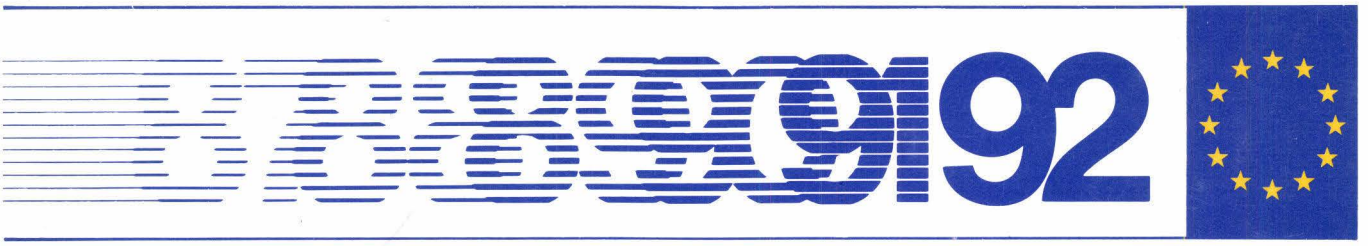
RESEARCH ON THE "COST OF NON-EUROPE"

BASIC FINDINGS

VOLUME 15



THE "COST OF NON-EUROPE" IN THE PHARMACEUTICAL INDUSTRY

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THE "COST OF NON-EUROPE" IN THE PHARMACEUTICAL INDUSTRY

by

Economists Advisory Group Ltd

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COMMISSION OF THE EUROPEAN COMMUNITIES

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The "Cost of Non-Europe"

in the Pharmaceutical Industry

Economists Advisory Group Ltd.

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ECONOMISTS ADVISORY GROUP

THE COST OF NON-EUROPE

IN THE PHARMACEUTICAL INDUSTRY

Executive Summary

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1 EXECUTIVE SUMMARY

1.1 The nature of the European pharmacuetical market and industry

1. In 1984 pharmaceutical sales within the Community, including Spain and Portugal, were approximately ECU25,750m at manufacturers' prices (Table 1), forming 9.5 per cent of health care costs and 0.79 per cent of combined gross domestic product (GDP). Of this total, 88 per cent of sales by value were obtained through a doctor's prescription, 14 per cent being consumed in hospitals and 74 per cent being dispensed through retail pharmacies. Only 12 per cent were bought over the counter,

2. There are large variations in the consumption of pharmaceuticals between the member states in the Community. Differences in income are only partly responsible. Equally important are differences in attitudes to drugs and in traditions of medical practice. These variations affect both the levels of consumption and the types of product consumed. There are strong similarities between Belgium, France, Italy and Spain, on the one hand, and Denmark, Ireland, the Netherlands and the UK on the other. The FRG has elements in common with both.

3. The supply of pharmaceuticals within the Community is highly internationalised. Taking the Community as a whole, 43 per cent of sales are by indigenous companies to their own national market. In every country the locally owned industry has a disproportionately large share of the local market. Only in France and the FRG, however, does it amount to more than 50 per cent. Supplies from companies based in other Community countries make up a further 23 per cent of the total, while 34 per cent come from firms based outside the Community, primarily in the USA and Switzerland.

4. Foreign companies supply drugs either through trade or by local production. In the Community the latter is the more important, amounting to about 40 per cent of all pharmaceuticals supplied. US and Swiss firms depend overwhelmingly on local production to supply their markets, while British and German companies also have substantial foreign facilities. Denmark, Ireland and the Netherlands are the only Community countries which are supplied mainly by imports from abroad.

TABLE 1 PHARMACEUTICAL CONSUMPTION WITHIN THE EUROPEAN COMMUNITY, 1984

Country	Total sales ECU (1)	Per capita ECU	As % GDP	As % health care costs (2)	By type and outlet (%)			Average price (UK=100) (4)	Relative volume Per capita (UK=100) (5)
					OTC	Ethical through retail pharmacies (3)	Ethical through hospitals		
BELGIUM	880	90	0.81	8.6	12	76	12	103	140
DENMARK	370	74	0.50	7.0	15	70	15	154	77
FRANCE	5600	102	0.81	8.8	9	78	13	76	216
FRG	7660	125	0.89	11.0	16	66	18	164	122
GREECE	449	45	0.95	20.2	←83→		17	73	99
IRELAND	160	46	0.67	8.8	5	80	15	115	65
ITALY	4440	78	0.91	12.4	8	79	13	57	221
NETHER-LANDS	660	46	0.38	4.1	← n/a →			145	51
PORTUGAL	350	35	1.08	18.9	←93→		7	low	n/a
SPAIN	1830	48	0.81	12.1	←88→		12	low	n/a
UK	3510	62	0.59	9.6	20	67	13	100	100
TOTAL	25750		0.78	9.5	12	74	14	91	152

(1) at manufacturers' prices
(2) 1983
(3) including dispensing doctors
(4) using the 1983 indices of the EC statistical office
(5) per capita spending/average price.

Source: Authors' estimates based on IMF and IMS data and OECD: Measuring Health Care 1960-1983

5. Production of pharmaceuticals within the European Community amounted in 1984 to ECU39,300m (Table 2). The sector is dominated by large companies with the resources to develop new active substances (NAS). The cost of doing so is currently at least ECU75m per NAS to reach the market, and requires annual sales of ECU150m or more. There are 60 such firms operating in the Community, of which 33 are based there. Of the remainder, 20 are American, four are Swiss and three Swedish.

6. These companies have a strong international orientation and operate on a world-wide basis. They are generally organised on multinational lines. Within the Community, marketing is always organised on a country-by-country basis. The manufacture of active ingredients is confined to a limited number of sites, but conversion into dosage forms is extensively decentralised. Basic and commercially sensitive research is highly centralised most commonly in the country of origin. Clinical and formulation development work, however, is often dispersed.

7. Many smaller companies operate in the Community. Most of them concentrate on generics or OTC products or exploit local markets with well-established remedies. Their innovative capacity is limited, and their focus national rather than international. Firms of this kind have 20-30 per cent of the market in France, the FRG, Italy and Spain, although they have largely disappeared in the UK.

8. On the basis of shares of the world market and of success in innovation, the pharmaceutical industry of the USA leads. That of Switzerland, although much smaller, is also in the first class. Among the companies based within the European member nations those of the FRG and the UK are very strong. French firms are less well placed, being excessively dependent on sales in the home market and in the franc zone, and the same is true, mutatis mutandis, of those of Italy. The research-based companies of Belgium, the Netherlands and Denmark have elements of competitive strength but are handicapped by their moderate size. The indigenous companies of the other Community nations are uniformly weak.

