ICEG EC

International Center for Economic Growth
European Center

# The Expected Effects of the EU Accession on the Pharmaceutical industry in Hungary

**By: Peter Tordai**

May 2003

Budapest

# Table of contents

## List of terms and abbreviations

| | |
|---|---|
| **API** | Active Pharmaceutical Ingredient |
| **Bioequivalent** | Formulations are said to be bioequivalent if the nature and extent of therapeutic and toxic effects are equal following the administration of equal doses. |
| **CADREAC** | Collaboration Agreement between Drug Regulatory Authorities in European Union Associated Countries |
| **CEE** | Central Eastern Europe |
| **COMECON** | Council for Mutual Economic Assistance |
| **EC** | European Council |
| **ECJ** | European Court of Justice |
| **EFPIA** | European Federation of Pharmaceutical Industries and Associations |
| **EGA** | European Generic medicines Association |
| **EMEA** | European Agency for the Evaluation of Medicinal Products |
| **EU** | European Union |
| **FDA** | Federal Drug Administration |
| **FDI** | Foreign Direct Investment |
| **GCP** | Good Clinical Practice |
| **GLP** | Good Laboratory Practice |
| **GMP** | Good Manufacturing Practice |
| **INN** | International Non-proprietary Name |
| **IP** | Intellectual Property |
| **MNCs** | Multi-National Corporations |
| **"Me-too" products** | Patented products with similar therapeutic effects targeting the position of the branded ethical drug |
| **MRP** | Mutual Recognition Process |
| **NBE** | New Biological Entities |
| **NCE** | New Chemical Entities |
| **OECD** | Organisation For Economic Co-operation and Development |
| **OEP** | (Hungarian) National Health Fund |
| **OGYI** | (Hungarian) National Institute of Pharmacy |
| **OTC** | Over The Counter, non-prescription medicines |
| **Parallel Trade** | Purchase of goods at low prices in one country and the subsequent resale of those goods at higher prices in another country |
| **PECA** | Protocol of European Conformity Assessment |
| **Pharmacovigilance** | Monitoring and continuous surveillance of the safety of an authorized medicinal product during its life on the market |
| **R&D** | Research and Development |
| **ROCE** | Return On Capital Employed |
| **SPC** | Supplementary Protection Certificate |
| **TRIP** | Trade Related Intellectual Property |
| **Visegrád countries** | Group of four EU applicant countries: the Czech Republic, Hungary, Poland and Slovakia |
| **WHO** | The World Health Organisation |
| **WTO** | World Trade Organisation |

# Introduction

The pharmaceutical industry's contribution to the European Union's GDP is only 1 percent. However, the industry is very important not only in providing significant advances in medical care, but also in its economic contribution through development and diffusion of technology, and its positive influence on the balance of trade.

The European pharmaceutical industry has been at the forefront of international competition for a number of decades, characterized by a strong and innovative presence. However, recent trends suggest that now it is lagging behind the United States and Japan in its rate of innovation and its competitive edge over both the US and Japan appears to have been eroded.

Meanwhile, CEE pharmaceutical markets were growing fast, providing new opportunities for the innovative pharma companies. Most of them have built up good positions in the last couple of years and faced excellent sales growth after having implemented the developed marketing techniques.

But the recession affected also the European pharmaceutical industry in the recent years, and put growing pressure on the reimbursement systems to cut spending.

Under these circumstances the accession of the CEE countries and their cheap generic players mean a threat for the European pharma companies.

However, Hungarian drug companies also fear the new situation because of numerous direct and indirect effects. A direct effect, which could have negative impact on them, is their expectation that large number of new drugs would be registered to their domestic market. The new competitors will sharpen the competition and could squeeze further the domestic companies' market share. One of the indirect effects of the accession is the potentially growing wages, which will certainly put their profitability under pressure.

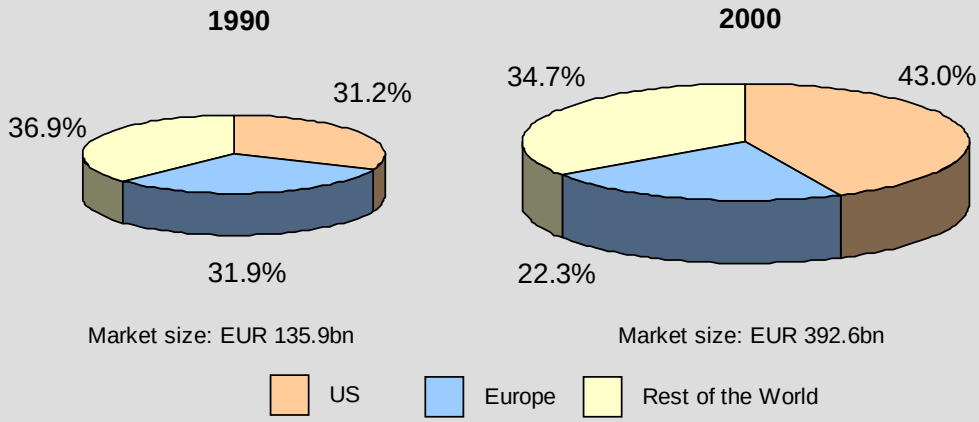
In our study, there are three major questions we would like to answer. First, how is the pharmaceutical market regulated in the EU, and what is the direct of development? Second, how can the legal harmonization effect the Hungarian pharmaceutical market? And third, what are the impacts of the accession on the major characteristics of the market, such as the market size, employment or trade balance?

# The pharmaceutical industry in the EU

The pharmaceutical industry in Europe is a strong industrial sector, which makes a significant contribution to Europe's industrial base. In 2001, the trade balance for the European Union was some EUR 29.5bn in Europe's favor and over EUR 18.8bn was spent on research and development, representing 100% increase over the previous 10 years. Over EUR 96bn worth of products left factories in the EU in 2001, representing 23% of global production. In 2001, the pharmaceutical industry was employing some 540,000 people in the European Union, including 88,000 people researching and developing pharmaceuticals.

However, the European pharmaceutical industry is losing competitiveness as compared to the US industry and there is a process of concentration of R&D into North America. Many indicators show that the competitive position of Europe, as a site for innovation and investment, is in decline compared to the situation in America and that the "brain-drain" is amplifying as Europe's most talented scientists are offered better opportunities abroad.

**Figure 1: World pharmaceutical market**




*Source: IMS Health*

Over the past 10 years, pharmaceutical R&D investments have doubled in Europe to reach EUR 18.8bn in 2001 but they have been multiplied by nearly five times in the US to reach EUR 30.3 billion in 2001. Over the same period, the average annual growth of pharmaceutical sales has remained below 10% in Europe, compared to 15% in the US. As a consequence of this, Europe's share of the world pharmaceutical market (which has tripled over the last 10 years) has decreased from 32% to 22%, whereas it has increased from 31% to 43% in the US. While a few of Europe's top pharmaceutical companies are still performing well, a growing number of the second tier companies face an uncertain future, because they cannot reach the required return du to the soaring costs of researching, developing and bringing a new medicine to market.

The reasons for which part of the pharmaceutical industry in the European Union appears to be losing global competitiveness are multiple and complex. First, the European pharmaceutical industry registers significantly lower productivity per worker than its US peer. The overall profitability and the industry's ROCE appear to be significantly higher in the US than in the European Union. However, a proper assessment of the extent of these differences faces significant measurement problems (transfer pricing, breakdown between pharmaceutical and other activities, etc.). The continued differences between the European markets lead to excess costs (such as higher marketing costs, higher distribution and administrative costs) and, in some cases, to excess production capacity. Most of the European pharmaceutical professional agree this could be offset by only a better operating Single Market.

We strongly believe the completing of the Single Market concept (and parallel to this preparing to the enlargement are the main tasks to resolve for the EU in order to improve the competitiveness of the industry

## Legislation and market regulation

The EU measures related to the medicines and the pharmaceutical market regulation are the following:

### Directives

Commission Directive 91/356/EEC of 13 June 1991 laying down the principles and guidelines of **good manufacturing practice** for medicinal products for human use

Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the **authorization and supervision of medicinal products** for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (OJ L 214, 24.8.1993, p. 1)

Directive 2001/20/EC OF the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of **good clinical practice** in the conduct of clinical trials on medicinal products for human use.

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to **medicinal products for human use**.

Amended by Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

Council Directive 89/105/EEC, of 21 December 1988, relating to the transparency of measures regulating the **pricing of medicinal products for human use** and their inclusion within the scope of national health insurance systems.

### Regulations

Council Regulation (EEC) No 2309/93, of 22 July 1993, laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a **European Agency for the Evaluation of Medicinal Products**.

Amended by Commission Regulation (EC) No 649/98 of 23 March 1998 amending the Annex to Council Regulation (EEC) No 2309/93

(EC) No 297/95 Council Regulation (EC) No 297/95, of 10 February 1995, on fees payable to the **European Agency for the Evaluation of Medicinal Products**.

(EC) No 540/95 Commission Regulation (EC) No 540/95, of 10 March 1995, laying down the **arrangements for reporting suspected unexpected adverse reactions** which are not serious, whether arising in the Community or in a third country, to medicinal products for human or veterinary use authorized in accordance with the provisions of Council Regulation (EEC) No 2309/93.

(EC) No 541/95 Commission Regulation (EC) No 541/95, of 10 March 1995, concerning the examination of variations to the terms of a **marketing authorization** granted by a competent authority of a Member State. Amended by Commission Regulation (EC) No 1146/98 of 2 June 1998 amending Regulation (EC) No 541/95

concerning the examination of variations in the terms of a marketing authorization granted by a competent authority of a Member State.

(EC) No 542/95 Commission Regulation (EC) No 542/95, of 10 March 1995, concerning the examination of variations to the terms of a **marketing authorization** falling within the scope of Council Regulation (EEC) No 2309/93.

(EC) No 1662/95 Commission Regulation (EC) No 1662/95, of 7 July 1995, laying down certain detailed arrangements for **implementing the Community decision-making procedures in respect of marketing authorizations** for products for human or veterinary use.

(EC) No 2141/96 Commission Regulation (EC) No 2141/96, of 7 November 1996, concerning the examination of an application for the transfer of **a marketing authorization for a medicinal product** falling within the scope of Council Regulation (EEC) No 2309/93.

(EC) No 141/2000 Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on **orphan medicinal products**.

(EC) No 847/2000 Commission Regulation (EC) No 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an **orphan medicinal product** and definitions of the concepts 'similar medicinal product' and 'clinical superiority'.

Currently, the pharmaceutical legislation of the EU has seven main goals. These are:

1. Guaranteeing a high level of health protection for European citizens, in particular by making safe, innovative products available to patients as quickly as possible.

2. Guaranteeing tighter surveillance of the market, in particular by strengthening pharmacovigilance procedures.

3. In the case of medicinal products for veterinary use, improving the level of animal health, in particular by increasing the number of medicinal products available.

4. Completing the internal market ("Single Market") for pharmaceuticals while taking globalization into account.

5. Setting up a legal framework, which fosters the competitiveness of European industry.

6. Meeting the challenges of EU enlargement.

7. Taking the opportunity to rationalize and, if possible, simplify the system ("better regulation"), thereby improving its overall consistency, its profile and the transparency of decision-making procedures.

## European Institutions

The main market regulator is the European Agency for the Evaluation of Medicinal Products (European Medicines Evaluation Agency, EMEA). Although the Agency already existed on paper at the end of 1993, it only became operational in February 1995.

Three registration procedures for pharmaceuticals were established according to the Regulation establishing a European Agency for the Evaluation of Medical Products:

- a centralized procedure, reserved for innovatory products and leading to a single Community wide authorization valid for all 15 Member States. The use of the centralized procedure will be compulsory for all medicinal products derived from biotechnology but available only at the request of companies for other innovatory products. Under this procedure applications will be processed by the Agency in London.

- a decentralized procedure, which will apply to the substantial majority of products, based upon the principle of mutual recognition, and covering a variable number of Member States.

- a national procedure, limited in principle to applications of local interest concerning a single Member State.

The national authorities have lost their regulatory powers in the case of biotechnology products. These products could be let to the market only by EMEA. The Agency is also dealing with the authorization of innovatory pharmaceutical products and it is expected that one of the issues that will be raised in the near future will be the definition of what is an innovative product. Policy implications related to this matter will be important in years to come.

