dozen countries which grant really enforceable pharmaceutical patents. In the rest of the world, there is, for pharmaceuticals, either no patent protection at all or, if there is, the available protection is so weak that it is not worthwhile to apply for it. In what is to follow, we shall deal with this situation.

Patent protection in various countries

When evaluating the status quo of the patent protection, we have to look specifically at the type of protection: Product per se protection, product-by-process protection, process protection. The strongest protection is the one for a product per se; the weakest is process protection.

Another important factor is the duration (term) of patent protection. It varies from 5 to 20 years, and it is obvious, in view of the long development period of a new drug (10-12 years) that "real" protection starts only with a term of at least 15 years.

A third factor for evaluation is the enforceability of protection. This is the most complicated problem, and we can quote mainly patent invalidity for nonworking of the invention in the country concerned, availability of compulsory licenses, and the compensation (if any) associated therewith, the chances of successfully preventing infringement before the courts, etc.

Keeping these three major factors in mind, we can say that adequate patent protection exists in Japan, Australia, South Africa, Austria, West Germany, France, Switzerland, Great Britain, Italy (in future!), and the U.S.A.

Inadequate patent protection exists in the Philippines, South Korea, Taiwan, Thailand, the German Democratic Republic, Hungary, Poland, the Soviet Union, Czechoslovakia, Yugoslavia, Nigeria, Morocco, Egypt, Canada and Argentina.

De facto no patent protection: India, China, Indonesia, Turkey, Saudi Arabia, Libya, Ghana, Venezuela, Mexico, Brazil, and the majority of other developing countries.

Developing Countries

Having regard to the above, the question poses itself as to why developing countries are so very much concerned about pharmaceutical patents, since it is a clear case that, in their part of the world, as well as in the majority of socialist countries, the pharmaceutical innovator already now has little or no protection at all. It is also difficult to understand why such important organizations as UNCTAD are so ardent in their demands to change the existing patent system in favor of developing countries. What is being requested by UNCTAD has already been in existence for quite a while!

But what are the consequences for developing countries, stemming from the fact of inadequate patent protection? Are the experiences made accordingly positive? Without aiming at a generalized statement, I should like to quote Mr. Ramachandran, Secretary to the Government of India, Department of Science and Technology, at the WIPO Colombo Symposium in 1977:

> The provision of endorsing the license with the words "license of right" also does not appear to be meeting the overall requirements of accelerating industrial development. Out of about 3,000 patents filed every year in India, 673 were endorsed with the words "license of right" during 1975-76. A major part of these (84%) related to chemical processes, 12% related to drugs and 4% related to articles of food. In the subsequent year, the number of licenses endorsed with the words "license of right" showed a steep decline to around 273, with approximately the same distribution in the different categories related to chemical processes, drugs and food articles. During the current year, the number of such licenses over a 10-month period is only of the order of 60, with almost the entire number in the chemical process sector. Thus, *it appears that the provision of the license of right has resulted in a situation where patents relating to these areas, namely chemical processes, drugs and food articles, are no longer being presented for registration.*

In brief, it appears that both the provision on "compulsory licenses" and that on "licenses of right" have not yielded the results expected of the patent system in India.

The interpretation of this statement is very simple: when the private pharmaceutical industry understood properly the implications of the new Indian Patent Law, it was realized that the de facto protection in the field of pharmaceuticals, agrochemicals and foods is practically nil. The costs involved in filing patents and paying for the process of prosecution would have been higher than any kind of return on the patents obtained.

The pharmaceutical industry then simply stopped filing patent applications in India and this situation will remain the same for as long as the Indian Patent Law is not changed. The question should now be posed whether the vacuum in the field of pharmaceutical patents in India has stimulated the inflow of foreign technology into that country.

I do not think that this question can be answered in the positive, and I should like again to express my surprise at the apparent aim of UNCTAD to erode or destroy the patent system.

AVAILABILITY OF PHARMACEUTICAL INNOVATIONS AND TECHNOLOGY FOR DEVELOPING COUNTRIES

We are seeking better ways and means for the transfer of technology to developing countries and to achieve this transfer under more favorable conditions. When speaking of favorable conditions, I think that it would do no harm to have a look at the conditions as they prevail today.