TABLE 2 PHARMACEUTICAL OUTPUT IN EUROPEAN MEMBER COUNTRIES, 1984

COUNTRY	PHARMA COMPANIES NUMBER (1)	PHARMACEUTICAL PRODUCTION				R&D EXPENDITURE		EMPLOYMENT (000)
		TOTAL ECUm	VALUE ADDED % (2)	TRADING PROFIT AS % SALES (3)	AS % CHEMICAL SALES (2)	TOTAL $m	AS % PHARMA SALES	
BELGIUM	80	1290	49	20	9.4	125	10	10
DENMARK	39	870	44	19	36.4	65	7	8
FRANCE	331	8530	30	5	19.6	1090	13	66
FRG	308	10140	46	12	12.4	1430	14	87
GREECE	90	405	20				<1	3
IRELAND	153	1040	69		52.4	15	5	4
ITALY	365	6300	41	11	21.0	380	6	64
NETHER-LANDS	47	1050				110	11	10
PORTUGAL	96	410					<1	3
SPAIN	370	2570	42	14	19.3	40	2	32
UK	333	6700	52	30	16.8	910	14	66
TOTAL	2212	34300	43	14	16.8	4165	11	353

(1) Manufacturers only

(2) 1983

(3) Authors' estimates based on 1983 Eurostat data.

Source: IMS, Eurostat, National sources

9. The pharmaceutical industry is subject to a very large degree of government regulation. The admission of new products to national markets is strictly controlled. Proof of safety, efficacy and quality is universally required. Regulation of this type is carried out on a national basis, although a considerable degree of uniformity within the Community has been attained through the various directives issued by the Commission since 1965.

10. Pricing policies designed to limit pharmaceutical expenditure are also normal in the member countries. They result from the heavy involvement of European governments and national agencies in the provision of health care. Only in the FRG and the Netherlands are prices largely uncontrolled. Elsewhere, they are fixed by various forms of official action (paragraphs 27-32). Positive lists, which limit reimbursement to specified products, and negative lists, which exclude certain drugs or therapeutic categories, are widely used. Average price levels vary very considerably within the Community. Differences of this kind have existed for many years. Prices are set on a national basis and little progress towards harmonisation has been made.

11. Other barriers towards the unification of the European market and industry are relatively unimportant. Tariffs and direct import restrictions have been eliminated, except in the cases of Portugal and Spain, where they are being phased out. Patent protection has been unified. Direct assistance to the local pharmaceutical industry in the form of subsidies and tax concessions is only significant in the case of Ireland. The discriminatory use of registration procedures and price controls is considered below.

12. Government regulation of the industry means that it forms apart of the political agenda. National administrations have divided aims. They wish to limit health care spending, of which pharmaceuticals form a minor but readily controlled part; at the same time they want to promote high-technology industries, of which the pharmaceutical sector is a successful example. There is therefore an inherent conflict of objectives.

13. In practice, Greece, Portugal and Spain, without a research-based industry, favour the interests of consumers unambiguously. Belgium and the Netherlands are inclined in the same direction; although they have such a sector, they appear to attach only a secondary importance to it. The FRG values its major companies, but is committed to a detached attitude to all types of industry. Denmark and the UK have a generally supportive attitude towards their own firms, which, however, make most of their sales abroad. The governments of France, and, to a lesser extent Italy, attach an equally strong importance to the interests of both consumers and producers, which have proved difficult to reconcile.

1.2 Registration and its problems

14. The object of registration is to make sure that a drug is safe, effective and of adequate quality before it is put on sale. The onus is on the applicant to satisfy the authority; the role of the latter is to evaluate the evidence put before it.

15. During the past 20 years the requirements of national regulatory authorities have converged as a result of action by the European Commission. There are now few differences in technical standards between them. All Community countries accept evidence obtained abroad and follow common guidelines. All provide abbreviated forms of registration for projects based on known ingredients. A uniform 120-day decision period has been agreed, to which 90 days are added if the product is referred to an advisory committee.

16. In practice, however, there are substantial differences between one country and another. Methods of evaluation vary, as do perceptions of the weight to be put on particular kinds of evidence. A large element of judgement is involved, which must be influenced by the local traditions of medical practice. Local clinical trials may not be officially required, but are often advisable to familiarise local opinion leaders with a new product.

17. There are also considerable delays in processing applications. Currently only France approaches the 120-day limit on occasion. The FRG and the UK take about two years, and Italy and Spain three or more. The Community average is currently 18-24 months. Such delays have tended to increase in recent years. They are attributed in the main to a lack of resources on the part of national registration authorities, aggravated in several nations by a large increase in the number of applications for generic products.

18. The large research-based companies respond to this situation by preparing the necessary dossier centrally, usually with the US Food and Drug Administration (FDA), the most demanding of authorities, in mind. The experimental work is organised so as to satisfy all requirements; thus, if local clinical testing is needed, it will be included in the overall programme. The dossier is then modified to suit the needs of each authority. They consider this to be a satisfactory if not ideal way to work.

19. The direct costs of multiple registration within the Community are limited. Based on the extra staff employed by the major firms, a figure of ECU40-55m seems reasonable. Extra clinical testing is not considered to be serious burden; as already noted, the results contribute to the central dossier, while the testing itself may help towards a favourable decision by the licensing authority and towards a better reception when the product reaches the market.

20. More important are the effects of delays in the registration process. Since it takes 9-12 years to develop an NAS, the opportunity costs of the money tied up in the process are considerable. A further delay increases the penalty correspondingly. Estimates based on data supplied by the FDA suggest that in 1984/5 the total costs imposed by the general failure to observe the 120-day limit were in the range of ECU30-200m, depending on the discount rate chosen, with a most probable range of ECU57-82m, corresponding to rates of eight and ten per cent respectively.

21. Another serious problem arising from delays in approval is the loss of revenue while the product is in patent. As yet there is no

general patent term restoration in the Community, and effective patent lives, weighted by national sales, average nine years. Estimates derived from average sales of new active substances during the years following their introduction suggest that the failure to meet the 120-day limit caused gross losses of ECU360-640m to their originators. The net losses are smaller, in part because costs of production must be deducted, and in part because of the continued sales of products which would otherwise be made obsolete.

22. The penalties due to the differences between member nations are less serious. As has been noted, with the partial exception of France, all greatly exceed the 120-day limit. If the minimum practicable time for the approval of an NAS under current conditions is taken to be one year, then the opportunity costs of delay drop to ECU20-28m and the net loss of sales to ECU100-175m. As far as registration is concerned, the total cost of the non-Europe is therefore ECU160-260m or 0.5-0.6 per cent of industry costs within the Community (table 3). Effective unification of the market would most benefit US companies since they introduce the largest number of new active substances.

23. Approaches to a more unified system of registration have focussed on two major alternatives - mutual recognition between states and pan-European registration agency. Research-based companies see considerable problems with both these approaches. There are doubts about the equality of the countries involved. There is some feeling that north European agencies carry more weight than south European ones. The differences of medical culture were thought to raise difficulties of mutual acceptability. Registration is not, however, thought to be used in a deliberately discriminatory way.

24. A single European agency would have the advantages of impartiality and uniformity of approach. In principle it could provide rapid decisions. It might, however, be excessively rigid and bureaucratic; the precedent of the FDA, EAG found, was not thought to be encouraging. There was some anxiety about the standards to be used; these would have to be high, but many feared a combination of the most severe elements of all national agencies. There was also concern about the political acceptability to the individual nations of a central authority.

25. It does not appear that a central registration authority would be much cheaper to run than the present system. The national agencies employ the equivalent about 1500 staff at a cost of ECU55-70m to which accommodation and related overheads should be added. Allowing for the higher salaries prevailing in the USA, this sum is comparable with the cost of the drugs and biologics division of the FDA. The European national registration agencies are generally under-staffed and savings through the creation of a single authority would therefore be limited.