## Intellectual property rights

Intellectual property rights are economic rights. They confer economic benefits on those who hold them. Those benefits should be proportionate to the benefit given to society. Generally the intellectual property system works well and is generally thought in the west to work fairly. Indeed, there are many questions considering the patent rights, which should be discussed.

All OECD countries have a basic harmonization of patent law, largely as a result of implementation of the obligations set out in TRIPs. EU Member States have achieved additional harmonization of extended patent term legislation. There are significant variations between EU Member States, and other OECD jurisdictions, as regards the scope and operation of permitted exceptions to exclusive patent rights.
The differences between EU Member States and other OECD countries such as the US and Australia in respect of the scope of patentability of second medical uses for known drug substances are such that the potential for patent litigation arising between generic companies and research based undertakings is greater within the EPC area.
It is widely accepted that patents are a fundamental incentive to innovative activities in pharmaceuticals and biotechnology. Both the US and the most of the European countries have provided relatively strong patent protection in pharmaceuticals. However in Italy, until 1978, patent law did not offer protection for pharmaceutical products: only process technologies could have been patented. As a result, Italian firms have tended to avoid product R&D and to concentrate instead on finding novel processes for making existing molecules. (Until 1992 that was the case in Hungary, too.)

Similarly, the establishment of clearly defined property rights also played a major role in making possible the explosion of new biotechnology firms in the US, since the new firms had few complementary assets that would have enabled them to reach returns from the new science without strong patent rights. In the US, a tight approbation regime in the biotechnology industry emerged quite quickly, for example through the Bayh-Dole Act in 1980 and through the granting of very broad claims on patents. In Europe, the scope for broad claims on patents is greatly reduced and usually process rather than product patents are granted.

A directive from the Commission that strengthens the protection offered to biotechnology was approved by the European Parliament in 2000. Still, considerable controversy surrounds this issue.

However, in our view the rationale for stronger protection to intellectual property in medical and especially biomedical research is not based on the traditional argument that the concession of broad property rights is an incentive to the production of knowledge. Rather, the argument is based on the assumption that property rights would favor the creation of markets for technology and hence a faster and more ordered diffusion and use of knowledge.

The move towards stronger IP protections through the TRIPS agreement presents complex issues. On the one hand there is evidence that strong patents can have a negative effect on affordable prices by delaying the entry of generic options. But on the other hand pharmaceutical industry continually raises concerns that the erosion of patent protections will undermine incentives for product development.

Since the developing market represents only a minor part of the global pharmaceutical market it is difficult to see how lower prices in this markets significantly impact MNC profits. The real fear of MNCs is that lower prices will undercut acceptance of higher prices elsewhere, and could lead to importation of comparatively cheap drugs to richer markets.

However, in our view the rationale for stronger protection to intellectual property in medical and especially biomedical research is not based on the traditional argument that the concession of broad property rights is an incentive to the production of knowledge. Rather, the argument is based on the assumption that property rights would favor the creation of markets for technology and hence a faster and more ordered diffusion and use of knowledge.

## Research and development

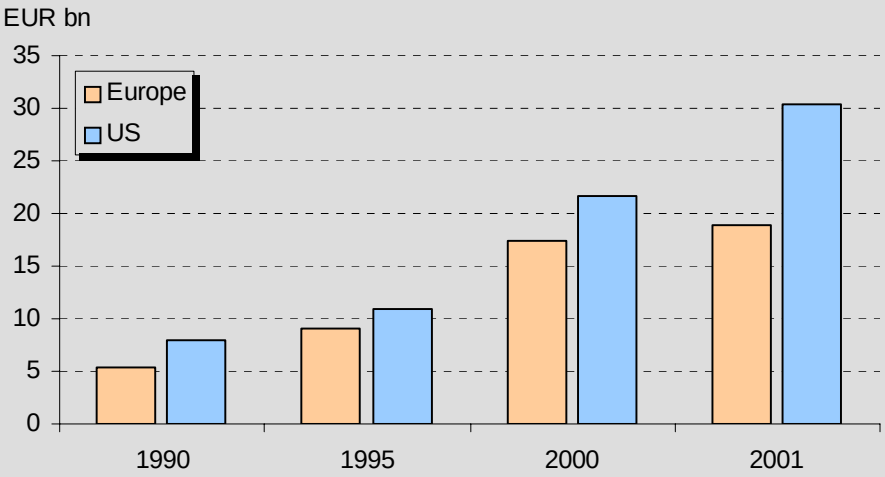
Over the last 20 years, R&D spending by pharmaceutical companies in Europe has risen more than seven-fold. In 2001 alone, the pharmaceutical industry has invested 18.8 billion -almost a fifth of all industrial research and development in Europe, and a higher percentage than any other industrial sector (including high-tech industries such as computers, electronics or aerospace).

Pharmaceuticals are an R&D intensive industry. R&D is associated with high financial risks since only a few out of a very large number of new molecules eventually make it to the marketplace, having to go through the lengthy development process and extensive pre-clinical and clinical trials. Regarding the authorization of new medicines, the regulatory authorities in different countries have achieved speedier review and approval; this also includes the EMEA's centralized procedure applied within the European Union.

Market entry does not guarantee commercial success. The cost, therefore, of developing a new drug is very high, with estimates of USD 300-600m, depending on the type of drug. The high cost inevitably forces the industry to globalize in an attempt to recoup its R&D costs from its marketable products.

European pharmaceutical R&D expenditure, measured as private sector outlays and taken as a proportion of the industry's sales, increased more than threefold within a decade, from about EUR 5.3bn in 1990 to over EUR 18.8bn in 2001. This figure includes R&D expenditure by European and non-European (mostly US and Japanese) companies. However, much higher increases have been recorded in the US (see figure).

**Figure 2: Pharma R&D expenditures in Europe and US**




*Source: EFPIA*

Over the past 30 years, the proportion of new and innovative molecules (in terms of New Chemical Entities) introduced in Europe has been falling both in absolute and relative terms. By contrast, NCEs introduced in the US have seen a consistently upward trend for the whole of this period.

In terms of ownership of biotechnology patents by private companies, US and Japanese companies are the largest holders, implying that they are also leading originators of knowledge in this field. Public institutions are a crucial source of discovery and knowledge both in the US and Japan. Through publicly funded R&D in specific areas, notably human genome, US and Japanese institutions are the leaders in (human genome) patent ownership.

However, as the number of pharmaceutical and/or biotechnology patents and NCE introductions are relatively crude measures of the industry's performance, additional indicators need to be considered, including the number of (bio)pharmaceutical blockbusters and the number of `international' drugs.

The pattern of limited success in European biotechnology, as demonstrated by the relatively poor results of public and private basic and applied research, continues in the area of commercial exploitation. Over 80% of the biotechnology blockbusters currently in the marketplace are of US origin. The deficit in European R&D in biotechnology may become even more serious in the future if the consolidation process in Europe continues, accompanied by greater investment in the US (and, possibly, Japan) at the cost of research conducted in Europe.

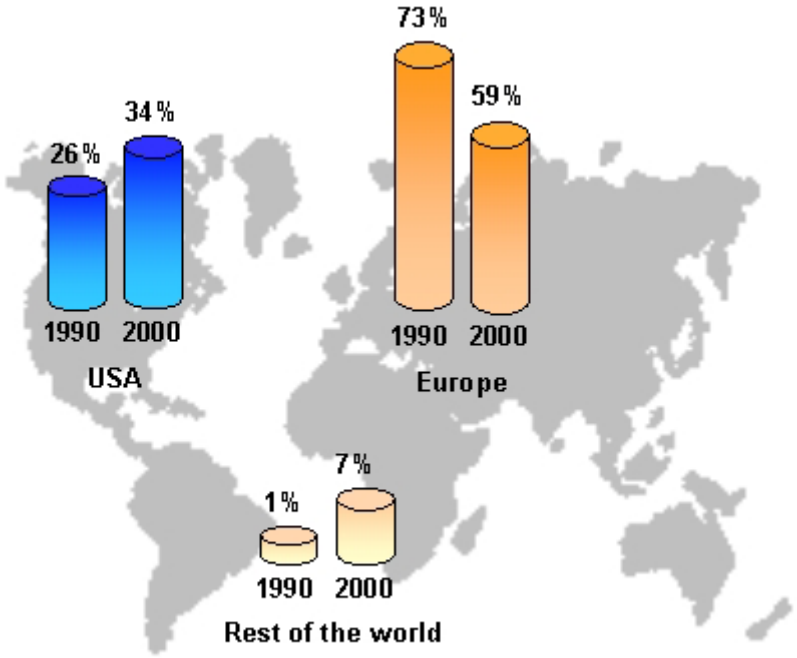
European companies had fewer internationally marketed pharmaceutical products in the recent years, as they lunched 79 new medicines in the 1997-01 period, compared to 89 in 1992-96. In contrary, US was able to increase the number of new medicines significantly during the 90s: 84 US NCEs succeeded on the world market between 1997 and 2001, up from 56 in the 1992-96 period.

American companies have also been more successful in disseminating their new medicines at international level: 62% of sales of new medicines marketed since 1997 are generated on the US market, compared with 21% on the European market and 7 % in Japan.

From the top selling 50 drugs currently on the market, US companies have developed 26 of them, European companies 21, and Japan only 3. In Europe, British companies account for 14 of these drugs, and their position in world rankings has risen steadily over the last two decades. In contrast, German companies perform in a less satisfactory manner. However, German firms top the list in terms of R&D expenditure and number of drugs under development, which may foreshadow future improvement on current performance.

European companies display a tendency to conduct a large part of their R&D outside their country of origin, as do US companies. This is not surprising since the pharmaceutical industry is multinational in its operations. Nevertheless, there is a tendency that R&D expenditures concentrate in the US. In 1990, major European research-based companies spent 73% of their worldwide R&D expenditure on the EU territory. In 1999, they spent only 59% in the EU. The USA was the main beneficiary of this transfer of R&D location.

**Figure 3:** Location of R&D spending by European pharmaceutical companies




*Source: EFPIA*

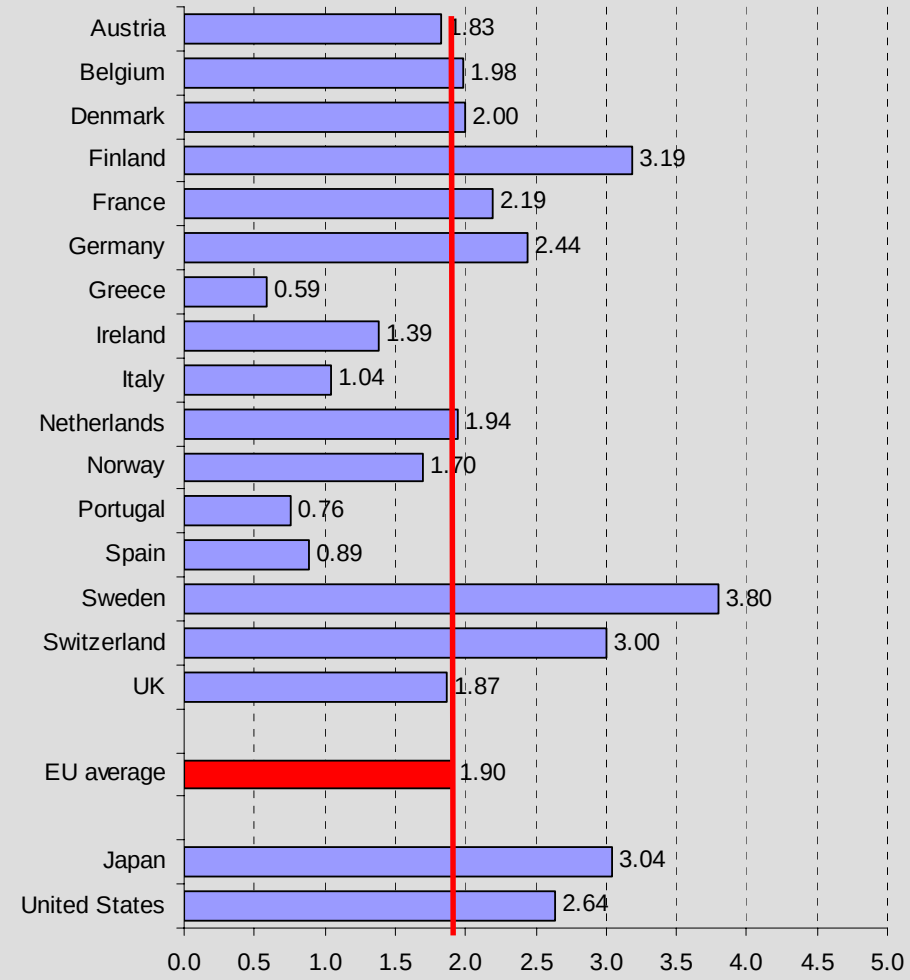
This evidence suggests that European companies rationalize their research effort in Europe and focus on one or two major research sites, whilst at the same time they attempt to strengthen their position in the US and Japan. European companies seeking to establish powerful strategic links particularly with American pharmaceutical groups, that will lead to the launch of joint products marketed profitably on both sides of the Atlantic. There is an increasing number of cooperative agreements between pharmaceutical multinationals and small new biotechnology firms, with the flow of investment running from Europe in return for technology transfer from US institutions.

