COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 25.11.1998
COM(1998) 588 final

COMMUNICATION FROM THE COMMISSION

on the Single Market in Pharmaceuticals

Commission Communication on the Single Market in Pharmaceuticals

Chapter 1
INTRODUCTION

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 (Resolution of 16 April 1996) and the Council (Resolution of 23 April 1996) 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.

In the meantime, several of the key actions identified in the 1994 Communication have been accomplished : the new Community procedures for the authorisation and supervision of medicinal products are fully operational, the ability to patent innovations in the field of biotechnology has been introduced, and some remarkable breakthroughs have been achieved in facilitating access to third country markets with the conclusion of the first phase of ICH (the International Conference on Harmonisation) and the signature of mutual recognition agreements with Canada and the United States.

There are encouraging signs that the action undertaken was necessary. After a late start, Europe's pharmaceutical biotechnology sector is now growing fast, although not so fast as its US counterpart. Employment in the European industry had been increasing by an average of 2,4 % a year for 20 continuous years, when this trend was abruptly interrupted in 1994 (13,500 jobs - 2,6% of total employment - were lost in that year); since 1996, employment has been is growing but, by 1997, it had not yet reached the level that had been attained in 1994.

Further steps are needed. The purpose of this Communication is to address the operation of the pharmaceutical market in the European Union. It is intended to contribute to – and to take forward – policy development in this area in the light of recent "Round Table" discussions between the Member States, the pharmaceutical industry and the Commission services on the completion of the Single Market in Pharmaceuticals and of the recent Council Conclusions on the operation of the Single Market in Pharmaceuticals, agreed in the Internal Market Council in May 1998.

The completion of the internal market is the single most important step needed to make Europe a more attractive R&D investment location, but it is not the only one. Action will have to be taken in parallel to address various other factors shaping the overall climate in which research and innovation take place, such as : access to venture capital; public funding of research; programmes to exploit synergies between the academia and industry or between basic and applied research; public understanding and acceptance of new technologies, including biotechnology and gene therapy. These matters are not addressed in this Communication, which is concentrating on the challenge of completing the Single Market in pharmaceuticals.

The purpose of the completion of the Single Market in pharmaceuticals is not just to provide an environment which is favourable 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. It must be clear that these policy orientations have to lead up to improvements in the provision of healthcare for all citizens. This has to be kept in mind at all

times, when policies are designed, recommended and implemented in this field, and a difficult balance has to be drawn between potentially conflicting objectives.

Issues relating to pharmaceuticals need also to be seen in the wider context of public health and of efforts to modernise and improve health systems. With increasing pressure on health systems, the Commission is already contributing to work to improve their efficiency, cost-effectiveness and quality. Details of this contribution are set out in the Commission Communication on modernising and improving social protection in the European Union COM(97)102.. The Commission's ongoing work on a future Community public health policy is also of particular relevance to the sector. The first strand of action proposed – improving information for the development of public health – aims to provide a comprehensive health information system and infrastructure for policy analysis and development. This could be used to examine issues such as patterns for prescribing pharmaceuticals, the cost effectiveness of both existing and new pharmaceuticals and the impact of other policies on the sector. The Commission expects to present concrete proposals for this new policy early in 1999. In addressing some specifics of the operation of the Single Market in pharmaceuticals, it is important, therefore, to see this Communication within the context of wider work that the Commission is taking forward in this area.

The efforts undertaken for the completion of the Single Market in pharmaceuticals must take into account the particular features of this sector : a research-based global for-profit industry; the traditional functions of demand split between the patient, the prescribing doctor and social security institutions meeting most of the cost as third-party payers; little private market provision; and high consumer expectations that they will have access to the benefits of medical advance at affordable cost. These efforts must also be consistent with the principle of subsidiarity : Member States have exclusive responsibility in the field of health care; they view both the provision of health and its financing as keys to social solidarity; and they have to meet public expenditure objectives, notably for the purpose of European Monetary Union.

There is, however, added value that action at Community level can bring to the economic regulation of the pharmaceutical sector, particularly in the context of the Single Market. This Communication seeks to set out the totality of the regulatory, social and industrial interests in play, in order to ensure that patients and consumers have access to the pharmaceuticals they need at affordable cost on the one hand and that appropriate incentives are available for innovation and industrial developments on the other.

The pharmaceutical industry in Europe

The pharmaceutical industry in Europe is a strong industrial sector which makes a significant contribution to Europe's industrial base. In 1997, the trade balance for the European Union was some 10½ billion ECU in Europe's favour and over 10 billion ECU was spent in 1997 on research and development in the European Union, representing a three fold increase over the previous 10 years. Over 87 billion ECU worth of products left factories in the EU in 1997, representing some 40% of global production. The market value (at ex-factory prices) of the European Union pharmaceutical market is just over 62 billion ECU (just under 30% of the world market); its retail value now exceeds 90 billion ECU; 56 billion ECU of this retail value is accounted for by payments by health care systems. In 1997, the pharmaceutical industry was employing some 487,000 people in the European Union, including 71,000 people researching and developing pharmaceuticals. In addition to a substantial research and development-based

sector, the pharmaceutical industry in Europe also has active sectors dealing in generic (i.e. patent-expired) and non-prescription ("over-the-counter") sectors.

Nevertheless, there are concerns, particularly in the global context in which this industry operates. The Commission's 1994 *Communication on the outlines of an industrial policy for the pharmaceutical sector in the European Community* (COM(93)718 final) expressed concerns that the competitiveness of the European industry appears to be weakening: 20 years ago Europe led the way in pharmaceutical research and development; more recently, to judge from patent filings at least, Europe has been overtaken by the US. The trend identified in the 1994 Communication has been confirmed by the latest data. Of the 47 new active substances launched on the World market in 1997, 19 (or 40 %) had been discovered and developed in Europe; 30 years ago, Europe's share of pharmaceutical discoveries was 65%. On the biotechnology side, Europe has made a particularly poor start compared with progress in the United States, as was noted in the 1994 Communication. Figures compiled in 1995 on the invention and marketing of biotechnology-derived new active substances put the US share at 76%, Japan's at 14%, and Europe's at 10%. There are however welcome signs that this is starting to change. Data based on a total of 770 biotechnology-derived medicines (including 206 genetically engineered ones) under development at the end of 1995 indicate that 25 % of the biopharmaceutical development work is currently located in Europe (63% in the US, 7% in Japan); in gene therapy specifically, 22% of the development work is located in Europe (70% in the US, 1% in Japan).

The reasons for which part of the pharmaceutical industry in the European Union appears to be losing global competitiveness are no doubt multiple and complex. The European pharmaceutical industry registers significantly lower productivity per worker than its US counterpart. The overall profitability and the return on capital employed appear to be significantly higher in the US than in the European Union, although a proper assessment of the extent and nature of these differences faces formidable measurement problems (because of 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, that could be off-set by a better operating (single) market.

The European pharmaceutical market

There are significant differences between the Member States of the European Union both in general macro-economic conditions (especially per-capita income and wealth) and in health systems. At an aggregate level of income, the majority of Member States lie within +/- 10% of the EU average. There are, however, a few Member States with average incomes per capita more significantly below the EU average. Incomes in the Applicant countries of Central and Eastern Europe are well below the EU average, and significantly below any current Member States.

There are also marked variances in the prevalence and incidence of major diseases, and – unsurprisingly – in the medical practices and medical treatments that address these diseases. Health care systems differ too, as does the share of health care expenditure represented by pharmaceuticals across the Member States. In general, there seems to be a well established positive link between health care expenditure and incomes; however differences in health care expenditure per capita appear to be greater than those in incomes per capita. Higher expenditure on health care as a whole can be related to higher expenditure on pharmaceuticals;

as this relationship is not perfect, it suggests that the demand for pharmaceuticals does differ across Member States. Further, the relationship between incomes and pharmaceutical expenditure appears to be weaker than that between income and total health care expenditure – an indication that other factors are important in determining expenditure.

Pharmaceutical expenditure within the EU is highly skewed towards a limited number of major markets. Hence the two largest (Germany, France) account for just over half the total EU market, and the largest four (Germany, France, Italy, United Kingdom) account for nearly 75% of the total EU market.

The nature and extent of use of in-patent, out-of-patent and non-prescription medicines varies significantly among Member States. In particular, the use of generic products varies considerably between Member States according to how they arrange the financial incentives within their health care systems for the supply, distribution and use of generics.

The cost of pharmaceutical distribution, including wholesale and retail pharmacy distribution differ widely among Member States. Together with the variations in the treatment of pharmaceuticals under indirect taxation rules, these costs significantly impact on pharmaceutical budgets. It would seem that considerable savings could be realised by adapting distribution channels to pro-competitive and less costly models.

The pricing of pharmaceuticals, free movement and parallel trade

The pharmaceutical market is regulated at a number of levels, in particular through the regulatory mechanisms for the Single Market and through action by Member States at national level to manage their health care systems. There is a wide diversity in the ways in which pharmaceuticals have been regulated within the health care systems in the different Member States.