One of the countries which was, and still is, very active as far as cooperation with developing countries is concerned, and particularly active in the field of technology transfer, is the Federal Republic of Germany. Various important German enterprises are actively engaged in technology transfer, for example to Brazil, where they have built large factories and employ many thousands of Brazilians. It is, therefore, perhaps a surprise to learn that, in the four years from 1972-1975, the total of all transfers from Brazil to Germany in the pharmaceutical field (royalties, dividends and profits) was only 0.9% of the turnover of these enterprises in Brazil.

Another figure demonstrates this situation even more clearly: The German pharmaceutical firms obtained from Brazil in 1975 a total of 9.43 million DM for royalties, transferred profits and profits from exports of raw materials and finished products to Brazil.

I wonder whether you would consider these 9.43 million DM to be excessively high or even exploitive. It corresponds, in fact, only to the costs of about 2.36 working days for research carried out in the German pharmaceutical industry! Similar figures can be produced for India or other developing countries, and I think that it is not exaggerating to say that there are few private Western pharmaceutical companies left which consider their engagement in the developing world to be profitable.

If we are interested in having specific figures as far as the economic engagement of the developed, market-economy countries is concerned, we can refer to a study prepared by Dr. Sronek, at the request of the UNCTAD Secretariat.

Value of total exports by regions of origin and destination
(Billions of U.S. dollars)

Origin / Destination	World	Developed market-economy countries	Socialist countries of Eastern Europe: Total	Socialist countries of Eastern Europe: USSR	Socialist countries of Asia	Developing countries
World						
1958-1960	117.0 (100%)	74.9 (64%)	11.4 (10%)	-	2.1 (1.9%)	27.8 (24%)
1968-1970	274.8 (100%)	192.6 (70%)	25.4 (9%)	-	2.8 (1%)	52.7 (19%)
1973	574.4 (100%)	409.3 (71%)	51.1 (9%)	-	5.6 (1%)	103.9 (18%)
Developed market-economy countries						
1958-1960	77.3 (100%)	53.6 (69%)	2.0 (3%)	-	0.5 (0.6%)	20.7 (27%)
1968-1970	195.2 (100%)	149.1 (76%)	6.1 (3%)	-	1.3 (0.7%)	38.0 (19%)
1973	407.8 (100%)	311.8 (76%)	16.2 (4%)	-	3.4 (0.8%)	73.7 (18%)
Socialist countries Eastern Europe						
1958-1960	11.7 (100%)	2.2 (19%)	7.2 (61%)	-	1.4 (12%)	0.9 (8%)
1968-1970	27.7 (100%)	6.3 (23%)	16.3 (61%)	-	0.9 (3%)	3.5 (13%)
1973	53.0 (100%)	14.1 (27%)	29.9 (56%)	-	1.6 (3%)	6.8 (13%)
Developing countries						
1958-1960	26.0 (100%)	18.8 (72%)	0.8 (3%)	-	0.2 (0.8%)	5.9 (23%)
1968-1970	49.7 (100%)	36.4 (73%)	2.1 (4%)	-	0.6 (1.0%)	10.2 (21%)
1973	108.7 (100%)	81.4 (75%)	4.1 (4%)	-	0.7 (0.6%(	21.4 (20%)

Source: UNCTAD, *Handbook of International Trade and Development Statistics, 1976,* table 3.1.

The interpretation of this chart is quite easy, and I shall therefore, not go into further details of it.

EFFORTS UNDERTAKEN BY U.N. ORGANIZATIONS TO PROMOTE TECHNOLOGY TRANSFER

In recent years, the United Nations and its organizations such as UNCTAD, UNIDO, WHO and partly WIPO have increasingly been concerned with the activities of transnational companies, with pharmaceuticals, with the protection of innovations in this particular field and with the transfer of technology to developing countries.

The overall objective of all these efforts is the idea of a New Economic Order, within which a more just distribution of the world's wealth is the final goal. Within all these activities, UNCTAD's efforts concerning an international code of conduct for the transfer of technology and, within this code, in particular the aspects of pharmaceutical patents and pharmaceutical trademarks is of special importance.