Important considerations for European companies investing in the US include the size of the US market, the opportunity to earn tax breaks against R&D expenditure in the US and meeting FDA regulations, which gains them entry to global markets. Such trends, suggest a strategic shift of importance from Europe to the US with implications for technology development, the creation of high-skilled employment and the overall shift of strategic decision-making towards the US.

The relative position of the US as a locus of innovation in pharmaceuticals has increased over the past decade compared to Europe. One notable difference between Europe and the US in the 1990s is that while the US have continued the development of a new research-intensive industry in the life sciences, Europe has been unable to complete the process of vertical specialization in the most innovative areas of the drug sector. Particularly, Europe has not really given rise to a full-fledged industry of innovation specialist companies and technology suppliers like in the US. The US pioneered the rise of a new organization of this industry, based on an effective division of labor between smaller and larger companies with different comparative advantages in the "exploration" and "exploitation" of new innovation opportunities.

Definitely, Europe has been less effective in encouraging the growth of new technology suppliers and innovation specialists since the early 1980s.

**Figure 4: R&D expenditure as a percentage of GDP (1999)**




*Source: EFPIA*

## Pricing, financing and reimbursement systems

### *The pricing of pharmaceuticals*

Without exception, there is no Member State without direct or indirect price controls for pharmaceuticals. The former may result in different prices for identical products, as ability and willingness to pay varies in the Member States, but no Member State can enforce the market-entry for any pharmaceutical product. Taking the example of innovative, patent-protected products it has to be realized though, that the demand side – always a national one – is negotiating prices with the supply side, enjoying the monopolistic advantages of comprehensive, world-wide protection of intellectual property rights as well as the exclusive world-wide marketing rights of their products.

The decisive reason, however, that price differences for pharmaceuticals do exist, is the pro-active price-differentiation policy by the industry itself: country by country as well as product by product. For a commercial industry this is only the logical consequence of fundamental economic principles. The implications of this policy have produced remarkable consequences during the last few years: Member States are in the same time parallel-importing as well as parallel-exporting countries (see below).

Seeing the price differentials and the growing parallel trade EC decided to accelerate the progress toward the Single European Pharmaceutical market. However, this effort came up against many difficulties.

Price harmonization within the EU are affected by the degree to which pressure can be lifted off companies to expand local manufacturing facilities unnecessarily, thus providing an opportunity for companies to achieve more economies of scale. Public procurement policies in various Member States also systematically tend to favor domestic over foreign suppliers.

While in some areas, the Commission has managed to make considerable progress towards a Single market, it has had to accept that Member States retain a substantial autonomy in the crucial area of pricing, reimbursement and user charges.

In addition, pricing and financing systems in the Union are far from similar. The Commission has attempted several times to introduce harmonizing legislation in this field, but it has failed to convince Member States to accept binding measures. The principle of subsidiary, introduced in the Treaty on the European Union has imposed further impediments to the creation of a Single Market in the pharmaceutical sector.

### *Transparency Directive*

The 'Transparency Directive' was in reality a procedural directive setting out a framework of procedures for decision-making but it was not a harmonizing Directive. Several issues were raised before and after its introduction which reflect the partial or incomplete harmonization in the pharmaceutical sector. These included, amongst others, the role of the level of prices as an impediment to free trade, price discrimination against imports, the use of average European prices and the definition of an excessive price.

### *Defining the level of prices*

The level of pharmaceutical prices as an impediment to free trade was raised by the Commission in Case C-249/88 Commission v Belgium. The Commission argued that the prices of medicines in Belgium were lower than in other Member States as a supportive argument to its claim that the rules of fixing of maximum prices for medicinal products were incompatible with EEC law. The Court's view is that it is a form of discrimination to apply the same mandatory pricing regime to goods with different production costs. The Court has ruled that Article 30 is infringed when an import is denied the opportunity to undercut the domestic product (unlawful minimum price fixing) or to trade at a reasonable profit (unlawful maximum price fixing).

### *Price discrimination against imports*

In the same case, the Court ruled that Belgium failed to fulfill its obligations under the EEC Treaty by permitting prices increases in return for undertakings on investment, research, employment and exports between 1983 and 1988. This was achieved through a system of program contracts which exempted pharmaceutical products covered by the program from the rules barring such products from approval for reimbursement where their price exceeds that of similar products by a given percentage.

By permitting prices to be granted in return for undertakings on investment, research, employment and exports pricing systems place imported products at a disadvantage and these measures are considered by the Court of Justice to have an effect equivalent to a quantitative restriction prohibited by Article 30 of the EEC Treaty.

## *The use of average prices*

Two Member States have introduced a system of average prices (Italy from 1994 and the Netherlands from 1996) and another three (Greece, Portugal and Ireland) 'look over their shoulders' at prices in other European countries.

In Italy, under the new system introduced in 1994, the prices are the average of those in Germany, Spain, France and the United Kingdom expressed in lire using the purchasing power parities (PPPs) for each country, which are considerably lower than the exchange rates. It was argued that if imports had taken place, the industry would lose money as they would have to pay at exchange rates and not (PPPs). The Commission stated that it has no objection in principle to the adaptation of Italian medicine prices to the average European price and suggested that it is for the Italian authorities to decide how they wish to calculate the average price of medicines, in compliance with the provisions of the 'Transparency Directive' and, as regards medicinal products imported from other Member States, Article 30 of the EC Treaty.

## *Excessive prices*

Multinational companies that practice discriminatory pricing to different national markets are susceptible to the charge of excessive pricing. According to the Court of Justice overpricing is defined as 'charging a price which is excessive because it has no reasonable relation to the economic value of the product supplied'. The Court has also said that the onus of proof of overpricing rests with the Commission or other persons alleging it.

The issue of excessive prices in the pharmaceutical sector was raised by the Danish presidency in 1993 following the introduction of a new product in the Danish market which was felt to be very high and called for discussions at Community level to ensure that Member States are not forced to accept unusually high prices for highly innovative products.

The response of the Commission was the establishment of a working party whose mandate was to clarify what is an excessive price. The working party failed to reach a definition but carried out a study, which indicated that whatever system of control has been implemented at national level, the pharmaceutical product concerned has been placed on the market in the Member States at similar prices.

The Commission pointed out that Member States introduced measures concerned with the level of reimbursement in order to contain expenditure and that this action confirms the Commission's own conclusions that action on reimbursement is more effective and has less of a distorting effect on the market than action on prices. The Commission did not comment explicitly on the problem of excessive pricing and its study rather indicates that similar prices in the Member States may reflect the regulator's inability to intervene and set a fair price.

This requires a comparison of the price with the full production costs. However, it is not easy to determine production costs, in particular in multi-product companies such as pharmaceutical companies where fixed costs such as Research and Development, capital investment and administrative and promotion costs are allocated between several products. There are also additional problems concerning transfer prices from the mother and the subsidiary company. Since these data are difficult to obtain, evidence on excessive pricing may be produced by comparing ex-factory prices in different countries for the same products. However, this can only be done in countries where prices are not regulated.

### *Types of co-payments*

Wide diversity exists in the forms of co-payments by which individuals and the state share the cost of prescribed ambulatory medicines in different EU countries. While the needy, the young, the old and those with chronic or life-threatening conditions are often supplied with medicines free, this is not universal. For example, in Denmark and Sweden only diabetes warrants free medicines but other serious conditions such as cancer, haemophilia and multiple sclerosis do not. It is therefore clear that the concept of social solidarity differs markedly within the

Six types of co-payment systems exist, often in combination, in the OECD countries. In 19 states some prescribed medicines are paid for in full. Four co-payment system — payments up to thresholds, proportional co-payments, supplements above the reimbursement price, and fixed rate co-payments — are found in roughly equal measure with 12-14 instances of each being identified.

*Threshold co-payment* systems sensitize patients to the cost of their medicines up to the threshold and preserve social solidarity by providing free or subsidized medicines above the threshold. Within the EU the thresholds range from around EUR 100 in the Netherlands to around EUR 700 in Germany. In Sweden introducing a threshold system in 1997 produced a major increase in demand for about three months before and a major reduction after the new scheme began. The new system appears to have lowered the demand trend line but without stopping the rising trend.

*Reference pricing* offers consumers' a distorted choice between paying something and paying nothing. In Germany since its introduction in 1989, the system has made significant and continuing savings for the sickness funds. In Denmark, the Netherlands and Sweden the evidence of significant savings being achieved by reference pricing is much less clear.

*Proportional co-payments* are found in 12 OECD countries. They embody the concept of social solidarity, but their impact in stimulating rational prescribing and choice by consumers seems limited because real price differences between competing products are diminished.

Increases in *fixed rate co-payments* can influence consumer demand but they do not enable prescribers or consumers to make reasoned choices between originals and generic medicines. They appear economically inefficient in containing the cost of the medicines bill and enhancing consumers' utility through choice.

*Free medicines* clearly have no role in sensitising consumers to the cost of medicines.

By contrast, the more a co-payment system sensitises consumers to the cost of prescribed medicines, the more likely it is to engage both prescribers and consumers in discussion about what is an optimal choice of product in each individual's circumstances. Such discussion may favour generics but this is uncertain, particularly in countries where the prices of originals have been held low by government intervention.

## OTC market (non-prescription medicines)

At retail prices, the global OTC pharmaceutical market was estimated to be worth USD 73.7bn in 2001. Europe was the largest market and accounted for around 32% of the global OTC pharmaceutical sales.

The market for OTC pharmaceuticals grew by only 3.8% in the last five years, but analysts expect to increase by an annual 7% in the next five years, and exceed USD 100bn by 2007. This growth would largely come from the US and emerging markets in Asia.

Growth in the US market will be driven by a rejuvenation of Rx-to-OTC switches. A third class of drugs to be available only under pharmacists' supervision might also be created to boost Rx-to-OTC switches in this market.

In revenue terms, the five largest OTC companies in the world are Johnson & Johnson, Pfizer, GlaxoSmith-Kline, Wyeth and Bayer. However, only Wyeth could be considered as an OTC professional, the main focus of the other four is the prescription drugs.

**Table 1: The world OTC market (1997-2002)**

| (EUR bn) | 1997 | 2000 | 2001 | 2002 | CAGR |
|---|---|---|---|---|---|
| US | 17.4 | 20.1 | 20.5 | 22.1 | 4.9% |
| Europe | 20.4 | 22.2 | 24.1 | 25.3 | 4.4% |
| Asia | 11 | 13 | 14.8 | 16.5 | 8.1% |
| Rest of the World | 16.1 | 14.8 | 14.4 | 14.6 | -1.9% |
| **Total** | **65.1** | **70.5** | **73.8** | **78.5** | **3.8%** |

*Source: Reuters Business Insight, The OTC Outlook to 2007*

The overall sales growth of the OTC products is much lower than that of the prescription drugs, and this is also expected for the next couple of years. In our view, this is the clear evidence that the OTC "industry" matures. Companies are seeking to expand sales for products by identifying and targeting emerging markets with untapped growth potential.

However, we see three more points to consider related to the expected performance of the OTC markets:

- Pharma companies use switches to protect the revenues of products even after the patent has expired. Switching strategies vary between national markets – drugs that may be available prescription-only in one country, may be available OTC in another.

- The increase in the elderly population has accelerated increases in healthcare expenditure of the principal providers in all markets. This has encouraged the imposition of cost containment measures, which have in turn boosted the number of ethical drugs switching to OTC status

- More widespread consumer acceptance of self-medication will be another major driver behind OTC market expansion. With increased awareness levels among consumers, self-medication for minor illnesses would become common.