26. From the standpoint of the pharmaceutical industry the key issue is the speed of the registration process. Any change which lengthened it would be opposed. Consumers would also benefit from the more rapid approval of new substances provided that safety standards were not lowered.

27. The CPMP procedure in force between 1978 and 1985 was not widely used because of doubts among large innovative companies about its advantages. The current procedure has arised considerably more enthusiasm, especially as it is thought to be potentially faster than the normal route.

1.3 Pricing systems, prices and price competition

28. As already noted, policies intended to control pharmaceutical expenditure are found in all member states of the Community. The methods used vary very widely as do average price levels. The only common factors are that all systems incorporate an element of patient copayment and the over-the-counter (OTC) products are exempt from regulation.

29. At one extreme, the FRG leaves pharmaceutical firms free to set prices as they wish. Total expenditure is limited by strong pressure on companies to limit price increases and on doctors to economise and by a negative list which excludes certain categories of comfort drugs from the reimbursement system. The situation in the Netherlands is very similar. Prices are high in both countries.

30. In the UK the profitability of pharmaceutical companies is controlled. A target level is set for the sector as a whole; the target for each firm depends on its research effort and on its contribution to the British economy. Subject to these constraints companies are allowed to set the prices at which their products are introduced. Irish prices are in practice tied to those in the UK. In both countries they are in the middle range.

31. In principle firms may set their own prices in France, but in practice admission to the national reimbursement system is strictly controlled. Products are dealt with on an individual basis. The price agreed between the manufacturer and the reimbursement authority depends on those of competitive products and on the company's local activities in France. Belgium has a similar system. Prices are low in both countries, and especially in France.

32. Denmark, Greece, Italy, Portugal and Spain control the prices of individual drugs by the use of cost-plus methods, and maintain positive lists. Prices are high in Denmark, below average in Italy and very low in the other three countries.

33. In every Community country except the FRG, the price at which a product is introduced cannot subsequently be changed without official permission. Such permission is often delayed, refused or made contingent on the company expanding its local activities.

34. As far as the adequacy of price levels is concerned, the attitude of the research-based companies is that sales in the Community market should ideally make a substantial contribution to world overhead costs, and in particular to the cost of innovation, and to profits. Prices in Denmark, the FRG and the Netherlands are considered to be 'satisfactory' form this point of view and those in the UK and Ireland 'adequate'.

35. Prices elsewhere are considered to be less than adequate. Those prevailing in France are thought to be strikingly low as were those in Italy until recently. Prices in Portugal and Spain are even lower. Nevertheless, the major firms continue to sell their products in these countries. The reason for this behaviour is that production costs are

relatively low, especially at the margin, while most other costs are fixed in the short run. It is therefore worth selling in any market in which direct costs are covered and some contribution is made to overheads.

36. Official data suggests strongly that total costs vary considerably between member countries. In Italy, Portugal and Spain, low prices are offset to some extent by low costs and in the FRG high prices are accompanied by high cost. The UK is unusual in combining above average prices with below-average costs, while the reverse is true of France. All measures suggest that prices in France are uncomfortably low from the standpoint of the French-based industry, which depends heavily on its local market. In contrast the UK industry is markedly profitable.

37. Consumer advocates claim, in opposition to the standpoint of the industry, that pharmaceutical prices are generally excessive and that the industry is inefficient in its use of resources. Central costs are inflated and conceal unnecessary activity, especially in marketing and administration. Prices would be more firmly controlled; alternatively, competition should be stimulated.

38. In relation to national income, total expenditure on pharmaceuticals is relatively low in Denmark and the Netherlands, and, to a lesser extent, in Ireland and the UK. It is high in France, Greece, Italy, Portugal and Spain. These variations result primarily from different attitudes to drugs rather than from differences in prices. For historical and cultural reasons the propensity to consume medicines is unusually high in southern Europe and low in northern Europe (paragraph 2). Such attitudes are difficult to change and must therefore influence national policies concerning the control of pharmaceutical expenditure.

39. In relation to national price levels, pharmaceutical products are unusually cheap in France, and were so, until recently, in Italy. This is not the case in Greece, Portugal and Spain. It is arguable that in the former countries prices are strictly controlled in order to limit total expenditure because it is impossible to reduce the volume of consumption. In the latter nations, however, low prices correspond to

low incomes. Prices in Denmark, the FRG and the Netherlands are high compared to other prices, perhaps because of the combination of free pricing, comprehensive health care services and a restrained attitude to medicines (table 1 and paragraph 38).

40. In so far as comparison with other parts of the chemical industry is possible, the pharmaceutical industry of the Community appears to use its resources with equal efficiency. In most member countries, however - France is the principal exception - it appears to be appreciably more profitable.

41. This is probably due to the ways in which price competition is limited by the arrangements for getting drugs to those who need them. Most products are available only on prescription (paragraph 1) and doctors see their prime duty as well-being of the patient rather than economy. The majority of the bill is paid by the state or the insurance agency. In most countries the distribution system incorporates definite monopoly elements. There is therefore scope for higher than normal profits.

42. To this extent consumer organisations have grounds for their criticisms. As presently constituted, the arrangements for discovering, making and distributing drugs are as a whole rather more expensive than is strictly necessary. The extra profits realised by the industry, however, do not appear large while the future benefits to be derived from its continued activities are very considerable. It is also arguable (paragraph 46) that price competition is increasing in certain significant parts of the pharmaceutical market. Moreover, it is obvious that radical alterations to the system would require a major political effort.

43. There is clear evidence that pricing systems may operate in a discriminatory way. As already mentioned (paragraphs 30-33), individual prices and profit margins depend in several member countries on the scale and nature of a company's local activities. This obviously discriminates in favour of indigenous firms; it also promotes the unnecessary decentralisation of particular functions, with

potential losses in economies of production (paragraphs 53-54).

44. Market distortions arise from the sharp differences in price level. The most obvious sign is parallel importing from low-price to high-price areas. It is seen in Denmark, the FRG, the Netherlands and the UK, the main sources of supply being France and Italy. The scale of this practice is quite small, however - it accounts for no more than 0.5 per cent of total Community sales - and has not increased recently. It is seen by the industry as an irritant rather than as a major threat.

45. Although prices do not play a major role in the competition between pharmaceutical products (paragraph 41), they nevertheless have an appreciable if subordinate part. In countries which permit free pricing, in-patent products are introduced at prices explicitly related to those charged by their competitors. Therapeutic advantages justify a premium price of up to 25 per cent over other medicines in the same therapeutic class.

46. A vigorous market in out-of-patent genric products has recently developed in those member countries where prices are high. Prices have been forced down and reductions in expenditure realised. Such products account for eight per cent by value of the UK market and ten per cent of that of the FRG and the Netherlands. It may be noted, however, that the market is highly imperfect and the originator is normally able to retain much of his sales even when charging a premium price. Official action to encourage generic products has been a sine qua non for the development of a successful generic sector.