. There are important differences between Member States, both in levels of prices and in levels of consumption (volumes). These differences can be explained by a number of factors, including : divergent medical cultures and prescribing patterns, price discrimination by pharmaceutical companies to reflect the differences in the ability to pay, and conjunctural factors such as inflation and currency fluctuations. One of the factors in these differences appears to be the extent to which Member States rely on price control as the main means for controlling aggregate costs – or whether a wider range of policies are used (including demand controls and efforts to influence prescribing patterns). Because total expenditure on pharmaceuticals has both a volume and a price component, relying on price-fixing to control expenditure does not necessarily deliver a lower aggregate spend on pharmaceuticals or a lower per capita pharmaceutical budget..

To the extent that price fixing by Member States results in the establishment of widely divergent prices, conflict can exist between the operation of price fixing mechanisms and the Single Market. Wholesale intermediaries buy products in lower priced parts of the European Union and sell them in higher-priced parts of the Union. In an effectively integrated market, the prices of tradable goods tend to converge towards a situation where arbitrage is no longer an issue; in this sector, since maximum prices are fixed in many Member States, the price convergence pressure on products already in the market will be towards lower prices, at least for out-of-patent products. Unless parallel trade can operate dynamically on prices, it creates inefficiencies because most, but not all, of the financial benefit accrues to the parallel trader rather than to the health care system or patient. However, parallel trade must equally be seen

as an important driving force for market integration and, consequently, for achieving the Single Market. In as far as the market structure does not provide for the financial benefits of parallel trade to be passed on to consumers and taxpayers, this can normally be ensured through adequate national measures.

Parallel trade has also, to an important extent, been stimulated by price differentials created by currency fluctuations. European Monetary Union is therefore an important step in reducing the risk of price distortions. For those Member States that participate in the Euro, currency movements after market launch, and the considerable effect that these fluctuations have had on parallel trade, will be a thing of the past.

Legal context

Concern about the interaction between European and national regulation of this sector (and parallel trade in pharmaceuticals) is not new. There have been a number of cases in the European Court of Justice seeking to establish whether price fixing by Member States is compatible with the free movement of goods in the European Union. The Court has noted that price control systems, although not in themselves contrary to the principle of free movement of goods, may nevertheless be so when the prices are fixed at a level such that the sale of imported products becomes either impossible or more difficult than that of domestic products – see in particular the judgement in *Roussel (case C-181/82).* In its most recent statement on these issues, in the judgement in *Merck v Primecrown (*cases C-267/95 and C-268/95), the Court noted that "distortions caused by different price legislation in a Member State must be remedied by measures taken by the Community authorities and not by the adoption by another Member State of measures incompatible with the rules on free movement of goods". In this judgement, the Court of Justice also confirmed that a patent holder may not impede the parallel importation of his own products from a Member State where the product could not be protected by a patent, unless he can prove that he is under a genuine, existing legal obligation to market the product in that Member State.

In a recent judgement *(Decker v Caisse de maladie des employés privés, case C120/95)* about consumers moving across borders to access health care products, the Court has noted that "aims of a purely economic nature cannot justify a barrier to the fundamental principle of the free movement of goods", going on to note, however, that "it cannot be excluded that the risk of seriously undermining the financial balance of the social security system may constitute an over-riding reason in the general interest capable of justifying a barrier of that kind". Taken together, these judgements indicate firstly that the fact that pharmaceuticals are used within the health care systems does not exempt them from the rules of the Single Market and secondly that companies normally exhaust their intellectual property rights at the time when they willingly place products onto any part of the pharmaceutical market within the European Union. .

Progress towards a Single Market in Pharmaceuticals

Over the past thirty years, there have been a range of developments towards a Single Market in pharmaceuticals, focusing on a number of relevant policy areas, in particular medicines licensing and the protection of intellectual property. The coming into force of the European Monetary Union will contribute to consolidating these developments, whilst the recent

successes in the external trade policy will allow European companies to use the Single Market as a springboard from which to launch into new third country markets.

- ***Medicines licensing***

  Since the 1960s, a comprehensive process for ensuring the safety, quality and efficacy of pharmaceuticals delivered to the European market has been developed. The provisions applicable include a core set of binding legislation and comprehensive guidance to the competent authorities and the regulated industry. These texts are brought together in a series of volumes entitled *The Rules governing medicinal products in the European Union*, which have recently been made available on the Internet (http://dg3.eudra.org/eudralex/index.htm). Current legislative developments include a proposal for a Directive on clinical trials and a Proposal for a Regulation on orphan medicinal products. Work is in hand to prepare a Proposal for a Directive on starting materials and to codify the entire pharmaceutical legislation in one single text.

  In 1995 two new Community procedures where established which now offer fast access to the whole of the European market in a single process, relying either on a common central evaluation by the European Medicines Evaluation Agency (EMEA) or on mutual recognition between Member States. The close collaboration between the Member States, the EMEA and the Commission that is a key factor in the success of this new system. Through the appropriate use of new information technologies and the pooling of the best available expertise provided by the National Agencies, this new system – perhaps the first example of an effective "networking administration" – is already setting the international benchmark for pharmaceutical evaluation and monitoring (pharmacovigilance). A comprehensive evaluation of the operation of the new system will be conducted in the year 2000; this will in particular provide an opportunity to address the need to speed up the decision-making process and to assess the overall contribution of the new procedures to the improvement of public health in the Community.

- ***Intellectual property***

  On the intellectual property side, Europe now has – through legislation that has been agreed by the Community institutions – the highest quality provisions for pharmaceuticals in the world. To compensate for the fact that it takes a long time to research and develop a new product, the pharmaceutical sector has been granted (through supplementary protection certificates) the right to extend its market exclusivity beyond the normal 20-year patent period, up to 15 years of effective protection from the date of first authorization in the Community (in the US, the comparable protection is for a maximum of 14 years). Legislation agreed this year by the Community institutions has introduced the ability to patent innovations in the field of biotechnology, a key field for this sector. The licensing process further protects the data used for license applications for 6, or more generally 10, years (whereas in the US, for example, such data exclusivity lasts for a maximum of 5 years). The Commission will present next year a proposal for a regulation to establish a Community patent, valid throughout the Single Market; this should facilitate the penetration of market by patented products, because of streamlined procedures.

- ***European Monetary Union***

  A large part of price divergence in Europe, and more specifically of price instability, is attributable to currency fluctuations. Depreciation of some currencies has widened the

market price gap between some Member States, creating further incentives for parallel trade. The advent of the Euro should help to provide a more stable environment in this respect, at least for participating Member States. It will however also make price differentials in the existing European market much more visible; this could in turn stimulate wholesalers and individual pharmacists to engage in cross border business. On the supply side, the development of an integrated capital market could reduce costs and improve access to funds, especially for innovative SMEs.

- *Access to third country markets*

  Technical requirements for the demonstration of the quality, safety and efficacy of a new medicinal products have been almost completely harmonised between the European Union, Japan and the United States, under the ICH (International Conference on Harmonisation). At the Fourth ICH Conference which took place in Brussels in July 1997 it was therefore decided that the three regions would now seek to agree in the way this information should be presented for the purpose of obtaining authorisation to place the medicinal product on the market; this would obviously save unnecessary duplication and re-working, thus decreasing the time and resources required for submission of regulatory documents, ultimately benefiting patients in the three regions and in the rest of the World. In the area of manufacturing, Mutual Recognition Agreements have been concluded with Canada, the United States, Australia and New-Zealand; they will allow substantial savings for manufacturers and, ultimately, for consumers and social security institutions, as inspections and batch controls are no longer duplicated with no benefit in terms of quality or safety. Similar arrangements are currently being negotiated with Switzerland and Japan. The effort will henceforth concentrate on the implementation of these agreements, on resolving the remaining trade barriers with some of the major partners (such as the problem of the acceptance of foreign data in Japan), and on improving access to the emerging markets of East Asia and Latin America.

The uncompleted agenda

As already indicated, there are several areas which deserve further attention : improving access to risk capital, especially for start up companies; providing better links between basic and applied research; monitoring the trend for large companies to link up or merge; eliminating the remaining barriers to entry in the main third country markets. But the operation of the Single Market in pharmaceuticals remains the single most important of the uncompleted parts of the agenda for establishing the European Union as a firm base for pharmaceutical innovation and sustainable industrial development.

Whilst it is clear that the responsibility for the funding, management and organisation of the health care systems is one that is firmly within Member State competence, there are aspects to the operation of these systems that relate to a wider European Union agenda, notably in respect of the contribution that free movement of goods makes towards the creation of the Single Market.

Of wider relevance still is an industrial policy concern that some of the mechanisms by which the financial viability of the health care systems is assured may unnecessarily distort the operation of the market leading to a reduction in the competitiveness of this sector in a global context. The key remaining issues relating to the completion of the Single Market in pharmaceuticals are thus largely ones within Member States' competence. Member States and

the Commission have a primary concern with the improvement of public health and with ensuring that patients and consumers have wide access to pharmaceuticals at affordable cost; these priorities have in turn to be reconciled with public expenditure objectives. Measures adopted for the completion of the Single Market must therefore be consistent with the principle of subsidiarity. Solutions will be found largely within the health care systems which are – and are set to remain – widely divergent.

The Frankfurt Round Tables

In order, therefore, to initiate a tripartite dialogue about solutions between Member States, industrial interests and the Commission, Commissioner Bangemann convened the Frankfurt Round Tables on the Completion of the Single Market in Pharmaceuticals.