## Generics

The term "generic" is widely used but its definition is not always clear cut. As a rule generic medicines are made by a manufacturer different from the maker of the original product. These generic manufacturers are specialist companies who do not carry out original R&D for the products they make. However, some original manufacturers also produce generic versions of their own products or are affiliated to specialist generic companies.

"Multi-source" products include both generics and the original products when the latter are off patent and still sold under their original name. The total market for "multi-source" products, therefore, is always larger than for "generics".

In light of these, the following definition can be given:

A "generic medicine" means a prescription medicine based on an active substance that is out of patent and which is marketed under a different name from that of the original branded medicine.

Health authorities apply a number of generics-specific instruments to control manufacturers' prices or the reimbursement prices of multi-source products. In 16 OECD countries the authorities control the reimbursement price by setting it at a given percentage below the price of the original. In 13 countries generic manufacturers are free to increase or decrease their prices at will, suggesting recognition that the prices of generics are, or could be, determined by market forces. In 10 countries, of which five are in the EU, the authorities have the power to increase or reduce the reimbursement price at will. In only six states do the authorities reduce the reimbursement price of an original when generics enter the market. Even if generic manufacturers have the freedom to set and change their prices, there is considerable pressure on them to conform to the reimbursement price in order to avoid making consumers pay a supplement. In these circumstances it is uncertain whether the health funds pay more or less overall than if they allowed market forces to determine the prices of multi-source products.

## Structure of EU's generics manufacturing industry

The EU's generics manufacturing industry seems fragmented though one dominant company has been identified in each of Austria, the Netherlands and Sweden. Independent manufacturers account for larger shares of national markets than do companies affiliated to research-based companies, but France and Sweden are exceptions.

In Japan the supply of generics appears very fragmented. In the USA the five largest companies among both the research-based affiliates and the independents command a share of about 30 per cent of the generics market. This suggests more concentration but no dominance in supply.

Sales and marketing expenditure as well as profit margins of generic companies in emerging EU generic markets such as France, Italy and Spain appear to be higher than in more mature EU generic markets such as the Germany, the Netherlands and the UK. In mature generic markets, prices to end-users may also be lower.

Market forecasts, such as IMS Health's recent projections, estimate the European generics market will grow around 15% in the next five years.

## Generic substitution

Generic substitution occurs when a pharmacist is permitted or required to substitute one medicine with another cheaper one using an identical or chemically similar active ingredient. The policy of the governments to encourage generic substitutions in order to safe their healthcare budgets evoked sharp debate between generic and innovative companies.

However, as healthcare budgets available for European governments are not growing at the same speed as healthcare expenditure, with the authorities resorting to cost-cutting through the encouragement of generic prescription and substitution.

## Parallel trade

Parallel trade of medicines is the purchase of drugs at low prices in one country and their subsequent resale at higher prices in an other country.

Parallel Trade in general is based on fundamental principles of the EU, as laid down in the Treaty of Rome (Articles 30 and 36):

- the principle of free movement of goods
- the principle of intellectual property rights

These corner-stones of one free common internal market in the EU are reflected in numerous, continuous decisions by the ECJ, implemented and guarded by the Commission. They are transformed into national law by the governments of the Member States and interpreted by rulings of national courts as well as executions through the relevant national authorities. Together they define the legal framework for Parallel Trade of medicinal products in the Member States.

By definition Parallel Trade could not exist without price differences for pharmaceuticals between the Member States.

The reasons for such price differences are two-fold:

- Price controls by governments and health providers

Active price-differentiation policies by the pharmaceutical industry

It is an axiom that for parallel trade to take place there must be a significant price differential between the two markets. However, price differentials alone do not necessarily lead to viable conditions for parallel trade. For parallel trade to be both viable and profitable, a number of other crucial market factors are also needed:

- Sufficient volume of drug supply – substitutable for the product in the destination market
- Commercial, economic and regulatory conditions (especially in the importing country) that allow adequate profits to be made
- Financially reasonable transportation costs between the supply market and the destination market
- Adequate legal and regulatory conditions to support the importer's rights
- Market acceptance by patients, pharmacists and wholesalers of the re-imported pharmaceutical product

As we mentioned, pharmaceutical parallel trade in Europe is based upon the principle of free movement of goods, which means that the various EU governments and regulatory bodies are committed to uphold traders' (parallel importers') rights. Additionally, all of the largest EU countries have some type of national healthcare insurance, including prescription drug benefits. Large budget deficits and an aging population have led to a variety of policies designed to control and reduce drug prices. Connive or even encourage the parallel trade is one of these policies.

However, according to innovative pharmaceuticals parallel trade is one of the key factors in undermining European pharmaceutical competitiveness. In their view parallel trade benefits neither social security systems nor patients, but deprives the industry from valuable resources to fund the research and development of new products.

Parallel imports are now reaching a significant percentage of the market in some European countries. Although difficult to calculate exactly, it is now estimated to affect sales of about EUR 3.5bn per annum, and could be costing the R&D based industry around EUR 1bn, much of which could have been reinvested in research and innovation.

Prices in the pharmaceutical sector in the EU are largely determined by national governments based on public policy considerations. Therefore, they do not reflect the normal interaction of supply and demand. Against this background, the encouragement of parallel trade is considered to be damaging by the innovative pharma companies.

Apparently, some examples back this argument. In Greece, parallel trade is leading to the shift of a significant percentage of supplies intended for one market to another country in the EU. This certainly causes some disorder of supply of medicines to patients.

Therefore we agree, the significant growth of parallel trade in recent years could have undermined the attractiveness of Europe as an environment for the pharmaceutical industry. Moreover, the forthcoming EU enlargement – given existing economic disparities between candidate countries and EU Member States – is likely to strengthen parallel trade.

We strongly believe the problem of the parallel trade will be resolved by the Single European Pharmaceutical Market, which is the long-term interest of each the governments, the pharmaceutical companies and the patients.

## Progress towards a Single Market in pharmaceuticals

In its 1994 Communication on the outlines of an industrial policy for the pharmaceutical sector in the European Community (COM(93)718 of 2 March 1994), the Commission expressed concerns that part of the pharmaceutical industry in the European Union may be losing global competitiveness, with consequent economic and social cost for Europe. In their responses to this Communication, both the European Parliament and the Council have stressed the importance of completing the internal market and establishing a stable and predictable environment in order to protect the health of patients, to ensure rapid access to the market and to encourage therapeutic innovation.

The purpose of the completion of the Single Market in pharmaceuticals is not just to provide an environment which is favorable for pharmaceutical innovation and industrial development, it is also to improve consumer choices in pharmaceuticals of the required quality, safety and efficacy, at affordable cost.

Over the past thirty years, there have been a range of developments in the EU towards a Single Market in pharmaceuticals, focusing on a number of relevant policy areas, in particular medicines licensing and the protection of intellectual property.

Single Market in pharmaceuticals is in fact far from complete, because competition is distorted by Europe's patchwork of national pharmaceutical pricing and reimbursement policies. The ECJ, in particular, has reminded Community institutions of the obligation to address trade distortions arising from national control of pharmaceutical prices, in order to ensure that the industry in Europe can continue to innovate and compete in world markets.

# The pharmaceutical industry in Hungary

## General overview

The Hungarian pharmaceutical industry with strong traditions is one of the oldest ones in Europe. As early as 1867 there had already been pharmaceutical enterprise operating in Hungary. At that time only London, Paris, Milan and Brussels had similar industry.

The Hungarian pharmaceutical industry survived quite well the world economic crisis of 1929-1933. By the end of the thirties there were 36 drug manufacturing companies operating in Hungary, some of which also had many subsidiaries abroad. However, the factories and laboratories were nationalized after the Second World War.

During the communism, as a member of COMECON, Hungary supplied drugs for the members of the block, especially for Russia. After the collapse of the former economic system and the liberalization of the domestic market Hungarian pharmaceutical companies moved towards Western Europe although their success was limited. The quality of their products mostly met the EU requirements, but the registration process and the lack of distribution channels often proved to be an insurmountable barrier to entering the market. Each company was privatized and – with the exception of Richter – found strategic investors.

At the start of the 90's the political and economic transition was followed by complete import liberalization: no longer were there administrative constraints on the appearance of foreign competitors on the domestic market as the import of pharmaceuticals was re-classed as customs free. Therefore foreign and domestic manufacturers were in the same position as regards the Hungarian subsidy system. As a result, following the transition, Hungarian pharmaceutical companies had to face a rapid loss of domestic market share. In line with this, the proportion of consumed pharmaceuticals manufactured in Hungary is now only 35% in contrast with 70% at the end of the 80s. Parallel with this, the concentration of the market also decreased.

A characteristic feature of the 90s is, that companies have changed their portfolio to purely human medicines. Diversification businesses have been wound up or sold. Over the years the number of those employed in the pharmaceutical industry has diminished from 20 thousand in 1990 to 12 thousand in 2002, whereas production has increased. Although productivity has been growing, it still is far from that of the most developed pharmaceutical manufacturers.

**Table 2: Therapeutic breakdown of the medicine consumptiun in Hungary (%)**

| Therapeutic group | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 |
|---|---|---|---|---|---|---|---|
| Drugs of the heart and circulatory system | 21.0 | 21.2 | 20.9 | 20.9 | 21.5 | 21.8 | 22.6 |
| Drugs of the central nervous system | 15.7 | 16.1 | 16.3 | 16.0 | 16.3 | 16.3 | 16.1 |
| Drugs of the intestinal tract and metabolism | 14.2 | 15.1 | 14.4 | 13.8 | 14.1 | 14.1 | 13.5 |
| Systemic drugs for infections | 14.1 | 13.4 | 12.4 | 12.5 | 10.9 | 9.5 | 8.6 |
| Drugs of the blood and blood making organs | 5.4 | 4.7 | 5.1 | 4.8 | 4.9 | 6.1 | 7.1 |
| Anticancer and immunmodulant drugs | 5.1 | 5.5 | 6.1 | 6.6 | 6.5 | 7.2 | 6.9 |
| Drugs of the skeleton and muscular system | 5.3 | 5.3 | 5.6 | 5.8 | 6.2 | 6.1 | 6.3 |
| Drugs of the respiratory organ | 6.2 | 6.3 | 6.2 | 6.4 | 5.8 | 5.4 | 5.2 |
| Drugs of urogenital system and sexual hormones | 2.9 | 3.2 | 3.4 | 3.8 | 4.2 | 4.2 | 4.5 |
| Drugs of the skin | 3.4 | 3.4 | 3.4 | 3.2 | 3.1 | 3.0 | 3.2 |
| Other (e.g. nutrients) | 3.1 | 2.8 | 2.9 | 2.7 | 2.7 | 2.6 | 2.7 |
| Systemic hormone-preparations | 2.2 | 1.8 | 1.8 | 1.8 | 2.2 | 2.1 | 1.9 |
| Drugs of the sensory organs | 1.1 | 1.1 | 1.3 | 1.4 | 1.4 | 1.3 | 1.3 |
| Homeopathic preparations | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 |
| Antiparasitics | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| **Total** | **100.0** | **100.0** | **100.0** | **100.0** | **100.0** | **100.0** | **100.0** |

*Source: MIS Consulting*

**Table 3: The market share of the major pharmaceutical companies (%)**

| Company | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 |
|---|---|---|---|---|---|---|---|
| 1. Richter | 9.7 | 10.7 | 10.2 | 9.6 | 9.0 | 8.9 | 9.1 |
| 2. Egis (group) | 11.7 | 10.6 | 9.7 | 9.2 | 8.6 | 8.0 | 7.9 |
| 3. Novartis (group) | 7.1 | 6.8 | 6.7 | 6.3 | 6.1 | 6.2 | 6.0 |
| 4. Sanofi-Synthelabo | 7.6 | 7.6 | 6.8 | 6.5 | 6.2 | 5.9 | 5.9 |
| 5. Teva (group) | 8.4 | 8.5 | 7.8 | 7.0 | 6.2 | 5.8 | 5.7 |
| 6. Merck Sharp & Dohme | 1.7 | 2.2 | 3.1 | 3.6 | 4.3 | 4.5 | 5.1 |
| 7. AstraZeneca | 2.2 | 2.6 | 3.3 | 3.8 | 4.4 | 4.7 | 4.8 |
| 8. Roche | 3.2 | 2.8 | 3.2 | 3.6 | 3.9 | 4.4 | 4.6 |
| 9. Pfizer (group) | 2.4 | 2.7 | 3.1 | 3.9 | 3.8 | 3.7 | 3.7 |
| 10. Lilly | 3.3 | 3.1 | 3.2 | 3.4 | 3.4 | 3.4 | 3.5 |
| 11. Schering (group) | 3.5 | 4.0 | 3.9 | 4.0 | 3.8 | 3.5 | 3.2 |
| 12. Aventis | 1.6 | 1.6 | 1.8 | 2.1 | 2.2 | 2.9 | 3.1 |
| 13. GSK (group) | 4.0 | 4.4 | 4.7 | 4.8 | 4.2 | 3.8 | 2.9 |
| 14. Pharmacia | 2.6 | 2.4 | 2.7 | 2.6 | 2.7 | 2.6 | 2.6 |
| 15. Janssen-Cilag | 1.9 | 2.2 | 2.2 | 2.1 | 2.4 | 2.6 | 2.6 |
| Top 5 | 44.5 | 44.2 | 41.2 | 38.7 | 36.1 | 34.8 | 34.7 |
| Top 10 | 57.4 | 57.6 | 57.2 | 56.9 | 55.9 | 55.5 | 56.3 |
| Top 15 | 70.9 | 72.2 | 72.4 | 72.4 | 71.1 | 70.9 | 70.6 |