47. The industry welcomes the transparency directive which it sees as a step to reduce and perhaps eliminate discriminatory practices and, in particular, pressures to enlarge local activities beyond what is commercially desirable. Progress towards convergence of national price levels within the Community is widely anticipated. There is some anxiety about the basis on which this might take place. The directive has been less enthusiastically received by consumer advocates, who consider that it will do little to limit the profits of the industry.

1.4 The operation of the multinational system

48. The major pharmaceutical companies operating in Europe are organised on a multinational basis (paragraph 4). This could be sub-optimal from an economic standpoint. The need to carry out operations in many locations could give to losses in economics of scale. The coordination of such an organisation could prove excessively expensive.

49. The research-oriented companies that there would be no worthwhile economies of scale in research from the unification of the Community market. There are indeed such economies in serious innovative research but they have already been realised. Such activity is normally concentrated in the firm's country of origin. Where a company has major research centres abroad, they have been placed there in order to exploit local expertise. Within the Community such centres are placed in the UK or, less frequently, in France. In a unified market there would be no immediate change in this policy.

50. Local development work is more decentralised. It does not appear, however, that this activity would be much affected by unification. Formulation research for specific markets is best carried out on the spot, where local advice and information is most effective and tests may be most readily arranged. As has already been seen (paragraphs 16, 18), local clinical research has promotional and even political functions as well as scientific ones, and may therefore be indispensable in practice.

51. The scope for economies in marketing are also very limited. Traditions of medical practice and patterns of consumptions vary markedly between member countries (paragraphs 1, 2) and different approaches are necessary for each market. Even more to the point, the key person in marketing is the salesman who calls on doctors to promote his company's products. If he is suitably persuasive, he must by definition be a native of the country in which he works. In practice marketing is always organised on a national basis, and no firm interviewed could see any alternative.

52. The possibility of economies in production are more considerable. The manufacture of pharmaceuticals involves two stages: the production of the active materials by extraction, synthesis or fermentation, and the conversion of these substances into dosage forms. The first of these steps is normally confined to a few sometimes a single site in Europe, but the second is often decentralised. A common reason is reported to be pressure from host governments, often expressed in the course of price negotiations (paragraphs 30-33, 42). Multinational companies agree that to meet these demands is often to sacrifice economies of production.

53. The equipment used for the formulation of active ingredients is relatively cheap but the building in which it is put, which requires elaborate air-conditioning and ultra-clean facilities is not. The total cost of a formulation plant depends not so much on the volume of output as on the product mix and on the technology used. Over a wide range of output, therefore, it may be taken as fixed. The number of such installations within the Community much exceeds need. American multinationals report that their European formulation plants were often working at between one third and one-half their capacity.

54. Assuming this to be generally true, then between one-half and two-thirds of all formulation plants belonging to the multinational companies are surplus to requirements. There are approximately 250 such plants within the Community. If they are conservatively valued at either ECU 10 or 20m each then the extra capital employed is in the range ECU 1250-3333m. If they were eliminated then, assuming a 10-year lifetime for this kind of installation, the annual saving would be ECU 125-333m.

55. If it is further assumed that the extra production could be provided by existing plants with no further labour then the reduction in employment may be tentatively estimated at a maximum of between 12,500 and 16,500 persons. Labour costs would drop by ECU 225-295m. The total saving in production costs would then be ECU350-630m, or 1.0-1.9 per cent of unit costs. If prices remained unchanged this would increase the trading profits of the Community industry as a whole by 7-14 per cent; alternatively spending on R & D might be raised by 8 - 15 per cent.

56. It should, however, be emphasised that these gains are markedly hypothetical. Multinational companies commented that in many cases their local activities were beneficial to them. In some countries, notably France, they are a condition of receiving an adequate price. In Germany, although pressures of this kind were absent, the free market permits relatively high prices which are advantageous in those export markets in which they are linked to those in the country of origin. More generally, firms feel an obligation to behave as corporate citizens of their host countries. Their local plants already exist, and it would be politically unacceptable and commercially damaging to shut them down.

57. Multinational companies do not think that there are appreciable direct costs in running Europe-wide networks of subsidiaries. Most of them remarked that the extra staff required to coordinate their operations were few.

58. The unification of the European market would therefore not be followed by large changes in the location of facilities. Some degree of concentration is seen as desirable but would happen slowly. Extensive action would have to await changes in pricing systems. Most companies indicated that they would continue to maintain production facilities in the five major countries of the Community.

1.5 The results of unification

59. The savings which might be expected from unification of the Community pharmaceutical market have been estimated in a variety of more or less plausible scenarios on an exploration of company attitudes. They are shown in table 3. In the first, no concentration of facilities takes place but economies due to unified and more rapid registration are realised (paragraph 22). In the second, multinational companies also withdraw all production facilities from Greece and Portugal. In the third, they further reduce the number of formulation plants which they operate by 50 per cent in France and by 25 per cent each in Italy and Spain. The production lost by these countries is transferred to the FRG and the UK.

TABLE 3 SAVINGS IN DIRECT COSTS OF OPERATION TO COMPANIES AND COUNTRIES THROUGH THE UNIFICATION OF THE COMMUNITY MARKET ON A 1984 BASIS

(For the three scenarios see para 59)

Origin of firms	FRANCE	FRG	UK	USA	SWITZ	OTHER	TOTAL
SCENARIO 1							
Savings to firms							
- m ECU: lower value	10.7	23.4	17.6	65.6	28.6	14.1	160
upper value	17.2	37.7	28.3	105.6	46.6	25.3	260
- As % unit costs							
lower value	0.19	0.26	0.51	0.91	1.34	0.22	0.48
upper value	0.30	0.40	0.82	1.47	2.10	0.39	0.77
SCENARIO 2							
Absolute saving m ECU							
Low value	18.5	29.6	23.8	84.3	31.7	15.7	204
High value	28.9	47.0	37.6	133.6	50.7	27.6	325
Reduction in unit Costs %							
Low value	0.32	0.34	0.70	1.17	1.43	0.24	0.61
High value	0.50	0.53	1.09	1.86	2.15	0.43	0.96
SCENARIO 3							
Absolute saving m ECU							
Low value	22.8	39.3	34.4	116.4	35.8	19.8	269
High value	46.2	88.6	61.9	227.7	65.8	42.7	533
Reduction in unit costs %							
Low value	0.40	0.44	1.00	1.62	1.68	0.30	0.79
High value	0.81	1.00	1.81	3.17	3.08	0.66	1.57

Source: Authors' estimates

60. The savings realised range from a minimum of 0.5-0.8 per cent of European unit costs to a maximum of 0.8-1.6 per cent. These savings would accrue primarily to companies operating on a multinational basis in a large number of member nations. They are proportionately greatest for US firms followed by those based in Switzerland and, at some distance, by the UK. Because these estimates relate to all companies of a particular nationality it should be remembered that this reduction in unit costs might be considerably higher or lower for individual firms, depending on their circumstances.

61. The funds so liberated might be used to increase investment in R & D, with a positive effect on competitive strength. For the Community as a whole research budgets could rise by between five and 18 per cent. However, as noted above, the main benefits would be felt by companies based outside the Community.