UNIDO's activities show certain parallels with UNCTAD's efforts. WHO is concerned with the problem of the availability of essential drugs for developing countries and especially with the availability of medicines against tropical diseases. Finally, WIPO is working on a revision of the Paris Convention, on the Establishment of Model Laws for Developing Countries on Patents and Trademarks, and on the drafting of a Licensing Guide for Developing Countries.

While in principle we should all welcome these activities and efforts, we should not hesitate to express our concern over the lack of objectivity and understanding of the functioning of transnational pharmaceutical enterprises and over a clearly recognizable switch toward a political approach to these very important problems.

The regulations aimed at are rather of a compulsory nature, putting the pharmaceutical innovator into a defensive position.

One of the main reproaches our industry has to make is that, although it is the major source of pharmaceutical innovations, it is deprived of the right to express its views properly. The result is that precisely those whose very property is being discussed cannot make their voices heard in an appropriate way.

Without going into further details, we should simply like to quote a conclusive paragraph from a recent resolution of the Fifth Conference of Heads of State or Government of Non-Aligned Countries in Colombo:

(c) that in the context of the revision of the industrial property systems, consideration be given to excluding pharmaceutical products from the grant of patent rights or alternatively the curtailment of the duration of patents for pharmaceuticals;

(d) the elimination, wherever possible, of brand names and the adoption of the generic names for pharmaceuticals; and provision of information only from official sources;

(e) the establishment by each developing country of its own pharmaceutical industry as appropriate, beginning with formulation and packaging and building up to more complex production activities;

In summarizing, we cannot avoid characterizing the feelings today of the private pharmaceutical innovator as a sense of unfair treatment by important U.N. organizations which probably believe that compulsion is the answer to the manifold problems of developing countries in the field of industrialization (in the field of pharmaceuticals) via expropriation of the private pharmaceutical industry's property rights.

OBSTACLES AND PROBLEMS IN THE TRANSFER OF TECHNOLOGY

I should like to quote the statement made above with respect to patent erosion. A vacuum in the field of patents is quite certainly an obstacle to the transfer of technology and to the transfer of know-how. Other obstacles are numerous, but the overall impression private pharmaceutical industry has today can be related to a statement made by the then Finance Minister of Sri Lanka in 1976: "What I have in mind is an export-oriented approach to foreign investment (technology is part of investment), under which the investor fades out once he has performed his catalytic function . . ." We have encountered similar attitudes in many other countries, and one should not be surprised to find us more hesitant to part with our costly technology.

Other obstacles are in the field of governmental registration of license or cooperation agreements, in the field of royalty transfer, in bureaucratic procedures or even in an absolute prohibition of the transfer of dividends or royalties. But since we find ourselves here in Belgrade, it might be of interest to go to some extent into the latest Yugoslav law which concerns long-term cooperation between Yugoslav enterprises and foreign partners.

This law, seen together with the law of January 1977 which regulates the introduction and the trade of medicines in Yugoslavia, is of such a nature that there is left little or no incentive for a private pharmaceutical enterprise to enter, or to continue, the transfer of technology to his Yugoslav partner. I now draw your attention to those paragraphs which our industry deems unacceptable and detrimental to future cooperation;

1. The Medicinals Law of January 1977 implies the ownership of the trademark of a drug introduced on the Yugoslav market by the Yugoslav enterprise. In many cases, these drugs were developed by western research-based transnational pharmaceutical companies, which established over many years internationally-known trademarks for their products, which are an important tool for the characterization of their products and are assumed to be a guarantee for the quality of these drugs. It is quite evident that these enterprises cannot give the ownership of these trademarks, but would be willing to license them to their Yugoslav partner. If this Medicinals Law is interpreted in the way it is today, it must be feared that western pharmaceutical enterprises will become hesitant as far as future cooperation with their Yugoslav partners is concerned.

2. The Law of August 1978 on long-term cooperation between Yugoslav and foreign enterprises contains a number of clauses which prohibit the drafting of cooperation contracts in the way as it was done up to now. Some of these clauses deserve to be mentioned here:

—2.1 In order to establish a close cooperation between the Yugoslav and the foreign, technology supplying firm, it was often mutually agreed that starting materials and intermediates for the final products be obtained from the innovator. The law on cooperation prohibits such clauses, and the innovator therefore has little or no control over the quality of the final product which is associated with the innovator's name and reputation.