*Source: MIS Consulting*

## *Health sector after 1990*

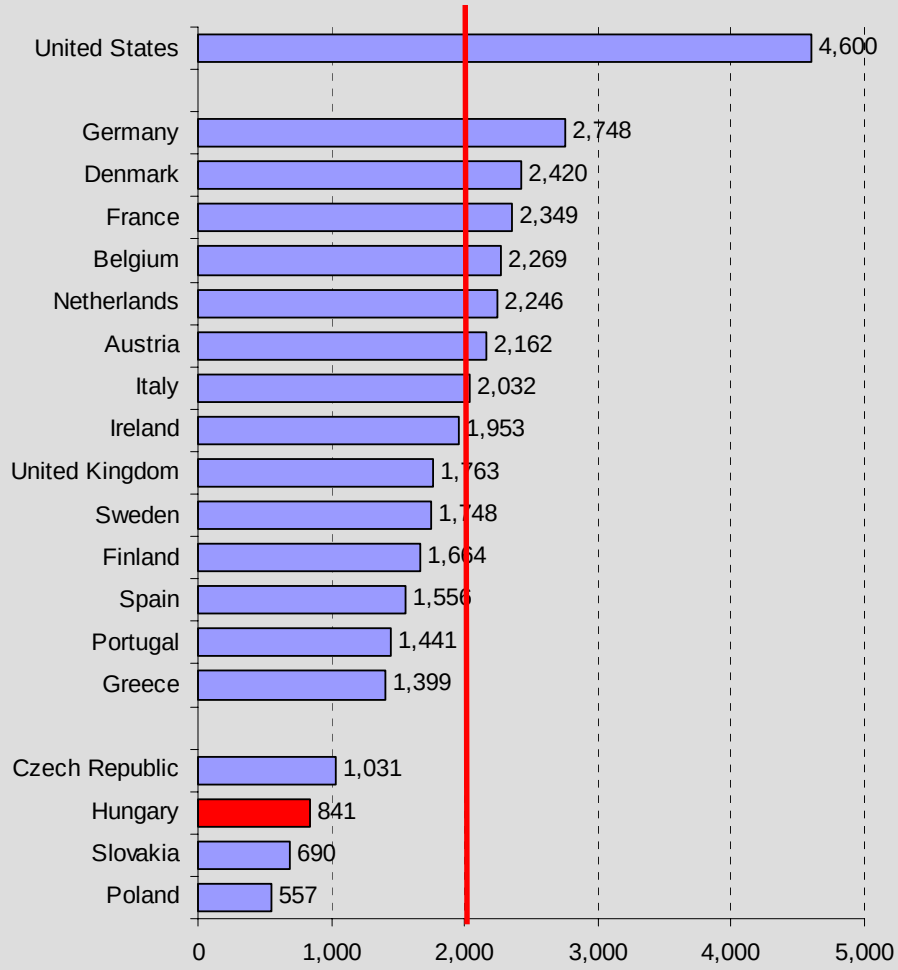
After the breakdown of the Eastern bloc in 1990, policy-makers in the CEE countries faced number of problems in their health care systems. The three main ones were i. the high numbers of some health care inputs (especially hospital beds, to a lesser degree physicians) but equally an undersupply (or at least unequal distribution) of others, i.e. the high technology, ii, low incentive levels for health care providers, which led to a certain under-performance of the health services, and iii, the excessively overcentralized structure of the health care system. To address these problems, a number of similar strategies was pursued in all countries, but no country managed to tackle all three issues successfully.

In Hungary, healthcare still belongs to those areas of the public sector where the major part of the reforms is yet to be completed. Indeed, in many areas reform has already begun. Social security was separated from the Central Budget in 1989, and the operation of health care enterprises was made possible. The family doctor, or GP, system was introduced in 1992 and in addition changes were made to the financing system in line with German and American methods. The reduction of hospital capacities started in 1995-1996. The Health Care Law was adopted in 1997. However, hospitals have not been privatized yet and are mainly owned by local governments.

Total (public and private) healthcare expenditure in Hungary is still low, not just compared to the average per capita figure of the EU, but compared to few CEE countries, such as the Czech republic or Slovenia. Hungary spends around 6.8% of its GDP to healthcare (calculated on Purchasing Price Parity), vs. 7.2% of the Czech Republic, 8.5% of the EU and 13.0% of the US.

However, more than 26% of the healthcare expenditures are spent on drugs, which is significantly higher than the average 15.5% of the EU.

**Figure 5: Per capita health expenditure (USD PPP, 2000)**




*Source: WHO*

## *Patent system*

The Hungarian patent system went through a substantial change in 1994: the process patent system was followed by the product patent system. The process patent system means that only the patented process is protected, the "molecule" itself is not. Under this system, Hungarian pharmaceutical companies were able to manufacture drugs protected by (product) patents in the developed world and sell these in countries with the same process patent system (mainly ex-COMECON countries).

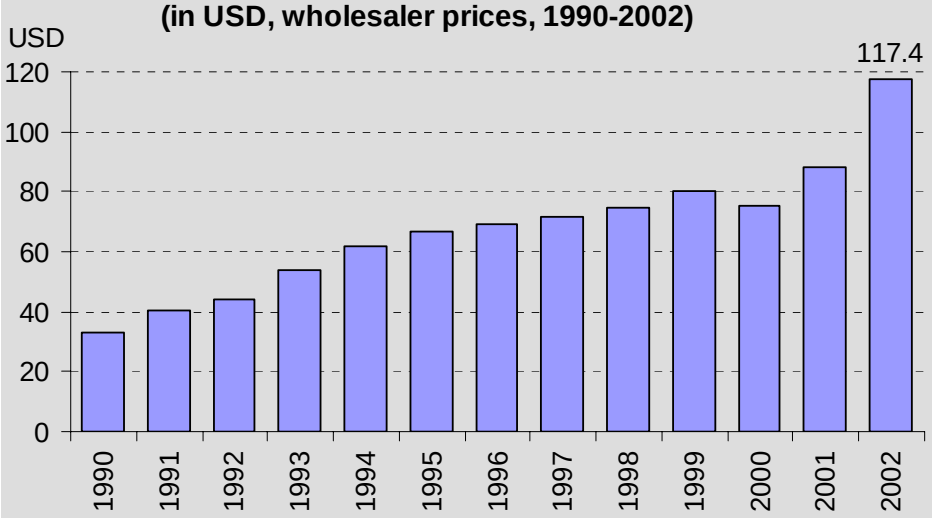
However, in 1994 foreign innovative manufacturers and the gradual application of EU standards enforced the introduction of the product patent system. Under the agreement of Hungary and the innovative drug companies, domestic pharma companies were allowed to keep their rights for selling the copies of certain licensed drugs in Hungary and finalize the process research already started. These allowances gave a chance for the Hungarian pharmaceutical industry to compete with the market-experienced MNCs in the last 5-7 years.

## *Drug consumption*

Hungarian GDP increased by 3.8% in 2001 and by 3.3% in 2002 in real terms. While a smaller proportion of GDP was taken up by health care in the 90s the trend reversed in 2000. This ratio was still 8.6% in 1993 and 6.1% in 1998, but reached 6.8% in 2000. As we mentioned before, expenditure on pharmaceuticals makes up around 25% of total health care spending.

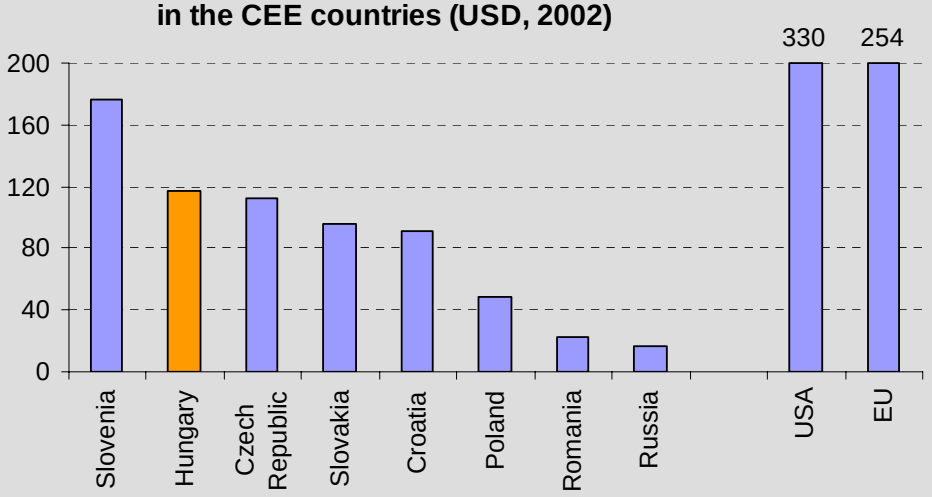
Turnover of domestic pharmaceuticals on manufacture prices was 15 times more in 2002 than in 1990, growing from HUF 21.8 billion to HUF 307 billion over the last twelve years. Last year, per capita consumption of pharmaceuticals equaled HUF 30,292 (USD 117). This level of consumption is still low compared to that of the EU countries; however, the Hungarian price level is also lower. In 2002, drug consumption rose by 33% in USD terms. However, it was partly due to the appreciating forint and the weakening US dollar. In HUF terms, the Hungarian drug market expanded by 19.8%.

**Figure 6: Per capita drug consumption in Hungary (in USD, wholesaler prices, 1990-2002)**



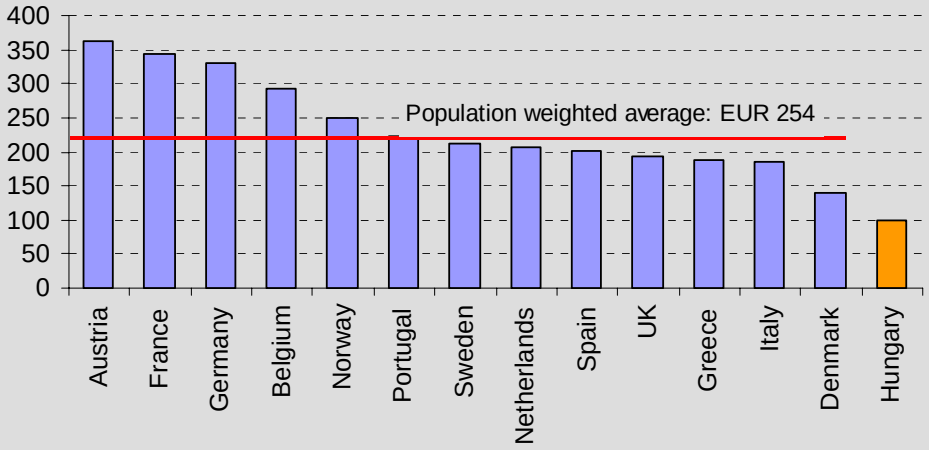

*Source: WHO*

**Figure 7: Per capita drug consumption in the CEE countries (USD, 2002)**



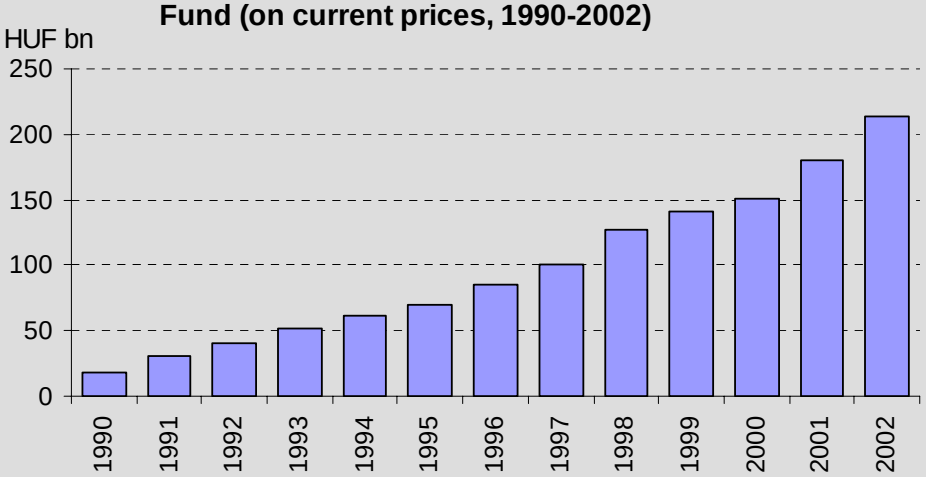

*Source: MIS consulting, miscellaneous sources*

**Figure 8: Per capita drug consumption in the EU countries (EUR, 1999, 2000)**




*Source: MIS consulting, miscellaneous sources*

**Figure 9: Reimbursement budget of the Health Insurance Fund (on current prices, 1990-2002)**




*Source: MAGYOSZ*

## Pricing of pharmaceutical products

The price of pharmaceutical products is set freely by companies in the Hungarian market. (87/1990 Act on setting prices) The wholesale and retail margin on pharmaceutical products is maximized by the Ministry of Health, which means that in practice the ex-manufacturer price can be set freely.