62. The effects of moves towards common pricing have been explored. Countries in which this entailed general increases in the price of pharmaceuticals would have to spend more on consumption but would simultaneously become more attractive as centres for production, since local production is always a major source of supply for the local market in the larger member countries of the Community. Countries in which prices fell would experience the reverse. Harmonisation on a basis which maintained total Community expenditure would benefit French and Italian firms and would have adverse effects on those of the FRG. UK, US and Swiss firms would break even. Harmonisation on a basis which reduced expenditure would be unambiguously unfavourable for all.

63. In the longer term the effect of unifying the European market will be to make the strong stronger and the weak weaker. Firms which have depended on the favour of their governments will suffer, while those who are already highly competitive will flourish even more. The elimination of marginal companies should concentrate resources on the more efficient and enable them to exploit the opportunities of the future the more profitably. Accelerated progress towards a two-tier pharmaceutical industry, in which companies are either very large or relatively small, seems probable.

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THE COST OF FRAGMENTATION IN THE EUROPEAN COMMUNITY'S PHARMACEUTICAL INDUSTRY AND MARKET

Full Report

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EXECUTIVE SUMMARY

1. In 1984 pharmaceutical sales within the Community, including Spain and Portugal, were approximately ECU25,750m at manufacturers' prices (Table 1), forming 9.5 per cent of health care costs and 0.79 per cent of combined gross domestic product (GDP). Of this total, 88 per cent of sales by value were obtained through a doctor's prescription, 14 per cent being consumed in hospitals and 74 per cent being dispensed through retail pharmacies. Only 12 per cent were bought over the counter,

2. There are large variations in the consumption of pharmaceuticals between the member states in the Community. Differences in income are only partly responsible. Equally important are differences in attitudes to drugs and in traditions of medical practice. These variations affect both the levels of consumption and the types of product consumed. There are strong similarities between Belgium, France, Italy and Spain, on the one hand, and Denmark, Ireland, the Netherlands and the UK on the other. The FRG has elements in common with both.

3. The supply of pharmaceuticals within the Community is highly internationalised. Taking the Community as a whole, 43 per cent of sales are by indigenous companies to their own national market. In every country the locally owned industry has a disproportionately large share of the local market. Only in France and the FRG, however, does it amount to more than 50 per cent. Supplies from companies based in other Community countries make up a further 23 per cent of the total, while 34 per cent come from firms based outside the Community, primarily in the USA and Switzerland.

4. Foreign companies supply drugs either through trade or by local production. In the Community the latter is the more important, amounting to about 40 per cent of all pharmaceuticals supplied. US and Swiss firms depend overwhelmingly on local production to supply their markets, while British and German companies also have substantial foreign facilities. Denmark, Ireland and the Netherlands are the only Community countries which are supplied mainly by imports from abroad.

TABLE 1 PHARMACEUTICAL CONSUMPTION WITHIN THE EUROPEAN COMMUNITY, 1984

Country	Total sales ECU (1)	Per capita ECU	As % GDP	As % health care costs (2)	By type and outlet (%)			Average price (UK=100) (4)	Relative volume Per capita (UK=100 (5)
					OTC	Ethical			
						through retail pharmacies (3)	through hospitals		
BELGIUM	880	90	0.81	8.6	12	76	12	103	140
DENMARK	370	74	0.50	7.0	15	70	15	154	77
FRANCE	5600	102	0.81	8.8	9	78	13	76	216
FRG	7660	125	0.89	11.0	16	66	18	164	122
GREECE	449	45	0.95	20.2	83		17	73	99
IRELAND	160	46	0.67	8.8	5	80	15	115	65
ITALY	4440	78	0.91	12.4	8	79	13	57	221
NETHER-LANDS	660	46	0.38	4.1		n/a		145	51
PORTUGAL	350	35	1.08	18.9	93		7	low	n/a
SPAIN	1830	48	0.81	12.1	88		12	low	n/a
UK	3510	62	0.59	9.6	20	67	13	100	100
TOTAL	25750		0.78	9.5	12	74	14	91	152

(1) at manufacturers' prices
(2) 1983
(3) including dispensing doctors
(4) using the 1983 indices of the EC statistical office
(5) per capita spending/average price.

Source: Author's estimates based on IMF and IMS data and OECD: Measuring Health Care 1960-1983

5. Production of pharmaceuticals within the European Community amounted in 1984 to ECU39,300m (Table 2). The sector is dominated by large companies with the resources to develop new active substances (NAS). The cost of doing so is currently at least ECU75m per NAS to reach the market, and requires annual sales of ECU150m or more. There are 60 such firms operating in the Community, of which 33 are based there. Of the remainder, 20 are American, four are Swiss and three Swedish.

6. These companies have a strong international orientation and operate on a world-wide basis. They are generally organised on multinational lines. Within the Community, marketing is always organised on a country-by-country basis. The manufacture of active ingredients is confined to a limited number of sites, but conversion into dosage forms is extensively decentralised. Basic and commercially sensitive research is highly centralised most commonly in the country of origin. Clinical and formulation development work, however, is often dispersed.

7. Many smaller companies operate in the Community. Most of them concentrate on generics or OTC products or exploit local markets with well established remedies. Their innovative capacity is limited, and their focus national rather than international. Firms of this kind have 20-30 per cent of the market in France, the FRG, Italy and Spain, although they have largely disappeared in the UK.

8. On the basis of shares of the world market and of success in innovation, the pharmaceutical industry of the USA leads. That of Switzerland, although much smaller, is also in the first class. Among the companies based within the European member nations those of the FRG and the UK are very strong. French firms are less well placed, being excessively dependent on sales in the home market and in the franc zone, and the same is true, mutatis mutandis, of those of Italy. The research-based companies of Belgium, the Netherlands and Denmark have elements of competitive strength but are handicapped by their moderate size. The indigenous companies of the other Community nations are uniformly weak.

TABLE 2 PHARMACEUTICAL OUTPUT IN EUROPEAN MEMBER COUNTRIES, 1984

COUNTRY	PHARMA COMPANIES NUMBER (1)	PHARMACEUTICAL PRODUCTION				R&D EXPENDITURE		EMPLOYMENT (000)
		TOTAL ECUm	VALUE ADDED % (2)	TRADING PROFIT AS % SALES (3)	AS % CHEMICAL SALES (2)	TOTAL $m	AS % PHARMA SALES	
BELGIUM	80	1290	49	20	9.4	125	10	10
DENMARK	39	870	44	19	36.4	65	7	8
FRANCE	331	8530	30	5	19.6	1090	13	66
FRG	308	10140	46	12	12.4	1430	14	87
GREECE	90	405	20				<1	3
IRELAND	153	1040	69		52.4	15	5	4
ITALY	365	6300	41	11	21.0	380	6	64
NETHER-LANDS	47	1050				110	11	10
PORTUGAL	96	410					<1	3
SPAIN	370	2570	42	14	19.3	40	2	32
UK	333	6700	52	30	16.8	910	14	66
TOTAL	2212	34300	43	14	16.8	4165	11	353

(1) Manufacturers only

(2) 1983

(3) Authors' estimates based on 1983 Eurostat data.

Source: IMS, Eurostat, national sources

9. The pharmaceutical industry is subject to a very large degree of government regulation. The admission of new products to national markets is strictly controlled. Proof of safety, efficacy and quality is universally required. Regulation of this type is carried out on a national basis, although a considerable degree of uniformity within the Community has been attained through the various directives issued by the Commission since 1965.