The first Round Table took place in December 1996; the second a year later. A wide range of interested parties have attended these events, including representatives from the Member States, the European Parliament, the full range of industrial interests both within the pharmaceutical industry and in related sectors such as the wholesalers.

The proceedings of the Round Tables – and the reports of two Working Groups that met in 1997 to prepare the second Round Table discussions – have been published, and are available on the Internet (http://dg3.eudra.org/frankf/index.htm).

Whilst not necessarily reflecting the views of Community institutions, the Frankfurt Round Table process has identified that there are a range of pressures that are growing in this sector and that act as factors towards change. These are in particular:

- The amount of money that Member States are spending on health care in general (and pharmaceuticals in particular) has been rising at a rate that is faster than the growth in their economies. At the same time, most Member State governments have been seeking to restrain government expenditure to meet the requirements for entry into European Monetary Union. The need for such fiscal discipline will continue with the Euro. Relaxation of price controls – particularly on in-patent products in countries with high volume consumption could create difficulties in controlling aggregate expenditure on pharmaceuticals.
- The product pipelines of the research-based industry are delivering a steady stream of new products into the market. The recent Council Conclusions on the Single Market in Pharmaceuticals, agreed at the Internal Market Council in May 1998, note that the prices of new pharmaceuticals should be related to "the therapeutic interest and cost effectiveness" of the specific innovation. Nevertheless, the available means of determining the "value-added" of a specific new product, particularly at market launch, are acknowledged to be relatively unsophisticated and demonstrate the usefulness of developing such mechanisms further in the near future.
- There are observable delays in new products reaching some parts of the European market after they have received marketing authorization; the pharmaceutical industry has recently claimed that products are entering certain parts of the European market up to 3 years after other parts. The reasons for these delays are unclear (although they may in part be found in the increasing amount of negotiation about pharmaceutical expenditure) and are hard to explain in the light of the specifications in the Transparency Directive (Council Directive 89/105/CEE of 21 December 1989) that pricing and reimbursement decisions should take a maximum of 180 days. A re-evaluation of the content of this Directive – which was always

intended as a provisional measure – may be becoming timely so that it can take into account new developments in this field.

- There are concerns expressed in some industry circles that the returns for new, patented products in Europe are starting to look comparatively unattractive in a global context. Conversely, the Member States are concerned that, unless savings can be made elsewhere within existing expenditure in the pharmaceutical sector or elsewhere in the healthcare system, the entry of new products onto the market represents additional calls on health budgets.
- The forthcoming enlargement of the European Union brings with it the prospect of a considerably larger market for pharmaceuticals – and the potential for a considerably increased generics industry. However, the average per capita income in the countries of Central and Eastern Europe is considerably lower than the average in the current Member States and raises therefore the question of how patients are to have access to affordable pharmaceuticals at prices which are realistic in the Single Market context.

The Council's Conclusions

In response to the Round Table discussions, and as a contribution to the process, the Council considered the Single Market in Pharmaceuticals in Conclusions that were agreed in the Internal Market Council on 18th May 1998. This was the first time that the Council has discussed the tensions at the heart of the Single Market in Pharmaceuticals. In its Conclusions, the Council invites the Commission to bring forward a Communication on these issues, but stresses the importance of "maintaining the established competencies between Member States and the Commission in particular with respect to ensuring the availability of health care to citizens and improving the effectiveness of the single market. The Council considers that Community policy should address the need to:

- ensure the effective further improvement in the operation of the Single Market in this sector based on the principles of free movement and competition;
- facilitate the delivery of health care in Member States at levels which are affordable and in ways which maximise as far as possible, patient access to medicines;
- recognise Member States' need to adopt economic measures to control the total costs of pharmaceutical expenditure;
- maintain the regulation n of the pharmaceutical sector to ensure the safety, quality and efficacy of medicines; and
- strengthen the competitiveness of the European pharmaceutical industry, in particular by encouraging research and development which is required for therapeutic improvement and cost-effectiveness."

The Council considers "that the development of the single market requires Member States to take account of European Union dimensions". It therefore invited "the Commission to address in its Communication how best to accommodate the requirements set out (...) above in ways consistent with Community rules". The Council further considers "that developments in Community policy should take account, in particular, of tensions regarding pharmaceutical prices and their convergence, and the divergent patterns of wealth in the Union, which are likely to increase with enlargement."

Chapter 2
APPROACHES AND SPECIFIC MEASURES

The tensions identified in the Round Table process do not lend themselves to easy solutions. In particular, Member State health care systems (for which the Member States are – and will remain – responsible) are widely divergent, both in their operation and in their proximity to the market.

The Round Tables have identified that one of the drivers of this discussion is the concern on the part of the industry about parallel trade. The Round Table dialogue has suggested that – in the out-of-patent sector - parallel trade can have positive effects for consumers and national health care systems by promoting price competition and thereby reducing prices. At the same time, it is reasonable to assume that parallel trade has a dynamic restraining effect, particularly on prices at the higher end of the European market; by contributing, therefore, to price competition for in-patent products, it can help social security systems to deal with the strong market power of certain products. Where parallel trade arises because of distortions caused by different price legislation, then the Court has indicated, in the Merck v Primecrown judgement, that remedies must be found by the Community authorities. These remedies must be consistent with the basic principle of market integration and can therefore not include measures the effect of which is to maintain or increase the partitioning of the Common Market along national lines. Consequently, solutions must be found which are compatible with the principles of the Single Market, rather than ones which would delay its completion.

Possible approaches

The Commission has considered various approaches, including the possibility that the current situation could be left to develop (Status-quo), a fully integrated approach (Full integration), and a middle way consisting in developing the co-operation between Member States and introducing normal market mechanisms in market segments which are sufficiently suitable for convergence (Staged introduction of market mechanisms).

- *Status-quo*

  If the current situation is simply left to develop, there is a distinct risk that this could result in a long-term segmentation of the Community pharmaceutical market, requiring important monitoring activities on the part of the Commission to observe price differentials (through benchmarking), to take action in respect of established breaches of the EC Treaty and of the Transparency Directive by Member States, and to continue to apply the competition rules to companies seeking to limit parallel trade. Whilst it must be acknowledged that the current situation has allowed the European Union to ensure a high level of social protection and of health protection to its population, it is unlikely that simply allowing this situation to develop will suffice to restore the global competitiveness of the European pharmaceutical industry and doubtful whether such monitoring activities are, in themselves, the simplest way to achieve the proper functioning of the Single Market.

- *Full integration*

  A fully integrated approach would seek to relieve the current tensions by forcing price convergence within the Single Market. This would probably require a centralised

European pricing procedure or, at least, very efficient co-operation between the Member States. Irrespective of whether this would be compatible with the principle of subsidiarity, it must be stressed that establishing an appropriate level of price across the Community would prove extremely difficult. Low levels would benefit immediate health care expenditure objectives (at least in the Member States where prices are currently high), but would provoke a steady diminution of Europe's contribution to global pharmaceutical R&D investment, leading ultimately to disinvestment from the European economy. High levels would reduce access to consumers and payers in those countries where economic and social conditions mean that such prices cannot be afforded.

- ***Middle way***

  The Round Table process has identified an approach to the regulation of this sector which distinguishes between the different sectors of the market, notably the market for medicines which are available without prescription; the out-of-patent sector; and the in-patent sector when the investment in research and development needs to be paid for. Within this framework, there are a number of possible options which Member States may wish to use in order to relieve the tensions that are growing in this sector. These measures, some of which are outlined in the following section, aim at introducing convergence through sustained co-operation between Member States and health care services providers. They also consist in building in normal market mechanisms whenever they can be left to operate without compromising the access to medicines at an affordable cost for all patients and consumers, and the Member States' ability to meet public expenditure objectives. The common features of these measures is their reliance on market transparency, open competition and patient empowerment

The Commission concurs with the conclusions of the Second Frankfurt Round Table and with the Internal Market Council's Conclusions of 18 May 1998 that a centrally administered European pricing system for medicines is undesirable and, currently, impracticable Therefore, as suggested at the Round Table and as recommended by the Council, the Commission considers that there is a potential for advancing the Single Market in ways which recognise the differing patterns and pace of development in different segments of the market (non-prescription, out-of-patent, and in-patent), through the staged introduction of normal market mechanisms whenever they can be implemented without compromising the access to medicines at an affordable cost for patients and consumers, and the Member States' ability to meet public expenditure and health care objectives, while fully recognizing the benefits of the Treaty rules on free movement of goods in all these segments..

The implications of enlargement should also be considered. Such a balanced approach would however facilitate the preparation of enlargement in the pharmaceutical sector, both from an economic and public health point of view.

Specific measures

The specific measures described here are not mutually exclusive, nor do they represent a "blueprint" that might be imposed onto the health care systems in the different Member States. Rather, they represent a series of options and devices from which better, less distorting, ways of meeting the range of objectives sought in this sector can be developed. Many of the more challenging measures are not implementable "over-night" and will take some time to develop

and operate effectively. All these possibilities need also to be considered in the context of wider efforts to improve the efficiency, quality and cost-effectiveness of health care systems in the Member States; indeed without such developments, some of these possibilities, pursued in isolation, risk bringing significant drawbacks both to the sound management of health care systems and to patient and consumers access to pharmaceuticals at an affordable cost. Most of the options discussed below are under the exclusive competence of Member States and it is therefore, in accordance with the principle of subsidiarity, for them to consider whether and when some of these measures could be introduced within their national health system.