However, the ex-manufacturer price of products at which they are reimbursed by the social security (social health insurance) is subject to negotiation between the pricing and reimbursement committee, formed by experts of National Health Fund, Ministry of Finance and manufacturers prior to the marketing of the reimbursed product. Changes in reimbursed prices, initiated by manufacturers, must be approved by the committee. For non-reimbursed medicines, the Ministry of Health is informed of price changes by either the manufacturer or the importer, and the price is published on a quarterly basis in the Official Gazette.

According to the current legislation, the price of reimbursable pharmaceutical products is negotiated by the National Health Insurance, usually once every year. Then the negotiated prices are presented to a committee, called the Price and Reimbursement Committee.

Each year, negotiations take place between the committee and each manufacturer to determine price increases for the following year. In advance of the negotiation period, the government targets price changes for the following year.

Price setting negotiations are in two, simultaneous parts. The first part introduces the wholesale price and therefore retail price that the expert committee will recognize. The second part assigns the medicines to a reimbursement category.

In the first phase, manufacturers propose a price to the National Health Insurance Fund, but do not provide "cost" information, as there is no rate of return regulation. The price negotiation occurs at the same time as the reimbursement classification, which is considered more important by the manufacturers. If the expert committee deems that the proposed price is too high and therapeutic criteria allow it, expert committee can put the product in a lower reimbursement category or grant reimbursement only if a particular specialist prescribes the drug. A registered drug does not necessarily obtain price reimbursement as the criteria of quality and efficacy may conflict with cost-containment. The committee can refuse to grant any reimbursement, especially if similar drugs are already on the market.

Until 1999, the outcome of the negotiation was ratified by the Ministry of Health. Currently, the Government based on proposal of the Minister of Finance and the Minister of Health ratifies the negotiation outcome. Details of the new product, its price and reimbursement level are published in the official Gazette.

From January 1998, manufacturers do not have to negotiate the price of those products that are not reimbursed by the National Health fund. The list of those medicines that are not reimbursed is published annually by the Ministry of Health.

According to 22/192 Order of the Ministry of Health, Social and Family Affairs, the wholesaler and retailer margins are not fixed but they are dependent on the ex-manufacturer price of a product. Margins are regressive, which means that there is a lowering margin for the more expensive products.

## Reimbursement of pharmaceuticals

Reimbursement categories for prescription medicines in Hungary are 100, 90, 70, 50 and 0 %. If prescribed by a specialist, medicines in 25 therapeutic areas are available with 100 % reimbursement and 41 categories are reimbursed to 90 %. The socially handicapped are entitled to certain medicines, which are being prescribed to them with 100 % reimbursement. These medicines are contained in a special list. Also entitled to free medicines are those serving in the army and those who suffered workplace accidents.

### Reimbursement

The reimbursement policy in Hungary came into force in February 1995. This reimbursement system applies to all Hungarian citizens. In line with the Transparency Directive (89/105/ECC) regarding transparency requirements of drug pricing and reimbursement policies, the principles of drug reimbursement were published in 1996, Welfare Gazette Number 25, as a ministerial statement. According to this regulation, drugs can be reimbursed at these varying levels: 0/50/70/90%. The bioequivalent generic products are reimbursed with a fixed amount based on the price of the least expensive alternative product included in the given group of similar products. Fixed reimbursement system has been introduced for 75 INN groups.

Applications for reimbursement of any product is submitted to the National Health Fund. Until 1999, this was the legal responsibility of the Ministry of Welfare (now Ministry of Health, Social and Family Affairs). Then the medical profession (Medical Chamber and consultants of the National Health Fund) is consulted

upon the question whether the drug is acceptable for reimbursement and if so at what level. In case of generics such consultation is not needed and practically any generics, which price is favorable compared to those products already in the market is accepted for reimbursement assuming the generic product is ready to be marketed. It happens hardly ever that the Medical Chamber's official statement is not to reimburse the pharmaceutical product. In 1999 there was a general policy direction set by the Ministry of Health that non-prescription products should be taken off the reimbursement list. The reimbursement decisions are published in a government decree and made public in the Official Gazette.

Since pharmaceuticals manufactured in Hungary are in general, lower priced than medications from foreign companies, medications on the social list are primarily products manufactured in Hungary.

Economic evidence is not explicitly required in reaching reimbursement decisions. A committee has been already set up to discuss methodological issues regarding economic evaluations for drugs, but it is not resulted yet in a developed system of economic evidence. It is likely that within the next couple of years in case of new innovative products and me-too products such evaluation will be required for reimbursement.

In Hungary, there are not any earmarked budgets for new and expensive pharmaceutical products, therefore many of them were simply kept out the reimbursement system.

## Cost-Sharing

As mentioned above, drugs can be reimbursed at the levels of 0, 50, 70, and 90 percent in Hungary. The bio-equivalent generic products are subsidized with a fixed amount, which is based on the price of the least expensive alternative product included in the given group of products. For 75 INN groups, fixed reimbursement has been introduced. In cases of choosing the higher priced brand-name drugs, the difference between the fixed amount reimbursed and the price has to be covered by the patient.

In general, there are two groups of patients who are considered to be exempt from co-payments. Firstly, individuals who suffer from sever chronic disease, and secondly, individuals who are eligible for public assistance. The list of medications that can be prescribed to the exempted group of individuals is published in the official Gazette of the Ministry of Health, and products considered for this list are assessed on both clinical effectiveness and price.

Around 30% of prescriptions are not subject to co-payments of patients. (This includes both disease specific groups and the low-income groups.)

## Category of maximum reimbursement for special diseases (90-100%)

Individuals who suffer from severe chronic disease can receive their medicines free of charge or reimbursement at a level of 90%. Prescriptions for these special conditions have to be prescribed by a specialist doctor. In addition, there is a special list of very expensive drugs that can only be 100% reimbursed if they are prescribed.

The list of these conditions is defined in a governmental decree. There are 23 conditions, which warrant 100% reimbursement (for example, diabetes, cancer or multiple sclerosis) and another 37 conditions make patients eligible to a 90% reimbursement (e.g. asthma, epilepsy and rheumatoid arthritis). Patients who suffer from cancer would get nearly all drugs reimbursed at the highest level, from soft pain-killers to the most expensive special cancer products. The treatment period may be limited for certain diseases: for instance, treatment for psychiatric diseases is covered for this special category for only six months.

## Category of 100% reimbursement for deprived people.

People who are in difficult social status and have low income can apply for a special card against which a shortened list of reimbursed products can be purchases free of charge. This special public care system was introduced in 1995. Beneficiaries of the scheme are the socially deprived people, i.e. those who earn the minimum monthly wage. They can only benefit from this subsidy only when the drug has been prescribed by a doctor, and when it has been dispensed by the pharmacy that they are registered with for this control. Usually low-price drugs from various therapeutic categories are included on this special list.

Approximately 5% of the population are eligible for public assistance and medicines free of charge, upon the decision of local government authorities. However, the central government provides the necessary funds for covering the co-payment on behalf of the patients.

Currently, the 100% reimbursement list currently contains some 600 products. The list is revised every year by a committee having from National Health Insurance Fund, Ministry of Health, general practitioners and pharmacists.

## Other reimbursement levels (90, 70, 50%)

Most diseases are currently reimbursed at a level of 70 or 50 per cent. In Hungary, there is also a fixed reimbursement system, where the amount reimbursed for bioequivalent products is equal to the reimbursement price that applies to the least expensive drug containing this compound. The existence of cheaper me-too products in the market means that their prices are often the reference prices for branded ethical products.

This system does not currently apply to drugs with the same therapeutic group (i.e. antihypertensives), but it can be introduced in certain tighter clinically categories (i.e. ACE inhibitors) when an ATC subgroup based fixed system is to be introduced because of budgetary restrictions. This system will probably increase the proportion of co-payments to be paid by patients but it is also likely to initiate doctors' opposition who usually prefer to prescribe more expensive branded products rather than generics.

## Category of no reimbursement (0%)

This category includes non-prescription drugs that are not subsidized and few prescription drugs, such as analgesics or sleeping pills, are not reimbursed either.

Since January 1998 it is possible for a drug to be marketed having to go through the pricing and reimbursement process, described above. Naturally, these drugs are not the subjects of any subsidy.

Athough, the pricing system certainly moved towards the transparency in the last ten years, the new government contravened the three-year price agreement in 2002. During the past several years the planned pharmaceutical budget had always proved to be insufficient and additional funds had to be set aside. With the move the new government wanted to set back the growing deficit of the National Health Fund.

However, the government's effort only moderately succeeded last year, and now there is no agreement on the schedule of the new reimbursement talks.

## Monitoring of prescribing policies of doctors

In Hungary there is a system of monitoring prescribing patterns of doctors. The use of the highly subsidized exempted medicines is monitored through this computerized system. High priced prescriptions, patients generating high monthly drug expenses, and physicians over-prescribing are selected for more scrutinized control. In 1999, professional bodies have been consulted on a plan aiming to encourage rational prescribing of drugs by providing financial incentives to physicians as part of the savings could be used in order to improve their practice. The final decision on the introduction date of this scheme has not been made so far.

OEP most recently mentioned that it initiated an inquiry against patients and doctors, who marked out with enormously high usage of certain expensive drugs.

## Generics

The prices of generics are regulated through the negotiation process during which reimbursement status is provided. In general, generics are priced 20% lower than the brand name reimbursable products, but prices tend to converge over time.

These products are reimbursed with a fixed amount based on the price of the least expensive alternative product included in a given group of similar therapeutic products.

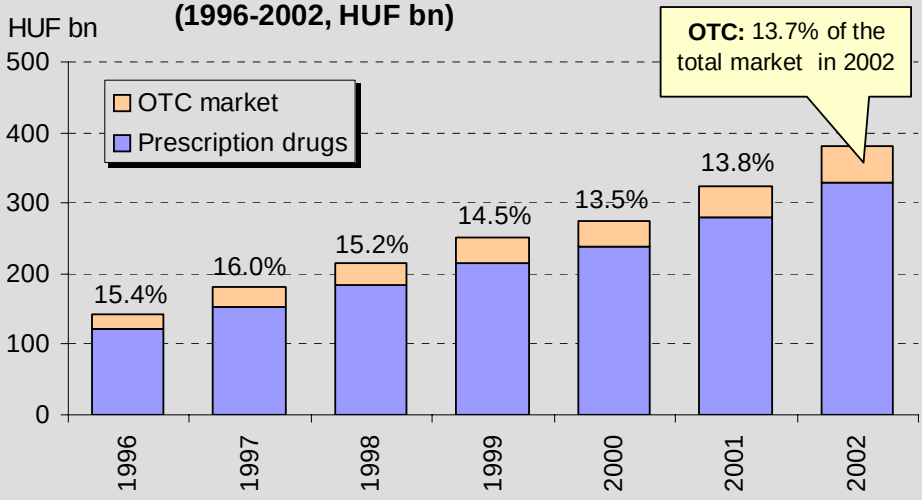
Generic substitution is currently allowed in Hungary. Pharmacists can substitute a branded product with a cheaper generic, unless the physician has explicitly requested on his/ her prescription that a branded product should be dispensed. There are no explicit incentives for physicians or pharmacists to prescribe or substitute with generics.