10. Pricing policies designed to limit pharmaceutical expenditure are also normal in the member countries. They result from the heavy involvement of European governments and national agencies in the provision of health care. Only in the FRG and the Netherlands are prices largely uncontrolled. Elsewhere, they are fixed by various forms of official action (paragraphs 27-32). Positive lists, which limit reimbursement to specified products, and negative lists, which exclude certain drugs or therapeutic categories, are widely used. Average price levels vary very considerably within the Community. Differences of this kind have existed for many years. Prices are set on a national basis and little progress towards harmonisation has been made.

11. Other barriers towards the unification of the European market and industry are relatively unimportant. Tariffs and direct import restrictions have been eliminated, except in the cases of Portugal and Spain, where they are being phased out. Patent protection has been unified. Direct assistance to the local pharmaceutical industry in the form of subsidies and tax concessions is only significant in the case of Ireland. The discriminatory use of registration procedures and price controls is considered below.

12. Government regulation of the industry means that it forms apart of the political agenda. National administrations have divided aims. They wish to limit health care spending, of which pharmaceuticals form a minor but readily controlled part; at the same time they want to promote high-technology industries, of which the pharmaceutical sector is a successful example. There is therefore an inherent conflict of objectives.

13. In pràctice, Greece, Portugal and Spain, without a research-based industry, favour the interests of consumers unambiguously. Belgium and the Netherlands are inclined in the same direction; although they have such a sector, they appear to attach only a secondary importance to it. The FRG values its major companies, but is committed to a detached attitude to all types of industry. Denmark and the UK have a generally supportive attitude towards their own firms, which, however, make most of their sales abroad. The governments of France, and, to a lesser extent Italy, attach an equally strong importance to the interests of both consumers and producers, which have proved difficult to reconcile.

14. The object of registration is to make sure that a drug is safe, effective and of adequate quality before it is put on sale. The onus is on the applicant to satisfy the authority; the role of the latter is to evaluate the evidence put before it.

15. During the past 20 years the requirements of national regulatory authorities have converged as a result of action by the European Commission. There are now few differences in technical standards between them. All Community countries accept evidence obtained abroad and follow common guidelines. All provide abbreviated forms of registration for projects based on known ingredients. A uniform 120-day decision period has been agreed, to which 90 days are added if the product is referred to an advisory committee.

16. In practice, however, there are substantial differences between one country and another. Methods of evaluation vary, as do perceptions of the weight to be put on particular kinds of evidence. A large element of judgement is involved, which must be influenced by the local traditions of medical practice. Local clinical trials may not be officially required, but are often advisable to familiarise local opinion leaders with a new product.

17. There are also considerable delays in processing applications. Currently only France approaches the 120-day limit on occasion. The FRG and the UK take about two years, and Italy and Spain three or more. The Community average is currently 18-24 months. Such delays

have tended to increase in recent years. They are attributed in the main to a lack of resources on the part of national registration authorities, aggravated in several nations by a large increase in the number of applications for generic products.

18. The large research-based companies respond to this situation by preparing the necessary dossier centrally, usually with the US Food and Drug Administration (FDA), the most demanding of authorities, in mind. The experimental work is organised so as to satisfy all requirements; thus, if local clinical testing is needed, it will be included in the overall programme. The dossier is then modified to suit the needs of each authority. They consider this to be a satisfactory if not ideal way to work.

19. The direct costs of multiple registration within the Community are limited. Based on the extra staff employed by the major firms, a figure of ECU40-55m seems reasonable. Extra clinical testing is not considered to be serious burden; as already noted, the results contribute to the central dossier, while the testing itself may help towards a favourable decision by the licensing authority and towards a better reception when the product reaches the market.

20. More important are the effects of delays in the registration process. Since it takes 9-12 years to develop an NAS, the opportunity costs of the money tied up in the process are considerable. A further delay increases the penalty correspondingly. Estimates based on data supplied by the FDA suggest that in 1984/5 the total costs imposed by the general failure to observe the 120-day limit were in the range of ECU30-200m, depending on the discount rate chosen, with a most probable range of ECU57-82m, corresponding to rates of eight and ten per cent respectively.

21. Another serious problem arising from delays in approval is the loss of revenue while the product is in patent. As yet there is no general patent term restoration in the Community, and effective patent

lives, weighted by national sales, average nine years. Estimates derived from average sales of new active substances during the years following their introduction suggest that the failure to meet the 120-day limit caused gross losses of ECU360-640m to their originators. The net losses are smaller, in part because costs of production must be deducted, and in part because of the continued sales of products which would otherwise be made obsolete.

22. The penalties due to the differences between member nations are less serious. As has been noted, with the partial exception of France, all greatly exceed the 120-day limit. If the minimum practicable time for the approval of an NAS under current conditions is taken to be one year, then the opportunity costs of delay drop to ECU20-28m and the net loss of sales to ECU100-175m. As far as registration is concerned, the total cost of the non-Europe is therefore ECU160-260m or 0.5-0.6 per cent of industry costs within the Community (table 3). Effective unification of the market would most benefit US companies since they introduce the largest number of new active substances.

23. Approaches to a more unified system of registration have focussed on two major alternatives - mutual recognition between states and pan-European registration agency. Research-based companies see considerable problems with both these approaches. There are doubts about the equality of the countries involved. There is some feeling that north European agencies carry more weight than south European ones. The differences of medical culture were thought to raise difficulties of mutual acceptability. Registration is not, however, thought to be used in a deliberately discriminatory way.

24. A single European agency would have the advantages of impartiality and uniformity of approach. In principle it could provide rapid decisions. It might, however, be excessively rigid and bureaucratic; the precedent of the FDA, EAG found, was not thought to be encouraging. There was some anxiety about the standards to be used; these would have to be high, but many feared a combination of the most severe elements of all national agencies. There was also concern about the political acceptability to the individual nations of a central authority.

25. It does not appear that a central registration authority would be much cheaper to run than the present system. The national agencies employ the equivalent about 1500 staff at a cost of ECU55-70m to which accommodation and related overheads should be added. Allowing for the higher salaries prevailing in the USA, this sum is comparable with the cost of the drugs and biologics division of the FDA. The European national registration agencies are generally under-staffed and savings through the creation of a single authority would therefore be limited.

26. From the standpoint of the pharmaceutical industry the key issue is the speed of the registration process. Any change which lengthened it would be opposed. Consumers would also benefit from the more rapid approval of new substances provided that safety standards were not lowered.

27. The CPMP procedure in force between 1978 and 1985 was not widely used because of doubts among large innovative companies about its advantages. The current procedure has arised considerably more enthusiasm, especially as it is thought to be potentially faster than the normal route.

28. As already noted, policies intended to control pharmaceutical expenditure are found in all member states of the Community. The methods used vary very widely as do average price levels. The only common factors are that all systems incorporate an element of patient copayment and the over-the-counter (OTC) products are exempt from regulation.

29. At one extreme, the FRG leaves pharmaceutical firms free to set prices as they wish. Total expenditure is limited by strong pressure on companies to limit price increases and on doctors to economise and by a negative list which excludes certain categories of comfort drugs from the reimbursement system. The situation in the Netherlands is very similar. Prices are high in both countries.