- ***Relaxation of price controls and the development of effective competition***

  As the Council pointed out in its Conclusions of 18 May 1998, there is a potential for advancing the Single Market in ways which recognize the differing patterns and pace of development in different sub-sectors of the pharmaceutical market : products which are available to patients without medical prescription (and for which reimbursement is, normally, not available), out-of-patent products (for which generic competition is possible) and in-patent products (in principle, these include the most innovative products).

  Non-prescription products

  The remaining price controls on pharmaceuticals sold without prescription could be removed, subject to appropriate accompanying measures to take into account differing therapeutic, economic and social circumstances of patients and their need to access a wide range of medicines. Consideration could also be given to accompanying measures aiming at reinforcing competition in this sector, such as the abolition of resale price maintenance, the relaxation of restrictions on the place of sale of non-prescription medicines and the relaxation of restrictions on the use of brand names for products switched from prescription-only to non-prescription. Such a relaxation, assuming that the market is competitive, could reduce marketing costs considerably by allowing companies to benefit from the economies of scale and scope that could come from cross-border marketing.

  Out-of patent products

  From an economic point of view, out-of-patent products are far closer than in-patent ones to products in normal markets, in which cost-containment can normally be achieved through price competition. Consideration could be given to the possibility of removing price control in this sector whilst stimulating competitive arrangements for the supply of generic products (see below). Clearly, the removal of price controls in this sector would require high levels of transparency of information about products.

  In-patent products

  In this sector of the pharmaceutical market, the evidence suggests that greater reliance on market mechanisms, and greater levels of price freedom for in-patent products available under health care systems, would require mechanisms of market competition able to ensure that Member State aggregate expenditure targets are met. Where specific products have few or no therapeutic alternatives, they are likely to have considerable market power. This is likely to influence the extent to which liberalization can be achieved without negative impact for patients and health care systems: liberalization can be expected to require much higher levels of price sensitivity on the part of prescribers and careful attention to budgeting. This would therefore require an examination of the financial incentives within the health care systems and, in particular, whether these incentives

increase competition or erode it, and the scope for developing greater price sensitivity on the part of prescribers and greater levels of price competition between products within the market. Two key points should be noted in this context.

Firstly, the removal of mechanisms for setting prices should not be considered as a "prior requirement" for developing greater competition within this sector. Whilst it is clearly the case that this industry competes strongly on innovation, and there are indications that price competition may be an increasing factor in the context of pricing decisions at market launch, there is relatively little dynamic price competition in this sector once a product has been launched onto the market. Without such dynamic competition and in a market with little transparency, there is a risk – and some anecdotal evidence in the case of this industry – that "market" pricing simply equates to higher prices where the health care system pays for brand image. There is scope for developing further the assessment of the relative effectiveness of healthcare interventions – often the information that is necessary to do this can only be generated once products are in more general use within healthcare systems.

Secondly: Although intellectual property rights legitimately prevent competitor products from entering the market during the patent period, they do not somehow "protect" products - even those still under patent - from mechanisms that might be developed to encourage price competition between products that are legally placed on the market.

A sustainable solution for the longer term may need not only to reduce the reliance on price fixing as the means of meeting budgetary objectives but also to introduce higher levels of competition into the market to free up resources to help to pay for new products.

Allowing for greater price freedom in this sector needs to take into account a range of legitimate objectives, including : that Member States need to be able to control how much is spent in aggregate on pharmaceuticals; that the R&D expenditure required to create innovative products needs an adequate level of profit in the pharmaceutical sector; and that patients should have access to pharmaceuticals. Thus, freeing-up this sector will have to be balanced with developments to ensure that these other legitimate objectives continue to be met or are met better than currently. This suggests in particular that removing price controls on all pharmaceuticals would require significantly increased levels of effective competition within the market in order to ensure continued control of aggregate expenditure : a *free* market does not imply an *unregulated* market.

The public health impact of any relaxation would also need to be taken into account, such as the benefits – in terms of advice and protection - that the consumer can gain from pharmacists. Reforms in this area need to be set within the wider context of improving the efficiency, cost effectiveness and quality of health systems more widely. The Commission is contributing to this debate by studying how and where market forces within health care systems can help save costs while promoting quality and access for all.

- ***Contractual policy***

Moving from a mechanism whereby prices are fixed by public authorities to a dialogue between public authorities and enterprises could constitute an appropriate method in order to reconcile price liberalisation and cost-containment in the health care sector. The contractual framework allows for a price negotiation which takes into account the interest of both industry and the Member States, in the context of multi-annual commitments covering the entire turnover obtained with the pharmaceutical portfolio of the contracting

company. Such a contractual policy allows to progress towards pricing freedom by exchanging consumption volumes which are not medically justified for greater freedom in respect of price determination. Provided that it is in conformity with the Treaty rules on free movement of goods and competition, this method, based on the extension beyond price fixing of the scope of the discussions to a wider range of subjects (prices/volumes/ promotion/R&D spending/priority choices in respect of public health), involving the entire pharmaceutical portfolio could allow for the establishment of levels of growth for pharmaceutical expenses which are compatible with the increase in the national wealth, the epidemiology and the need to meet the cost of major pharmaceutical innovations.

- ***Profit control***

  A profit control policy can produce similar results whilst allowing to the industry to decide to launch new products at the price they deem appropriate as long as the profits obtained are in line with public health and social protection objectives. Such system is also based upon negotiations between interested parties on a level of profit which allows reasonable prices, competitive development and sustainable research. For such a policy to be acceptable for all, it should distinguish clearly between what belongs to the health service and what belongs to the private sector, take into account the capital employed, in particular in respect of R&D, as well as promotion expenses.

- ***De-listing and greater patient co-payment for certain products***

  De-listing of certain indications or treatment areas which are considered to be appropriate for self-treatment, or moving them to lower reimbursement classes, might help to achieve greater cost-consciousness in the use of medicines and thereby contribute to savings in reimbursement budgets. Such an effect might be strengthened by a reduction in the reimbursement of products of lesser therapeutic evidence. Clearly, a savings effect would only arise within an indication-based model of pharmaceutical prescribing whereby pharmaceutical treatments for minor illnesses were de-listed from reimbursement; in the absence of such a prescribing model, de-listing might simply result in the use of more expensive prescription products to treat the same indication. At the same time, consideration needs to be given to the widely differing therapeutic, economic and social circumstances of patients and in particular their need for access to basic products which can help relieve some of the effects of long-term treatments (in particular in cancer and AIDS).

  Some consideration is timely of the extent, at the margin, for patients to make greater contributions, in certain circumstances, to meeting the costs of prescribed pharmaceuticals. In the Commission's view, particular care is needed in any reflections by Member States or industry concerning any idea of transferring financial burdens to the patient: the principles of social solidarity that underpin the health care systems in the Member States are an asset to the European Union and the consumer should expect to continue to benefit from such principles.

- ***Reference pricing***

  Setting ceilings or reimbursement levels by therapeutic categories may help containing pharmaceutical expenses. Under such systems, social security institutions accept to cover or reimburse the cost of pharmaceuticals in a given therapeutic category up to the reference price, which is normally fixed against the cheapest products in the category,

which are thus fully reimbursed. The difference between the reference price and the actual price of any product in the category can be considered as a form of patient co-payment. When circumstances allow, reference prices should be preferred to price controls, to the extent that they spur, rather than stifle, competition : they encourage companies to bring prices in line with the reference prices or justify the higher price requested, and leave it to the doctor/patient to choose between a cheaper medicine at no extra cost or a more expensive one for which a co-payment will be required.

- *Encouraging generic competition*

  The Frankfurt Round Tables has identified that a more competitive generic market has an important contribution to overall competition in the pharmaceutical sector. Many of the measures that are mentioned more generally in this section on specific measures are of relevance to the generic sector. However, of particular importance to this sector are:

  - encouraging the prescribing by doctors and the dispensing of generics by pharmacists so as to stimulate consumer choice;
  - increasing consumer awareness of the availability of generic medicines;
  - ensuring that the licensing process for generic products operates speedily to ensure that consumers have access to lower prices generics as soon as possible after patent protection of the original product expires;
  - developing financial mechanisms within the health care systems in ways that favour price competition between generic products and originator brands.

- *Involvement of prescribers*

  Greater competition in the pharmaceutical sector requires a higher involvement of prescribers which decide, for most of the market, both on whether a product should be used and, if so, which product. Mechanisms, such as prescription budgets, together with information about the comparative cost of products with the same therapeutic interest, can help to increase price sensitivity on the demand side, which is a prerequisite for a more competitive pharmaceutical market.

- *Access to market*

  Steps should be taken to improve the speed with which products access the market after they have received their marketing authorizations. This should include an examination – with a view to taking any appropriate legal steps - of the reasons why licensed products are not entering the market until long after the deadlines for pricing and reimbursement negotiations stipulated by the Transparency Directive (which imply that pricing and reimbursement negotiations should be completed within 180 days).