—2.2 The foreign innovator is rather upset by clauses of the new law which aim at great freedom of exportation of the final products now to be granted to the Yugoslav partner. Since the majority of the western enterprises are active in the majority of developed and developing countries, they now realize that they would be competed within their traditional markets by their Yugoslav partners. Planning for their future activities would become difficult or impossible, and it is this clause which, in future, will lead to great hesitance of Western enterprises to enter into new cooperation agreements with Yugoslav partners.

— 2.3 In the past, Western enterprises who wished to establish cooperation with a Yugoslav partner supplied the latter with all the necessary available information which, otherwise, was part of their trade secrets. The new law on cooperation, as we understand it today, de facto prohibits secrecy agreements between the Yugoslav and his foreign partner, giving the former the right — after a three-year period from the termination of the cooperation contract — to give away secret know-how and other information to anybody he wishes to choose.

— 2.4 In addition to the above clauses, the law on cooperation prohibits any kind of restrictive clauses concerning specific starting materials or intermediates, specific trademarks, specific manufacturing processes and specific marketing channels.

In summarizing, it can be concluded that the law on cooperation gives all the advantages stemming from cooperation to the Yugoslav partners of a Western enterprise, neglecting the legitimate interests of the latter. The consequences for future cooperation have already been mentioned in the introduction to this chapter.

FRUITFUL COOPERATION BETWEEN INNOVATORS AND DEVELOPING COUNTRIES IN THE FIELD OF PHARMACEUTICALS

At the beginning of this short presentation, I stressed the fact that private pharmaceutical enterprises are domiciled in a few countries only, while all peoples of this world should be in a position to profit, as far as the health care is concerned, from all the innovations which we are fortunate enough to have today in the field of drugs. The question remains, however, how to achieve this goal.

I believe that we have to realize that a private pharmaceutical enterprise like all enterprises in the free-market system, can survive only as long as its operations are profitable. In the field of pharmaceuticals, the question of survival is linked with extremely high costs of research and development, with the very high risks associated with the investment needed for these activities, and the fact that this industry suffers today from the very low number of positive innovative results. These enterprises are not in a position to give away the rare results of their research work without an adequate return on their investments.

It has often been said at UNCTAD conferences and in individual discussions with delegates from developing countries that this return on investment and compensation of research costs should be borne by developed countries only. Should this modus be established, it would undoubtedly lead to higher prices for drugs in developed countries and, in the majority of these countries, to higher costs for the governmental or semi-governmental health services.

I do not think that such an approach would have a realistic chance of success, since already now our pharmaceutical enterprises find themselves under increasing pressure from the respective national health services, from the health insurance companies and even from their respective governments. What is then the answer to this problem?

We have to accept the fact that developing countries must achieve a higher rate of industrialization, which should lead to a reduction of unemployment and to an improvement of economic conditions. Such a development would certainly be in the interests of developed countries as well. But I do not think that such a development can be financed or implemented by private industries in general and, in the pharmaceutical field, by the western private pharmaceutical companies.

Nor do I believe in the possibility of U.N. organizations like UNCTAD, UNIDO or WHO being able to force the pharmaceutical industry to give away its costly technology for practically nothing.

What remains, as I see the problem, is the necessity for a dialogue between developing countries and the pharmaceutical industry. But this dialogue will only be fruitful if the pressure exercised today by UNCTAD and other U.N. organizations and by certain governments of some developing countries ceases to prevail. Negotiations usually proceed well if both parties feel the right climate for a dialogue and if they are not under the impression that they are being forced into something which is against their interests.

We know well from past experience that the only contracts and treaties that are honored are those which are fair and acceptable to both parties concerned. What we see today in the field of pharmaceuticals and especially in the field of the transfer of pharmaceutical technology is not what we would consider to be acceptable, and I would like to close these considerations with the hope that all parties involved finally realize that pressure and compulsion are not likely to create the climate and good will which are a prerequisite for fruitful cooperation.

In this connection I should like to stress again the importance of the Yugoslav initiative to bring all of the involved parties together, so that a fruitful dialogue can start, hopefully leading to a better understanding of the various problems of the parties concerned.