30. In the UK the profitability of pharmaceutical companies is controlled. A target level is set for the sector as a whole; the target for each firm depends on its research effort and on its contribution to the British economy. Subject to these constraints companies are allowed to set the prices at which their products are introduced. Irish prices are in practice tied to those in the UK. In both countries they are in the middle range.

31. In principle firms may set their own prices in France, but in practice admission to the national reimbursement system is strictly controlled. Products are dealt with on an individual basis. The price agreed between the manufacturer and the reimbursement authority depends on those of competitive products and on the company's local activities in France. Belgium has a similar system. Prices are low in both countries, and especially in France.

32. Denmark, Greece, Italy, Portugal and Spain control the prices of individual drugs by the use of cost-plus methods, and maintain positive lists. Prices are high in Denmark, below average in Italy and very low in the other three countries.

33. In every Community country except the FRG, the price at which a product is introduced cannot subsequently be changed without official permission. Such permission is often delayed, refused or made contingent on the company expanding its local activities.

34. As far as the adequacy of price levels is concerned, the attitude of the research-based companies is that sales in the Community market should ideally make a substantial contribution to world overhead costs, and in particular to the cost of innovation, and to profits. Prices in Denmark, the FRG and the Netherlands are considered to be 'satisfactory' form this point of view and those in the UK and Ireland 'adequate'.

35. Prices elsewhere are considered to be less than adequate. Those prevailing in France are thought to be strikingly low as were those in Italy until recently. Prices in Portugal and Spain are even lower. Nevertheless, the major firms continue to sell their products in these countries. The reason for this behaviour is that production costs are

relatively low, especially at the margin, while most other costs are fixed in the short run. It is therefore worth selling in any market in which direct costs are covered and some contribution is made to overheads.

36. Official data suggests strongly that total costs vary considerably between member countries. In Italy, Portugal and Spain, low prices are offset to some extent by low costs and in the FRG high prices are accompanied by high cost. The UK is unusual in combining above average prices with below-average costs, while the reverse is true of France. All measures suggest that prices in France are uncomfortably low from the standpoint of the French-based industry, which depends heavily on its local market. In contrast the UK industry is markedly profitable.

37. Consumer advocates claim, in opposition to the standpoint of the industry, that pharmaceutical prices are generally excessive and that the industry is inefficient in its use of resources. Central costs are inflated and conceal unnecessary activity, especially in marketing and administration. Prices would be more firmly controlled; alternatively, competition should be stimulated.

38. In relation to national income, total expenditure on pharmaceuticals is relatively low in Denmark and the Netherlands, and, to a lesser extent, in Ireland and the UK. It is high in France, Greece, Italy, Portugal and Spain. These variations result primarily from different attitudes to drugs rather than from differences in prices. For historical and cultural reasons the propensity to consume medicines is unusually high in southern Europe and low in northern Europe (paragraph 2). Such attitudes are difficult to change and must therefore influence national policies concerning the control of pharmaceutical expenditure.

39. In relation to national price levels, pharmaceutical products are unusually cheap in France, and were so, until recently, in Italy. This is not the case in Greece, Portugal and Spain. It is arguable that in the former countries prices are strictly controlled in order to limit total expenditure because it is impossible to reduce the volume of consumption. In the latter nations, however, low prices correspond to

low incomes. Prices in Denmark, the FRG and the Netherlands are high compared to other prices, perhaps because of the combination of free pricing, comprehensive health care services and a restrained attitude to medicines (table 1 and paragraph 38).

40. In so far as comparison with other parts of the chemical industry is possible, the pharmaceutical industry of the Community appears to use its resources with equal efficiency. In most member countries, however - France is the principal exception - it appears to be appreciably more profitable.

41. This is probably due to the ways in which price competition is limited by the arrangements for getting drugs to those who need them. Most products are available only on prescription (paragraph 1) and doctors see their prime duty as well-being of the patient rather than economy. The majority of the bill is paid by the state or the insurance agency. In most countries the distribution system incorporates definite monopoly elements. There is therefore scope for higher than normal profits.

42. To this extent consumer organisations have grounds for their criticisms. As presently constituted, the arrangements for discovering, making and distributing drugs are as a whole rather more expensive than is strictly necessary. The extra profits realised by the industry, however, do not appear large while the future benefits to be derived from its continued activities are very considerable. It is also arguable (paragraph 46) that price competition is increasing in certain significant parts of the pharmaceutical market. Moreover, it is obvious that radical alterations to the system would require a major political effort.

43. There is clear evidence that pricing systems may operate in a discriminatory way. As already mentioned (paragraphs 30-33), individual prices and profit margins depend in several member countries on the scale and nature of a company's local activities. This obviously discriminates in favour of indigenous firms; it also promotes the unnecessary decentralisation of particular functions, with potential losses in economies of production (paragraphs 53-54).

44. Market distortions arise from the sharp differences in price level. The most obvious sign is parallel importing from low-price to high-price areas. It is seen in Denmark, the FRG, the Netherlands and the UK, the main sources of supply being France and Italy. The scale of this practice is quite small, however - it accounts for no more than 0.5 per cent of total Community sales - and has not increased recently. It is seen by the industry as an irritant rather than as a major threat.

45. Although prices do not play a major role in the competition between pharmaceutical products (paragraph 41), they nevertheless have an appreciable if subordinate part. In countries which permit free pricing, in-patent products are introduced at prices explicitly related to those charged by their competitors. Therapeutic advantages justify a premium price of up to 25 per cent over other medicines in the same therapeutic class.

46. A vigorous market in out-of-patent genric products has recently developed in those member countries where prices are high. Prices have been forced down and reductions in expenditure realised. Such products account for eight per cent by value of the UK market and ten per cent of that of the FRG and the Netherlands. It may be noted, however, that the market is highly imperfect and the originator is normally able to retain much of his sales even when charging a premium price. Official action to encourage generic products has been a sine qua non for the development of a successful generic sector.

47. The industry welcomes the transparency directive which it sees as a step to reduce and perhaps eliminate discriminatory practices and, in particular, pressures to enlarge local activities beyond what is commercially desirable. Progress towards convergence of national price levels within the Community is widely anticipated. There is some anxiety about the basis on which this might take place. The directive has been less enthusiastically received by consumer advocates, who consider that it will do little to limit the profits of the industry.

48. The major pharmaceutical companies operating in Europe are organised on a multinational basis (paragraph 4). This could be sub-optimal from an economic standpoint. The need to carry out operations in many locations could give rise to losses in economies of scale. The coordination of such an organisation could prove excessively expensive.

49. The research-oriented companies say that there would be no worthwhile economies of scale in research from the unification of the Community market. There are indeed such economies in serious innovative research but they have already been realised. Such activity is normally concentrated in the firm's country of origin. Where a company has major research centres abroad, they have been placed there in order to exploit local expertise. Within the Community such centres are placed in the UK or, less frequently, in France. In a unified market there would be no immediate change in this policy.