  There are also reports of long delays in issuing licenses for generic products in some Member States. The review of the European licensing system in 2000 provides an opportunity to consider the licensing of generic medicines in greater depth and for developing the access of generic products to specific health care systems and the demand for generic products within those systems.

- *Market transparency*

  The Transparency Committee already provides an appropriate forum for Member States to exchange information about, and to discuss, mechanisms that are successfully addressing the issues raised by the Single Market in this sector. This discussion could usefully address not only the systems for paying for pharmaceuticals but also the systems for pharmaceutical distribution. The Transparency Committee also offers the basis for promoting greater transparency of pharmaceutical prices (the *EudraMat* database of pharmaceutical prices is now operational).

  There is a need to underpin discussions and policy-making with better empirical data than is currently available to the Commission and to national regulators. Benchmarking price levels and movements, volumes, margins and discounting arrangements would allow to develop useful economic data and analysis for the formulation of future policies and for the preparation of Enlargement.

  Work might also be undertaken on how to improve the assessment of relative effectiveness of pharmaceuticals and on how to exchange that information between regulators. The EMEA and the European Commission Joint Research Center are currently working up a pilot project to collate and make available electronically summaries of product characteristics and patient leaflets. The Council has itself noted the relative absence of reliable data in this area: this may need to be addressed, if necessary by setting out requirements for data disclosure in legislation.

  Whilst there is a need for certain market restrictions to safeguard high standards of qualitative and professional information in the retail pharmaceutical distribution sector, national bans on distance selling of non-prescribed pharmaceuticals could be re-examined in the light of the principle of proportionality. When cross-border marketing restrictions are combined with remuneration systems that favour the sale of high-cost products, competitive pressures in the internal market to offer the best value (in terms of price/quality) pharmaceuticals and pharmacy services risk being neutralised.

Electronic commerce and information to patients

The pressures for change that have been identified in the Round Table process can be expected to fall on all parts of the pharmaceutical sector, not just the pharmaceutical industry itself. The pharmacy service in many Member States accounts for over 25% of the final cost (excluding taxation) of a pharmaceutical. It may be only a matter of time (and ability to enter the market) before new systems for delivering products to the consumer – particularly through the increasing possibilities of electronic commerce – cause regulators to consider what savings might be made in this part of their expenditure on pharmaceuticals.

There are two key aspects of the pharmaceutical sector that are likely to be particularly affected by development of electronic commerce : the wholesaling of pharmaceuticals (where electronic commerce may reinforce the considerable consolidation in the wholesaling function currently underway in the European Union), and, where authorised, the sale of pharmaceuticals to patients (and the effects on pharmacists). Developments in these area raise the prospect that the delivery of prescription medicines could be performed through electronic commerce mechanisms at considerably less cost to the health care systems so long as there is no detrimental effect on safety: of particular relevance here is the public health implications of

global trade in pharmaceuticals in particular where the public health interest requires medical supervision of the prescribing and use of a given product.

A range of more general issues can be expected to be raised by developments in the area of electronic commerce. These issues notably include the prospect that advertising legally placed on the Internet in the United States (which allows *direct to consumer* advertising of prescription pharmaceuticals) will be accessed in the European Union where such advertising is explicitly banned. The issue of direct to consumer advertising needs to be examined in greater depth;. The context of such consideration, however, is unlikely to be simply that of advertising directly to patient; the wider issue of what information is made available about products – especially for the purposes of independent third party assessment of relative effectiveness – will also need to be addressed in this context.

Enlargement

The issue of the Single Market in pharmaceuticals is being raised with the countries of Central and Eastern European in the context of the preparations for Accessions negotiations. A more developed dialogue between the current Member States, the applicant countries and the pharmaceutical industry is important to ensure that all the interests in this sector can engage constructively in the complex set of issues, relating to health policy, industrial policy, competition and market policies that the Single Market raises in this sector. In particular, there needs to be a thorough consideration of the implications arising from lower abilities to pay for pharmaceuticals given that levels of GDP per head in these countries are lower – often substantially lower - than the average of the current EU-15. The Commission could, therefore, arrange a dedicated discussion conference in 1999 on the pharmaceutical market aspects of accession to ensure full understanding of the challenges ahead.

Chapter 3
CONCLUSION : LOOKING FORWARD

The completion of the Single Market in Pharmaceuticals raises a complex set of issues that do not lend themselves to easy solutions. This is an area of direct and central relevance both to Europe's industrial base in pharmaceuticals and to the financial viability of the health care systems on which the European citizen relies. This Communication has aimed to stimulate discussion about these issues with all interested parties. The approaches that are developed as a result of these discussions must be developed in full respect of the principles and priorities established by the EC Treaty, in a manner consistent with the principle of subsidiarity.

The Round Table dialogue has, in this respect, been valuable, in particular in identifying factors for change but also in establishing a forum to discuss better regulation of this sector. But, to be meaningful, that discussion now needs to be taken forward within clearer parameters. The third Round Table, in December 1998, provides an opportunity for testing whether the interested parties can agree not only on some basic assumptions which will allow this debate to move forward constructively but also on a process for handling future discussions.

The first key question has to be whether the parties to this discussion can agree a set of common objectives founded on agreed basic assumptions. Without this, there is little point in continuing the process. This Communication confirms the basic principle that pharmaceuticals should not be exempted from the Single Market because they are used in health care systems; furthermore it notes that the existence of price control systems are not themselves contrary to the principle of free movement of goods. Parallel trade acts as an important driving force for market integration where there are important differences in prices between Member States. These differences must be addressed in a way that is consistent with the principles of the Single Market and cannot justify measures the effect of which is to maintain or increase the partitioning of the common market along national lines. The aim of ensuring sufficient overall revenue to the pharmaceutical industry to allow continued funding of research and development has to be considered within the context of Member State responsibilities to promote health and treat illness within limited budgets, access at an affordable cost for patients and consumers and the principles of the Single Market.

The Commission has considered various approaches which could be pursued, including the possibility that the current situation could be left to develop, subject to adequate monitoring and a fully integrated approach . Both these approaches have drawbacks, which have been outlined;. There is, however, a middle way consisting in reinforcing co-operation between Member States and health care service providers and introducing normal market mechanisms in market segments which are sufficiently suitable for convergence, whenever this can be done without compromising the access to medicines at an affordable cost for patients and consumers, and the Member States' ability to meet public expenditure objectives . A range of specific measures can be considered in this context; most of them relate to the exercise of exclusive competence of the Member States. In accordance with the principle of subsidiarity, it is therefore for the Member States to decide whether these measures could or should be adopted.

The Round Table meeting in December 1998 could be used to discuss the feasibility of the various options identified in this Communication to build the consensus for change – taking into account the different segments of the pharmaceutical market, the need to encourage competition, and the requirement that Member States must be able to ensure the financing of

their health care systems.The specific measures addressed in this Communication are intended to serve as the basis for advancing practical solutions. Some of the approaches discussed in this Communication are easier than others. The focus now needs to be on achievable developments that work in the context of the existing health care systems and the Single Market. Policy development by consensus is better than trying to impose solutions in this area; however, the Treaty requires the development and maintenance of a Single Market.

If the interested parties wish to pursue this agenda within these parameters, the practical next steps might be:

- Discussions between the Commission and the Member States to develop ideas for greater reliance on market mechanisms to meet regulatory objectives and to develop increased competition in the context of individual national health systems; these discussions should complement a dialogue between the Member States and the major stakeholders, including patients and consumer associations, to seek to identify ways of addressing these issues within their domestic health care systems: these discussions might be given a greater focus by the agreement of action plans. The outcome of these discussions, and the action plans, might be part of the discussions of future Round Tables.
- In the light of progress in the above discussions and negotiations, the Commission will assess whether the Transparency Directive requires modification. Key parts of that assessment would concern the reasons for delays in launching products onto the market and consideration of whether the Directive needed updating to take account of evolutions in health care systems since the original Directive was agreed.
- As stated in the Commission Communication on the development of public health policy in the European Community COM(1998)230, future work should address and promote co-operation on the evaluation of the therapeutic value of pharmaceuticals, in particular in comparison to alternatives, as well as the systematic collection and analysis of data on the utilization of data and brands, especially prescription and consumption patterns.

A more developed dialogue between the current Member States, the applicant countries and the pharmaceutical industry is important to ensure that the applicant countries can consider fully the implications for their health care services of entry into the Single Market. The Commission could , therefore, arrange a dedicated discussion conference in 1999 on the pharmaceutical market aspects of Accession to ensure full understanding of the challenges ahead.