In 2000 original preparations and license products claimed about 25 % of the Hungarian pharmaceutical market, the rest was made up from generics.

## OTC products

The Prices of OTC products are freely set up. Therefore, OTCs are not reimbursed, unless they are included into the special list of drugs, which are available free of charge for low-income groups. OTC products are allowed to be sold by licensed pharmacies only.

**Figure 10: Sales of OTC drugs on retail prices (1996-2002, HUF bn)**




*Source: MIS consulting*

The main products in this category are vitamins, food supplementary products, baby-care and nutrition and medical nutrition etc.

According to the Hungarian law, OTC products could be advertised with certain limitations, while prescription drugs are kept off advertising. Mail order and trade of pharmaceuticals over the Internet are also prohibited.

*Margins to wholesalers and pharmacists*

In 2000, there were more then 20 large wholesalers, around 2050 retail pharmacies and 340 branches in Hungary. The mark-up of wholesalers and pharmacies is tightly regulated. The system used by Hungary applies a sliding scale, which means a decreasing gross margin percentage for more expensive medications. In 1999, the average margin was 6.0 % for wholesalers and 17.8 % for retail pharmacies.

# Market participants

## National Institute of Pharmacy (OGYI)

OGYI is the Hungarian authority for the registration of pharmaceutical products. There are over 5,000 drugs has been already registered in Hungary by OGYI, of which more than 500 new products were registered in last year.

Normally, the registration process takes 6-18 months. However, Hungary recognizes the EU centralized procedure. Drugs with EU registration are licensed by the Hungarian Drug Institute within 3 months after all required documents were presented.

The Hungarian Pharmaceutical Manufacturers Association (MAGYOSZ) is a national organization representing the professional interests of the pharmaceutical industry. It operates under the 1989. II. Law on the rights of Unions.

MAGYOSZ was established in 1990. Its main tasks include reconciliation and representation of professional interests, monitoring local and foreign pharmaceutical research, development, production, trade and economic activities and advising the members accordingly. It initiates, coordinates, and organizes a concerted action when it comes to enforcing members' interests.

## National Health Insurance Fund (OEP)

OEP was funded to finance the reimbursement of drugs in Hungary. In recent years OEP has covered 70-75% of Hungary's drug expenses and patients the remaining 25-30%. Each year, the OEP (as the primary drug purchaser in Hungary) and pharmaceutical firms have negotiated the price of more than 2,000 prescription drugs.

In 1999, the government declined to participate in the negotiations and placed a cap on drug spending. In 2000 the OEP was to switch to funding only "evidence-based medicines", checking the efficacy of the 400 drugs on which it spends 90% of state-subsidies.

Along with the country's total healthcare budget, the drug budget has been decreasing in real terms. Still, drug pricing is a hot political issue in Hungary. Hungarian citizens became accustomed to inexpensive drugs during four decades of the communist era and most still feel entitled to low cost drugs as well as free medical services.

# Potentials impacts of the EU accession on Hungary's pharmaceutical industry

The health status in most Candidate Countries is lower than in the EU and threats to health are increasing. The health status had been deteriorating even before 1990, but unwanted social effects of the transition worsened the health status in most Candidate Countries.

For the statistically most reliable health indicators (life expectancy and infant mortality) most Candidate Countries lag behind the EU. While in the 70's the difference in life expectancy between most of the Candidate Countries and the EU was on average 2-3 years, it now exceeds 6 years. Several Candidate Countries experienced a drop in life expectancy in the early 90's but for most of them the situation is now improving. For almost all the Candidate Countries mortality is significantly higher than in the EU. The most important causes of death are similar to those in the EU, namely diseases of the circulatory system, cerebrovascular diseases and cancer. Even though the gap in infant mortality has narrowed, the levels are still significantly higher than in the EU.

In terms of health systems, the candidate countries systems have faced severe financial and structural challenges over the past decade. Most countries suffered temporary breakdown of their economies, which has translated into a shortage of resources for the health sector. In response to the financial situation and new thinking in health systems management countries have also started undertaking analyses of staffing levels and health systems organization to see where more effective use of limited resources might be made. In financial terms, the EU countries spend on average nearly twice as much of GDP on health as do the candidate countries.

In light of the moves towards EU enlargement issues such as possible staff migration, patient demands, differing health priorities, adequacy of surveillance and disease prevention and control and others need to be considered. Issues such as consumer safety and tobacco legislation, already addressed in a number of EU laws, also need to be reviewed.

Therefore, it is very likely that the healthcare reform will accelerate in many countries, which would have considerable impact on the pharmaceutical market, too. The countries should meet the transparency criteria with their reimbursement systems, and the MNCs will be able to lunch their new drugs easier to the pharma markets. Because of this, the enlargement means threats for the Hungarian pharmaceutical sector.

However, it also means opportunities. Marketing of the products of the Hungarian drug companies in the EU will be easier, too. Although best-sold products of these companies in Hungary are legal copies of some patented original drugs. Currently, these copies are not marketable in the EU, but it will be in few years, when their patent will expire. That time, Hungarian companies could start selling these products with some advantage over their generic competitors.

## Employment

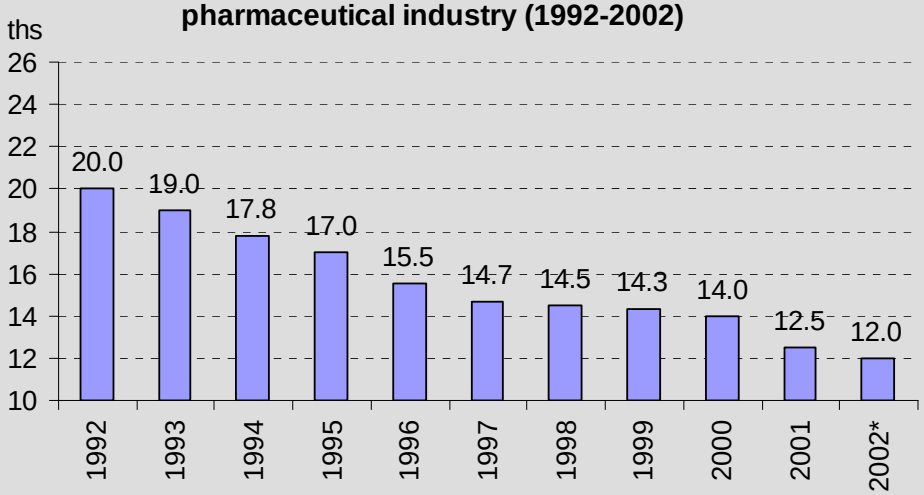
We believe the EU accession would have marginal impact on the employment in the Hungarian pharmaceutical sector. However, we see both positive and negative impacts with moderate importance. These are the following:

- Following the privatization the necessary layoffs in the production and the administration of the Hungarian companies have been done.

- Continuous strengthening of the forint after the widening of the floating band in 2001 set back the competitiveness of the Hungarian companies, which forced them to initiate new layoffs. In 2001, the employment in the Hungarian pharma sector decreased by roughly 10%.
- Currently, sales/employee ratio is close to USD 100,000 in Hungary vs. the average of ca. USD 300,000 of the major pharma MNCs. We believe this fact is due to i) the lower labor costs and ii) the much more labor-intensive structure of the Hungarian pharma industry and iii) the lower size of the domestic companies.
- The coming EU accession will certainly put pressure on the companies to rise the wages. This could lead to new wave of layoffs in the pharmaceutical sector as well. However, we expect only a moderate decrease in the employment, as the labor-capital switch is rather limited.
- The continuous boom in the number of doctor visitors (which is driven by the growing number of pharmaceutical companies, the growing number of products and overall, the growing size of the Hungarian pharmaceutical market) could partly compensate for the fall in the number of the administrative staff.
- The lower Hungarian wages and the supply of well-qualified chemical, medical, biological and clinical professionals could allure MNCs to establish research affiliates in Hungary. Few years ago, AstraZeneca was the first company, which opened its Central-European research center close to Budapest. After joining the EU, the tests made in Hungary would be more easily accepted by European regulators. We believe, these could encourage developed companies to make their laboratory/clinical trials in Hungary and hire Hungarian professionals.

Overall, we expect the fall in the employment to slow down gradually in the next two years, and to start growing thereafter.

**Figure 11: Number of employees in the Hungarian pharmaceutical industry (1992-2002)**

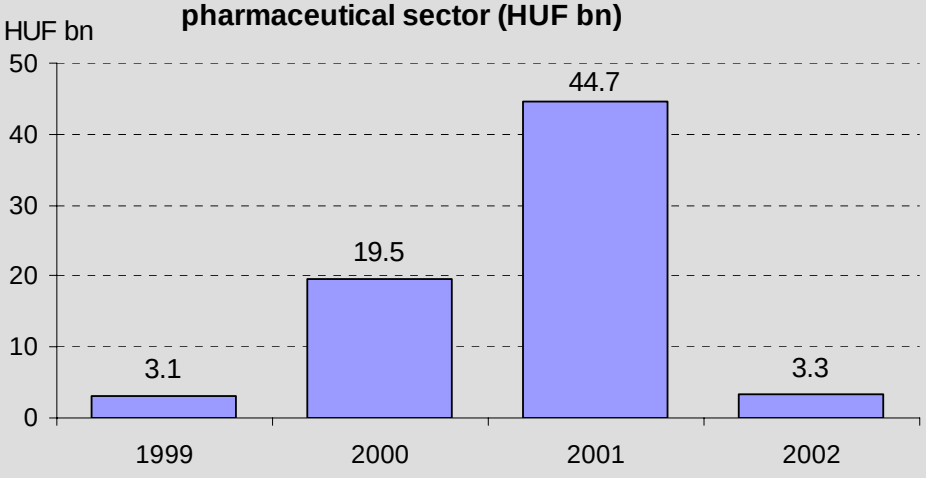



*Source: MAGYOSZ, *estimate*

## Foreign direct investment

Foreign direct investment was significant in mid 90s when most of the Hungarian pharmaceutical companies were privatized. Since than, there were only mere investments placed in the sector. (Unfortunately, the available figures also contain the investments in the Hungarian petrochemical sector. Without the huge capital inflow to the two major Hungarian petrochemical companies in 2000-2001, the figures would show a stable annual investment of HUF 3–4bn in the pharmaceutical sector).

**Figure 12: Foreign direct investment in the chemical/ pharmaceutical sector (HUF bn)**

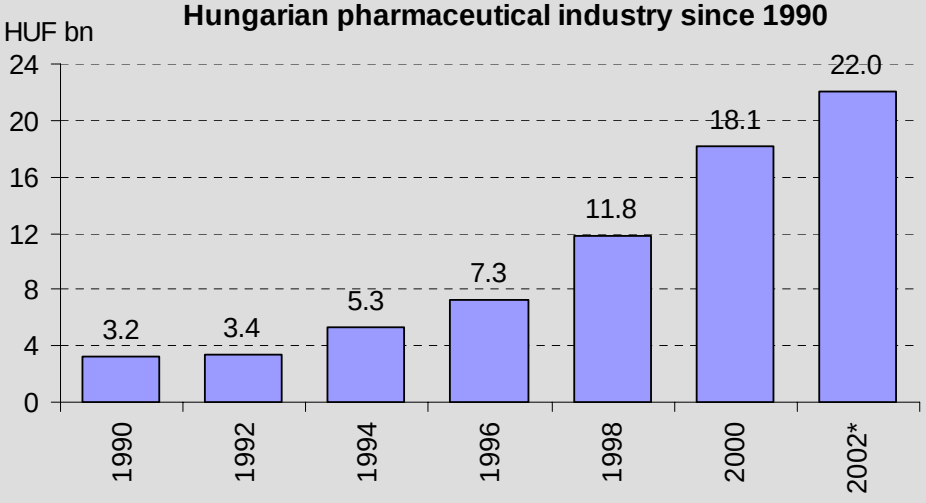



*Source: National Bank of Hungary*

The EU accession of Hungary would have only moderate positive impact on the FDI in the pharmaceutical industry. MNCs are unlikely to invest in production facilities, but rather to R&D centers and distribution networks.