ANNEXES

Annex 1

Key figures (European Union, Applicant countries, OECD)

	Population (million)	Total GDP ($ billion)	GDP per capita ($)	Pharmaceutical market ($ billion)
Belgium	10	228	22,546	2,70
Denmark	5	173	33,185	1,10
Germany	81	1,835	22,539	21,80
Greece	11	100	9,576	1,20
Spain	39	559	14,264	7,60
France	58	1,538	26,462	25,30
Ireland	4	52	14,576	0,40
Italy	58	1,018	17,797	12,10
Luxembourg	0,5	11	27,053	0,10
Netherlands	15	395	25,591	4,20
Austria	8	233	28,844	2,10
Portugal	10	83	8,368	1,30
Finland	5	126	24,651	1,00
Sweden	9	229	25,779	2,80
United Kingdom	59	1,104	18,848	8,40
Bulgaria	8	10	1,127	0,20
Czech Republic	10	46	4,402	1,00
Estonia	2	2	1,132	0,03
Hungary	10	41	4,033	0,60
Latvia	3	4	1,767	0,05
Lithuania	4	6	1,495	0,10
Poland	39	93	2,402	1,40
Romania	23	30	1,324	0,20
Slovak Republic	5	17	3,220	0,10
Slovenia	2	14	7,024	0,10
United States	263	7,246	27,538	84,00
Japan	125	4,591	36,739	53,20
Switzerland	7	304	42,989	2,90

Source : EPISCOM Data

Annex 2

Health expenditure and pharmaceutical expenditure (as % of GDP)

	Health expenditure (% of GDP)	Pharmaceutical expenditure (% of GDP)	Pharmaceutical expenditure (% health exp.)	Pharmaceutical expenditure ($ per capita)
Belgium	7,6 %	1,4 %	13 %	267
Denmark	7,7 %	0,7 %	12 %	215
Germany	10,4 %	1,3 %	11 %	269
Greece	7,1 %	1,8 %	25 %	118
Spain	7,4 %	1,5 %	16 %	193
France	9,9 %	1,7 %	17 %	435
Ireland	7,0 %	0,7 %	10 %	111
Italy	7,6 %	1,4 %	14 %	209
Luxembourg	7,1 %	0,8 %	12 %	260
Netherlands	8,5 %	0,9 %	13 %	272
Austria	7,9 %	1,1 %	10 %	260
Portugal	8,2 %	2,2 %	18 %	127
Finland	7,3 %	1,1 %	11 %	192
Sweden	8,6 %	1,1 %	16 %	315
United Kingdom	6,7 %	1,2 %	10 %	143
Bulgaria	n.a.	n.a.	35 %	25
Czech Republic	n.a.	n.a.	28 %	94
Estonia	n.a.	n.a.	28 %	20
Hungary	n.a.	n.a.	30 %	63
Latvia	n.a.	n.a.	29 %	19
Lithuania	n.a.	n.a.	25 %	19
Poland	n.a.	n.a.	19 %	36
Romania	n.a.	n.a.	23 %	10
Slovak Republic	n.a.	n.a.	17 %	23
Slovenia	n.a.	n.a.	13 %	52
United States	14,0 %	1,1 %	7 %	319
Japan	n.a.	n.a.	20 %	425
Switzerland	10,2 %	0,8 %	11 %	396

Data : 1997 - Source : OECD Health Data 98 + EPISCOM Data

Annex 3

Total and public expenditure on health and on pharmaceuticals

	Total expenditure on health	Public expenditure on health	Total expenditure on harmaceuticals	Public expenditure on pharmaceuticals
Belgium	16 412	14 397	2 942	1 338
Denmark	10 953	7 142	1 003	507
Germany	195 335	152 912	24 822	18 010
Greece	6 546	5 073	1 740	290
Spain	33 891	26 686	6 791	5 055
France	117 334	94 630	19 931	12 222
Ireland	3 924	2 911	389	304
Italy	74 875	52 293	13 416	5 405
Luxembourg	903	835	106	85
Netherlands	26 904	19 385	2 945	1 882
Austria	14 349	10 329	2 028	1 196
Portugal	6 743	4 036	1 773	1 120
Finland	7 304	5 727	1 107	515
Sweden	17 107	14 194	2 230	1 588
United Kingdom	63 078	53 332	10 432	6 599
European Union	**595 658**	**463 882**	**91 655**	**56 116**
United States	815 024	380 376	72 002	10 479
Japan	261 323	205 737	54 353	35 849
Switzerland	23 529	16 465	1 791	1 094

1996 data – in Million ECU
Source : OECD Health Data 98

Annex 4

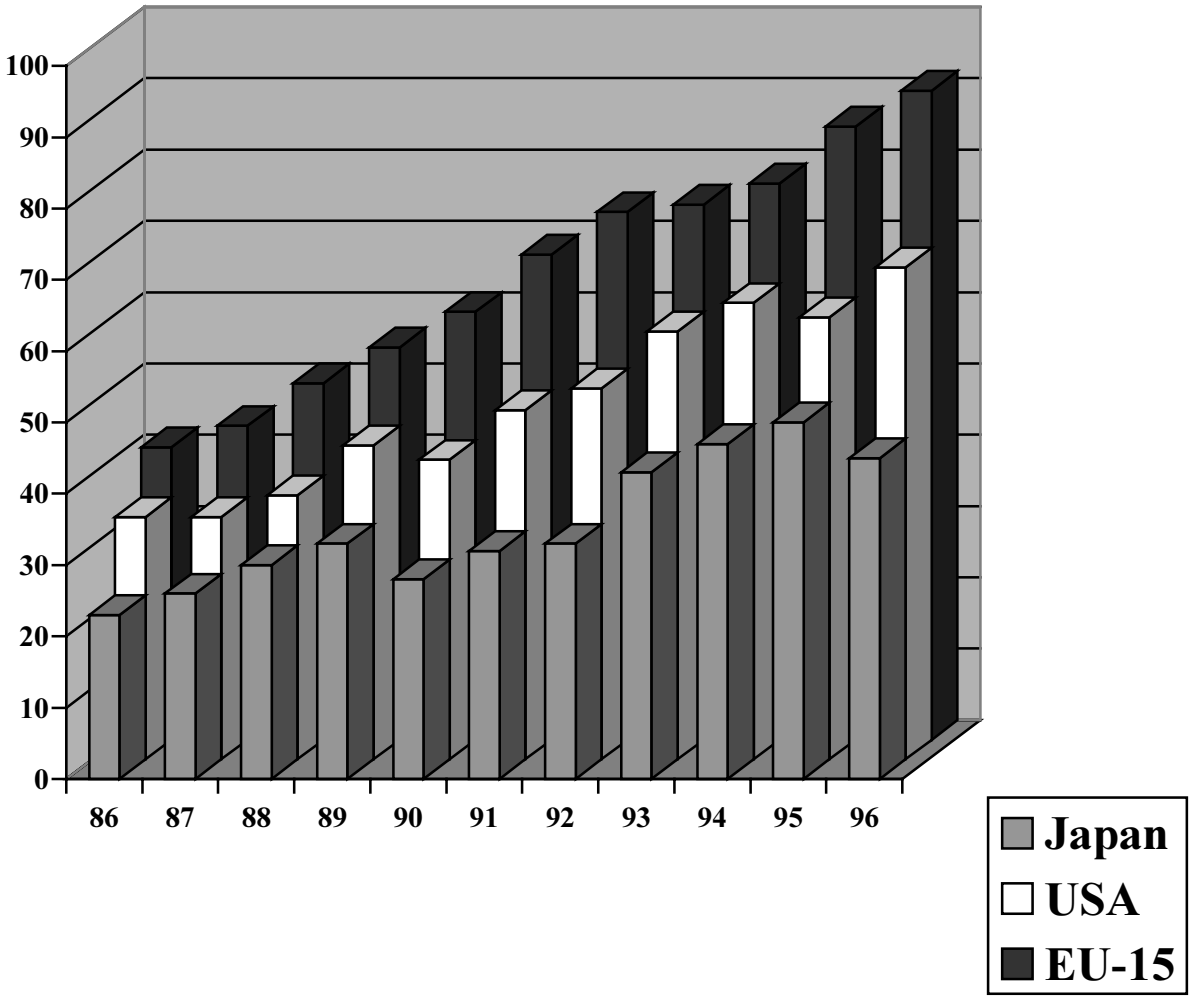
Pharmaceutical production, imports, exports and trade balance

	Production (ECU million)	Imports (ECU million)	Exports (ECU million)	Trade balance (ECU millions)
Belgium	3 595	3 127	4 241	1 114
Denmark	2 004	748	2 105	1 357
Germany	17 449	6 150	10 187	4 037
Greece	470	561	65	- 496
Spain	5 996	2 378	1 355	- 1 023
France	20 113	4 931	5 838	907
Ireland	2 301	585	2 201	1 616
Italy	11 505	5 441	753	8 908
Luxembourg	n.a.	n.a.	n.a.	n.a.
Netherlands	3 664	3 095	3 292	197
Austria	1 086	1 688	1 356	- 332
Portugal	418	568	133	- 435
Finland	566	541	189	- 352
Sweden	3 637	1 086	2 657	1 571
United Kingdom	15 111	3 821	6 585	2 764
European Union	**87 915**	**9 590**	**18 725**	**9 135**
United States		3 997	5 121	1 124
Japan	50 142	3 834	1 500	- 2 334
Switzerland	10 706	3 881	10 194	6 313

1996 data – in Million ECU
Source : OECD Health Data 98

Annex 5

Evolution of production in the pharmaceutical industry (1986-1996)



Figures : billion ECU, current prices
Source : Eurostat

Annex 6

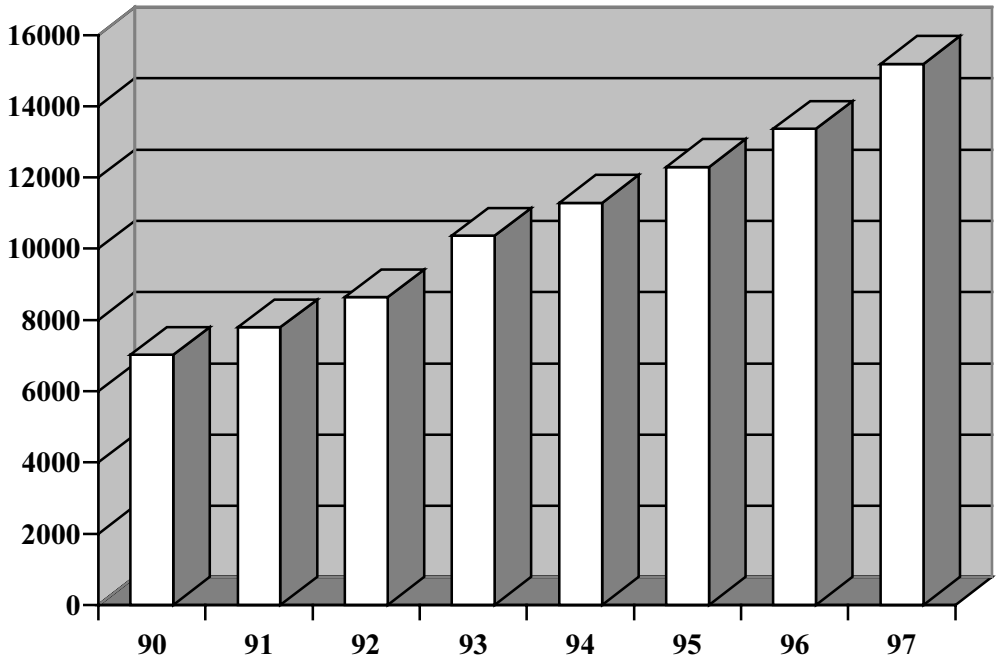
European Union trade balance in pharmaceuticals

	Exports from the European Union	Imports into the European Union	Trade balance of the European Union
United States	3,226	3,394	- 168
Switzerland	2,181	4,028	- 1,847
Japan	1,627	666	961
Australia	660	101	559
Canada	496	96	400
Norway	390	123	267
China	289	306	- 17
CEEC	1,521	169	1,352
CIS	574	6	568
Mediterranean Basin	1,583	114	1,469
Latin America	1,292	128	1,164
OPEC	1,210	13	1,197
Others	3,676	446	3,230
Total	18,725	9,590	9,135

1996 data – in ECU millions
Source: Eurostat, SITC 54 Rev. 3

Annex 7

Evolution of European Union trade balance in pharmaceuticals (1986-1996)



Figures : million ECU
Source : EFPIA member associations

Annex 8

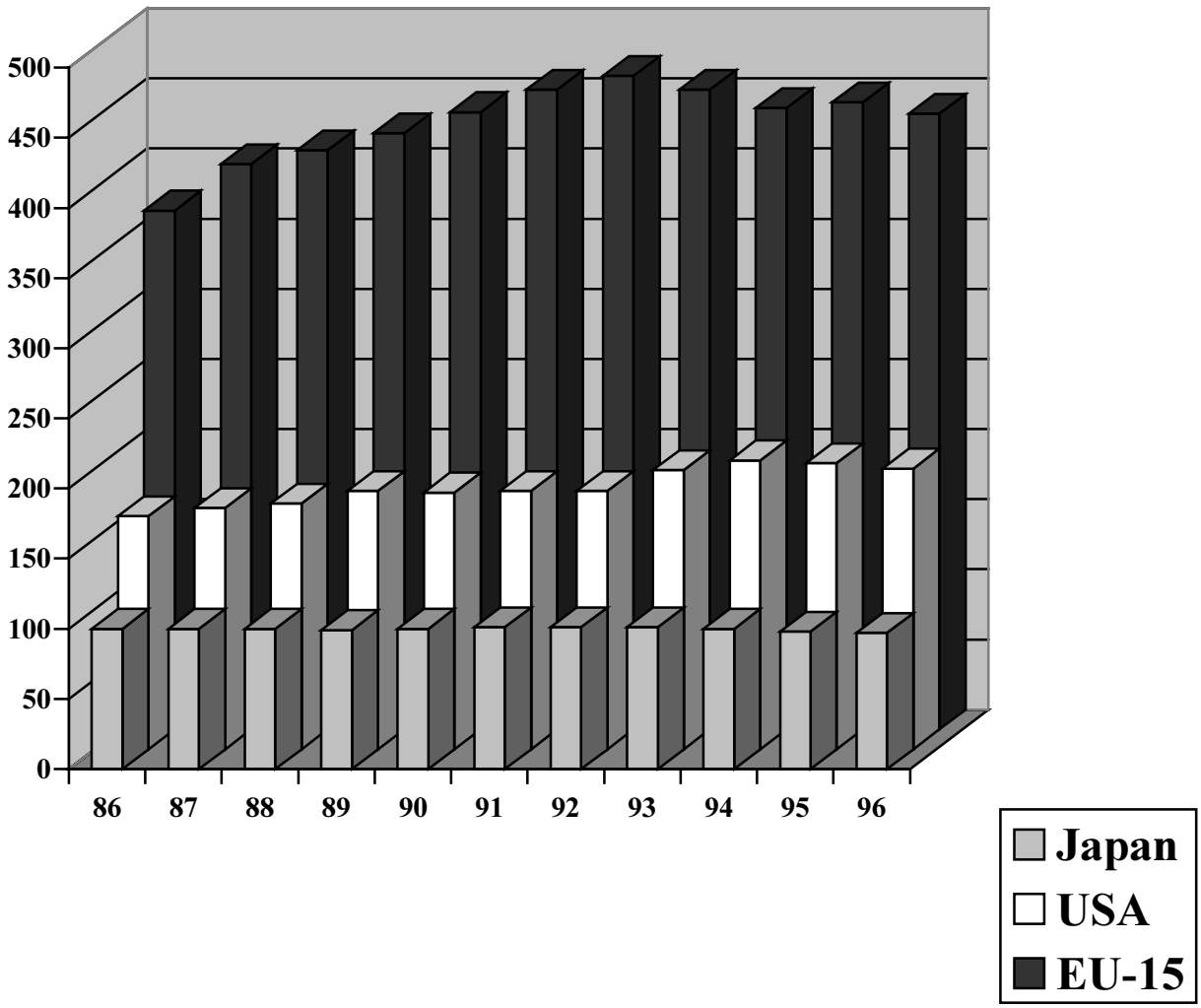
Pharmaceutical employment and R&D investment

	Total employment (units)	Employment in research (units)	Investment in research (ECU million)	Market value at ex-factory prices (ECU million)
Belgium	20 117	1 996	413	2 197
Denmark	15 672	4 045	361	811
Germany	115 500	14 826	2 700	15 735
Greece	7 800	n.a.	n.a.	1 027
Spain	38 500	2 320	260	5 305
France	87 600	14 900	2 150	13 875
Ireland	10 900	n.a.	n.a.	362
Italy	64 119	5 441	753	8 908
Luxembourg	n.a.	n.a.	n.a.	n.a.
Netherlands	13 500	2 250	260	1 908
Austria	9 260	n.a.	n.a.	1 196
Portugal	9 000	n.a.	n.a.	1 429
Finland	5 606	1 173	81	1 118
Sweden	16 000	5 300	1 052	1 814
United Kingdom	74 000	19 000	2 553	6 425
European Union	**487 574**	**71 251**	**10 549**	**62 259**
United States	203 009	49 409	13 314	58 255
Japan	160 300	30 700	5 221	47 164
Switzerland	26 700	16 465	1 791	1 094

1997 data, except : Ireland, Portugal and UK (1996) and Japan (1995)
Source : EFPIA, PhRMA, JPMA

Annex 9

Evolution of employment in the pharmaceutical sector (1986-1996)



Figures : thousand units
Source : Eurostat (Japan, USA), EFPIA (EU-15)

Annex 10

In-patent and out-of-patent products (% of reimbursable packs)

	In-patent products	Out-of-patent products multi-source	Out-of-patent products single-source	Non-prescription reimbursable products
Belgium	16 %	34 %	49 %	0 %
Denmark	10 %	54 %	24 %	12 %
Germany	5 %	40 %	22 %	33 %
Greece	9 %	48 %	30 %	13 %
Spain	15 %	36 %	36 %	13 %
France	8 %	30 %	56 %	6 %
Ireland	n.a.	n.a.	n.a.	n.a.
Italy	31 %	43 %	25 %	1 %
Luxembourg	n.a.	n.a.	n.a.	n.a.
Netherlands	16 %	58 %	18 %	8 %
Austria	13 %	34 %	49 %	4 %
Portugal	3 %	50 %	47 %	0 %
Finland	11 %	49 %	40 %	0 %
Sweden	n.a.	n.a.	n.a.	n.a.
United Kingdom	11 %	46 %	28 %	15 %
European Union	**12 %**	**36 %**	**42 %**	**10 %**