Therefore, similar to AstraZeneca, other companies could also appear in the next couple of years with the intention to establish R&D center in Hungary. However, according to our estimates, it would increase the FDI only by few billion forints.

**Figure 13: Development of the R&D expenditures of the Hungarian pharmaceutical industry since 1990**

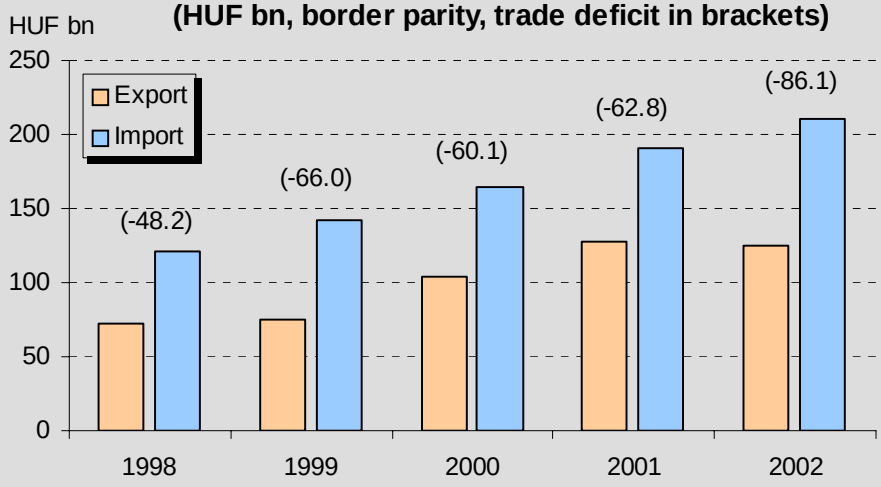



*Source: MAGYOSZ, *estimate*

## Trade balance

The trade deficit of the Hungarian pharma sector continuously widened during the 90s. The reason of this was the booming import driven by the spread of the relatively new innovative drugs on the Hungarian market. In the last five years, the deficit stagnated at around HUF 60bn, but boosted in 2002 mainly due to the adverse effect of the strengthening Hungarian currency and the weak US dollar. Roughly half of Hungary's export of medicines is based on USD, which weakened by 19.4% compared to the Hungarian forint in 2002 (end of year figures).

**Figure 13: Trade balance of pharmaceutical products (HUF bn, border parity, trade deficit in brackets)**




*Source: Central Statistic Office*

In 2003, we expect the deficit to broaden above HUF 100bn as a result of the further strengthening forint.

However, we also believe, that deficit will stagnate in 2004 and 2005 because of the following reasons:

1. From the current level, further strengthening of the Hungarian currency seems to be limited. This could stop further decrease of the competitiveness of the export.
2. The growth of the main export markets of Hungary (Russia, CEE countries) the growth rate will probably exceed the growth rate of the Hungarian pharmaceutical market (for which IMS Health forecasted 9% CAGR for the next five years)
3. We see the current trend of the Hungarian pharmaceutical market (viz. the change in the consumption structure in favor of the new original drugs) to continue in the next couple of years. The EU accession could strengthen this trend with the acceleration of the mutual recognition and the more transparent regulation of the reimbursement system. These could lead to a further increase in the share of the import drugs on the Hungarian pharmaceutical market.

In our view, the above mentioned points will result in a stagnating trade deficit in the following years after Hungary's EU accession.

## Legislation

Act 25 of 1998, which came into force on 1 January 1999, concerns medicines for human use and specifies the basic measures governing medicines, their supply and the rights of medicine consumers. The Act takes into consideration international legal regulations including EU legislation. The main points of the Act are:

- The monitoring of compliance with marketing requirements as well as supervision is the responsibility of the National Institute of Pharmacy.
- The process of registration may not take longer than two years from submission of application. Marketing authorization is valid for 5 years and may be extended for additional 5 year periods.
- Medicines not registered in Hungary, but registered in another country by a competent national or international Authority, may only be applied for medical purposes when their use is supported by an appreciable therapeutical interest. Marketing authorization is always required.

With the Act and other regulations, Hungary practically accepted the EU legislation and regulation practice. For instance, all the GLP, GMP and GCP standards have already inserted to the Hungarian law.

Intellectual property standards and enforcement are similar to that existing in the EU and compatible with the provisions of GATT/TRIPs. This includes a 20- year term for product patents plus up to five years Supplementary Protection Certificate (SPC), as well as effective data protection and adequate means of enforcement.

The most crucial point during the talks was the question of parallel trade. EU aimed at to prevent its pharmaceutical markets being flooded with cheaper versions of products sold in the Hungarian market (where prices will generally be much lower than in the current member states). One of the tools was the approval of the SPC. In Hungary, the mechanism would give protection to holders of a patent or SPC for medicines authorized in an EU member state before a patent or SPC could have been obtained for the product in Hungary after January 1, 2000.

We consider meeting the Transparency criteria of the EU as the main task for the Hungarian drug market regulation in the following months.

## Recent developments of the Hungarian drug regulation

Similar to the last couple of years the healthcare budget in Hungary seems to be underestimated in 2003. Since the major cause of the overspending is the strong rise in the medicine consumption and therefore the subsidies paid on that, the government and the National Health Fund is going to change the current price regulation system in order to curb public deficit. There is still no decision made on the issue, but pharma professionals agree that the new pricing mechanism would determine the growth of the Hungarian pharmaceutical market in the next couple of years.

## *Therapeutic fixed amount reimbursement system*

The National Health Fund (OEP) would like to see a gradual change in the system without taking into consideration the sensitive political background of the issue. Seemingly, OEP intends to introduce therapeutic group reference pricing in Hungary, which generated heavy disputes in the question even in the EU countries. Therapeutic fixed reimbursement system means that the forint-based reimbursement of all the medicines belonging to the same therapeutic group (ATC 4 or ATC 5 level) but having different active ingredients, thus being different in their characteristics is determined on the basis of the lowest cost per defined daily dose. The sum reimbursement would base

This system is hardly acceptable for market participants, because of different reasons:

1. The therapeutic fixed reimbursement system, if introduced, would substantially increase patients' burdens by compelling them to purchase their accustomed medications on much higher prices. Without changing their drugs to another, patients would not feel a reformed reimbursement system but a drastic rise in drug prices. It is still a question, whether the doctors would be willing/able to convince patients to use a new drug. In some cases it is not possible, therefore a certain rise in prices is very likely.

2. The doctors deny the plan of OEP since it will obviously hurt their freedom of therapy. They argue that the active ingredients in the same therapeutic group may have different indications and these drugs may greatly vary in their effect and adverse reactions. OEP also plans to monitor the doctors' prescription practice, since there were many abuses over the past few years. Therefore it seems that the tensions between the pharmacists/doctors and the Health Fund is growing.

3. Innovative drug companies feel the therapeutic fixed reimbursement system would limit the patients by access to medicines.

4. Doctors and pharmacists argue there is no acceptable method for determining therapeutically equivalent doses of different medicines belonging to the same ATC group. The use of WHO's DDD (average defined daily dose) is not acceptable for many, because it disregards the differences stemming from the different indications.

5. It is still unclear that the introduction of the therapeutic fixed reimbursement system how many saving would bring for OEP. If prescriptions will be shifted to non-reference groups' prices are likely to surge.

Although therapeutic group reference pricing for the time being lowers the prices of medicines sold in the given therapeutic group, it does not impact on other components of the rise of medicine consumption costs. Where it has been introduced (Germany, Sweden, Denmark, Holland), it caused the average price and the sales volumes fall in the given group, at the same time the non reference priced product groups saw the prices and sales increasing, which went together with the surge of total drug sales.

Extending therapeutic group reference pricing to products under patent protection is contrary to a European Union court judgment. These measures have, in the mean time, been repelled in many countries because they failed to bring about the anticipated results.

# Summary

In our study, we overviewed the pharmaceutical sector of the EU including its competitiveness, legislation and the regulation. We found that there the sector has been lost its competitiveness in the last couple of years due to structural problems and the lack of a Single Market, which makes the parallel trade possible and therefore causes growing losses for the companies.

We also found that the legislation moves towards the Single Market slowly, as the pharma MNCs are more interested in forcing the national governments to put administrative barriers into the parallel trade and keep the difference prices on each national market. This could have an impact also to the Hungarian market, where prices will probably remain lower than in the current member states, after joining the EU.

In the second part of the study we showed the main characteristics of the Hungarian healthcare system and the pharmaceutical market. We found that the health status of Hungary is very poor compared to the EU countries. However, the pharmaceutical market is relatively developed compared to the other CEE countries, mainly because of the traditionals of the industry and the growing need of new and more effective pharmaceutical treatments.

Practically, Hungary has accepted the EU legislation and regulation practice. GLP, GMP and GCP standards have already inserted to the Hungarian law. Intellectual property standards and enforcement are similar to that existing in the EU and compatible with the provisions of GATT/TRIPs. This includes a 20-year term for product patents plus up to five years Supplementary Protection Certificate (SPC), as well as effective data protection and adequate means of enforcement. The approved patent mechanism would give protection to holders of a patent or SPC for medicines authorized in an EU member state before a patent or SPC could have been obtained for the product in Hungary after January 1, 2000. Among the tasks of the Hungarian legislation we considered meeting the Transparency criteria of the EU as the most significant.

We stated that accessing the EU means both threats and opportunities for the Hungarian pharmaceutical industry. Registration procedure will be easier for the foreign companies and this could squeeze further the market share of the domestic producers. However, on the other hand, the generic pharma market of the EU could provide good opportunities for the Hungarian pharmaceuticals.

We believe, the EU accession of Hungary could have only moderate positive impact on the low FDI in the pharmaceutical industry, as MNCs are unlikely to invest in production facilities, but rather to R&D centers and distribution networks. We also believe the EU accession would have marginal impact on the employment in the Hungarian pharmaceutical sector.

The accession could strengthen growing trend of the pharmaceutical sales in Hungary with new products lunching the market due to the acceleration of the mutual recognition agreements and the more transparent regulation of the reimbursement system.

Overall, we fund that joining the EU will certainly accelerate the development of the Hungarian pharmaceutical market and will likely provide more opportunities than threats for the domestic companies.

# References

EFPIA**:** Prospects for European Competitiveness

Presentation made by Brian Ager at the Economist, London, 12-13 February 2003

EFPIA, 2001, The Pharmaceutical Industry in Figures,

The European Federation of Pharmaceutical Industries and Associations, Bruxelles.

A. Gambardella, L. Orsenigo, F. Pammolli,2001, Global Competitiveness in Pharmaceuticals. A European Perspective

http://europa.eu.int/comm/enterprise/library/enterprise-papers/pdf/enterprise_paper_01_2001.pdf

Graham Lewis, Vice President of IMS Health: The generics market – Current and Future Status

European Generics Association November 21, 2001

NERA, 1998, Policy Relating to Generic Medicines in the OECD,

National Economic Research Associates, London.

PhRMA, 2002, Pharmaceutical Industry Profile, PhRMA, Washington DC.

http://www.phrma.org/publications/publications/profile02/industryprofile2002.pdf

DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on the Community code relating to medicinal products for human use, of November 6, 2001

Reinhard Busse: Health Care Systems in EU Pre-Accession Countries and European Integration

Arbeit und Sozialpolitik, 5-6/2002, p. 41.

Jelena Markovic: The European Pharmaceutical Industry – Opportunities and Challenges

Business Briefing: Global Healthcare, 2002 Issue 3

Poullier j., Hernandez P., Kawabata K., Savedoff, W. D.: Patterns of Global Health Expenditures

EIP/HFS/FAR Discussion Paper No. 51 World Health Organization November 2002

CMS Cameron McKenna, Andresen Consulting: Evaluation of the operation of Community procedures for the authorisation of medicinal products, a study on behalf of the European Commission, October 2000

Ministry of Education: Research and Development in Hungary, Budapest, October 2002

GVH: A gyógyszerpiac szabályozásának versenypolitikai kérdései, Budapest, January 2003

Commission of the European Communities: Regular report on Hungary's progress towards accession. Brussels,9.10.2002 SEC(2002)1404 2002

Committee on Economic and Monetary Affairs and Industrial Policy : Report on the communication from the Commission on the Single Market in Pharmaceuticals, Brussels April 21, 1999