Source : Merck & Co, Inc. analysis of 1996 IMS data

Annex 11

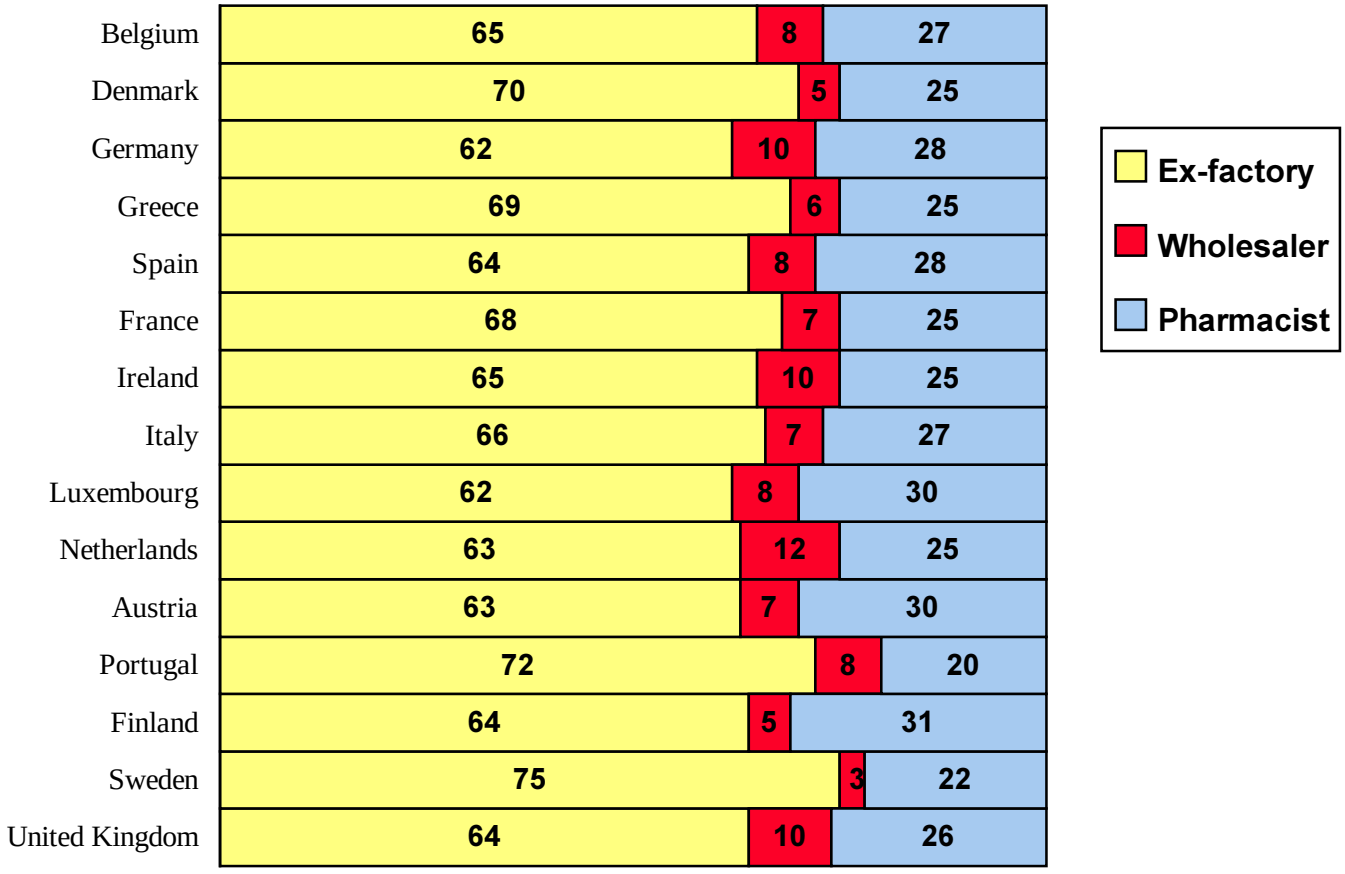
Self-medication and non-prescription pharmaceuticals

	Inhabitants per pharmacy	Self-medication (market share)	Non-prescription (market share)	VAT rate on non-prescription medicines
Belgium	1,922	17,6 %	19,8 %	6,0 %
Denmark	17,966	16,0 %	16,0 %	25,0 %
Germany	3,890	17,7 %	32,1 %	16,0 %
Greece	1,450	n.a.	n.a.	8,0 %
Spain	2,150	12,7 %	15,5 %	4,0 %
France	2,560	10,9 %	32,2 %	5,5 %
Ireland	3,080	20,0 %	21,0 %	21,0 %
Italy	3,460	8,2 %	13,9 %	10,0 %
Luxembourg	5,063	n.a.	n.a.	5,0 %
Netherlands	10,400	9,0 %	12,5 %	6,0 %
Austria	4,036	9,5 %	11,2 %	20,0 %
Portugal	4,250	10,8 %	10,8 %	5,0 %
Finland	6,482	14,9 %	14,9 %	12,0 %
Sweden	9,780	9,4 %	10,3 %	25,0 %
United Kingdom	4,730	20,1 %	24,0 %	17,5 %
Bulgaria	3,283	n.a.	n.a.	22,0 %
Czech Republic	6,435	16,0 %	16,0 %	5,0 %
Hungary	5,073	16,2 %	16,2 %	0,0 %
Romania	5,630	27,0 %	27,0 %	11,0 %
Slovak Republic	5,250	17,8 %	21,0 %	6,0 %
Slovenia	n.a.	12,0 %	12,0 %	5,0 %

1997 data
Source : AESGP Facts and Figures, 1998

Annex 12

Price structure (Wholesaler and Pharmacist margins)

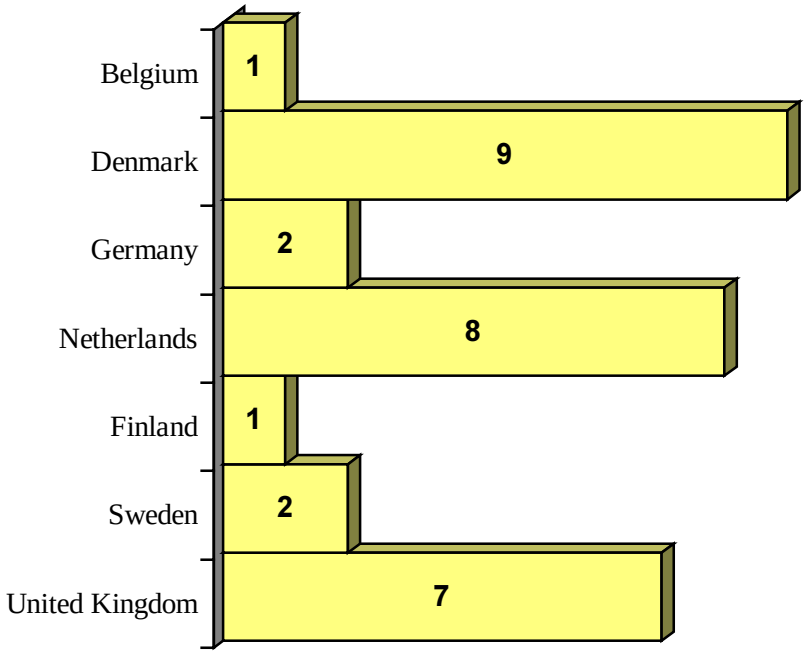


as % of Retail price (VAT excluded)

Source : GIRP European Pharmaceutical Data 1997 (except : Ireland)

Annex 13

Parallel imports (as % of total market)



Source : GIRP European Pharmaceutical Data 1997 (IMS)

Annex 14

Pharmaceutical sales, operating profits, R&D spend (Top 20 firms in 1996)

	Sales (million $)	Operating Profit (million $)	Margin (%)	R&D spend (million $)	R&D/sales (%)
Merck & Co	18,475	5,541	27,9	1,487	7,5
Glaxo-Wellcome	14,284	5364	37,5	1,988	13,9
Novartis	9,110	2,911	24,0	1,711	18,8
Bristol-Myers Squibb	8,702	2,871	33,0	1,276	14,7
Hoechst Marion Roussel	8,455	1,461	17,3	1,453	17,2
Pfizer	8,188	3,090	32,1	1,522	15,8
SmithKline Beecham	8,148	2,019	24,8	1,204	14,8
American Home Products	7,924	2,770	24,5	1,100	13,9
Roche	7,808	n.a.	n.a.	1,574	20,2
Rhone-Poulenc	7,686	932	12,1	1,100	14,3
Bayer Group	7,679	1,214	15,8	1,127	14,7
Johnson & Jonhson	7,188	2,477	34,5	1,093	15,2
Pharmacia & Upjohn	7,176	1,420	19,8	1,266	17,6
Eli Lilly	6,799	2 ,031	27,6	1,190	16,2
Abbott Laboratories	6,307	1,898	30,1	-	-
Astra	5,657	1,773	31,3	1,024	18,1
Schering-Plough	5,050	1,606	28,4	733	13,0
Takeda	4,573	965	21,1	580	8,6
Corange	4,226	561	13,3	566	13,4
Zeneca	4,170	1,296	31,1	668	16,0

Source : Chemical Insight, Late December 1997