50. Local development work is more decentralised. It does not appear, however, that this activity would be much affected by unification. Formulation research for specific markets is best carried out on the spot, where local advice and information is most effective and tests may be most readily arranged. As has already been seen (paragraphs 16, 18), local clinical research has promotional and even political functions as well as scientific ones, and may therefore be indispensable in practice.

51. The scope for economies in marketing are also very limited. Traditions of medical practice and patterns of consumptions vary markedly between member countries (paragraphs 1, 2) and different approaches are necessary for each market. Even more to the point, the key person in marketing is the salesman who calls on doctors to promote his company's products. If he is suitably persuasive, he must by definition be a native of the country in which he works. In practice marketing is always organised on a national basis, and no firm interviewed could see any alternative.

52. The possibility of economies in production are more considerable. The manufacture of pharmaceuticals involves two stages: the production of the active materials by extraction, synthesis or fermentation, and the conversion of these substances into dosage forms. The first of these steps is normally confined to a few sometimes a single-site in Europe, but the second is often decentralised. A common reason is reported to be pressure from host governments, often expressed in the course of price negotiations (paragraphs 30-33, 42). Multinational companies agree that to meet these demands is often to sacrifice economies of production.

53. The equipment used for the formulation of active ingredients is relatively cheap but the building in which it is put, which requires elaborate air-conditioning and ultra-clean facilities is not. The total cost of a formulation plant depends not so much on the volume of output as on the product mix and on the technology used. Over a wide range of output, therefore, it may be taken as fixed. The number of such installations within the Community much exceeds need. American multinationals report that their European formulation plants were often working at between one third and one-half their capacity.

54. Assuming this to be generally true, then between one-half and two-thirds of all formulation plants belonging to the multinational companies are surplus to requirements. There are approximately 250 such plants within the Community. If they are conservatively valued at either ECU 10 or 20m each then the extra capital employed is in the range ECU 1250-3333m. If they were eliminated then, assuming a 10-year lifetime for this kind of installation, the annual saving would be ECU 125-333m.

55. If it is further assumed that the extra production could be provided by existing plants with no further labour then the reduction in employment may be tentatively estimated at a maximum of between 12,500 and 16,500 persons. Labour costs would drop by ECU 225-295m. The total saving in production costs would then be ECU350-630m, or 1.0-1.9 per cent of unit costs. If prices remained unchanged this would increase the trading profits of the Community industry as a whole by 7-14 per cent; alternatively spending on R & D might be raised by 8 - 15 per cent.

56. It should, however, be emphasised that these gains are markedly hypothetical. Multinational companies commented that in many cases their local activities were beneficial to them. In some countries, notably France, they are a condition of receiving an adequate price. In Germany, although pressures of this kind were absent, the free market permits relatively high prices which are advantageous in those export markets in which they are linked to those in the country of origin. More generally, firms feel an obligation to behave as corporate citizens of their host countries. Their local plants already exist, and it would be politically unacceptable and commercially damaging to shut them down.

57. Multinational companies do not think that there are appreciable direct costs in running Europe-wide networks of subsidiaries. Most of them remarked that the extra staff required to coordinate their operations were few.

58. The unification of the European market would therefore not be followed by large changes in the location of facilities. Some degree of concentration is seen as desirable but would happen slowly. Extensive action would have to await changes in pricing systems. Most companies indicated that they would continue to maintain production facilities in the five major countries of the Community.

59. The savings which might be expected from unification of the Community pharmaceutical market have been estimated in a variety of more or less plausible scenarios on an exploration of company attitudes. They are shown in table 3. In the first, no concentration of facilities takes place but economies due to unified and more rapid registration are realised (paragraph 22). In the second, multinational companies also withdraw all production facilities from Greece and Portugal. In the third, they further reduce the number of formulation plants which they operate by 50 per cent in France and by 25 per cent each in Italy and Spain. The production lost by these countries is transferred to the FRG and the UK.

TABLE 3 SAVINGS IN DIRECT COSTS OF OPERATION TO COMPANIES AND COUNTRIES THROUGH THE UNIFICATION OF THE COMMUNITY MARKET ON A 1984 BASIS

(For the three scenarios see para 59)

Origin of firms	FRANCE	FRG	UK	USA	SWITZ	OTHER	TOTAL
SCENARIO 1							
Savings to firms							
- m ECU: lower value	10.7	23.4	17.6	65.6	28.6	14.1	160
upper value	17.2	37.7	28.3	105.6	46.6	25.3	260
- As % unit costs							
lower value	0.19	0.26	0.51	0.91	1.34	0.22	0.48
upper value	0.30	0.40	0.82	1.47	2.10	0.39	0.77
SCENARIO 2							
Absolute saving m ECU							
Low value	18.5	29.6	23.8	84.3	31.7	15.7	204
High value	28.9	47.0	37.6	133.6	50.7	27.6	325
Reduction in unit Costs %							
Low value	0.32	0.34	0.70	1.17	1.43	0.24	0.61
High value	0.50	0.53	1.09	1.86	2.15	0.43	0.96
SCENARIO 3							
Absolute saving m ECU							
Low value	22.8	39.3	34.4	116.4	35.8	19.8	269
High value	46.2	88.6	61.9	227.7	65.8	42.7	533
Reduction in unit costs %							
Low value	0.40	0.44	1.00	1.62	1.68	0.30	0.79
High value	0.81	1.00	1.81	3.17	3.08	0.66	1.57

Source: Author's estimates

60. The savings realised range from a minimum of 0.5-0.8 per cent of European unit costs to a maximum of 0.8-1.6 per cent. These savings would accrue primarily to companies operating on a multinational basis in a large number of member nations. They are proportionately greatest for US firms followed by those based in Switzerland and, at some distance, by the UK. Because these estimates relate to all companies of a particular nationality it should be remembered that this reduction in unit costs might be considerably higher or lower for individual firms, depending on their circumstances.

61. The funds so liberated might be used to increase investment in R & D, with a positive effect on competitive strength. For the Community as a whole research budgets could rise by between five and 18 per cent. However, as noted above, the main benefits would be felt by companies based outside the Community.

62. The effects of moves towards common pricing have been explored. Countries in which this entailed general increases in the price of pharmaceuticals would have to spend more on consumption but would simultaneously become more attractive as centres for production, since local production is always a major source of supply for the local market in the larger member countries of the Community. Countries in which prices fell would experience the reverse. Harmonisation on a basis which maintained total Community expenditure would benefit French and Italian firms and would have adverse effects on those of the FRG. UK, US and Swiss firms would break even. Harmonisation on a basis which reduced expenditure would be unambiguously unfavourable for all.

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1 INTRODUCTION

1.1 Terms of reference

This study was commissioned by DGIII of the European Community in a contract with Economists Advisory Group Ltd (EAG) dated 24 August 1987. The terms of reference are those set out in EAG's submission to DGIII dated 26 June 1987 and are given below:

- to review the present structure and organisation of the pharmaceutical industry within the European Community;

- to analyse of the costs and benefits of present institutional arrangements;

- to estimate the consequences in the short and longer term of the unification of the Community pharmaceutical market.

1.2 Method

The report is based on a review of the extensive literature of the world pharmaceutical industry which already exists including that commissioned by DGIII in 1983; on data collected from a large number of authoritative sources, notably the World Drug Marketing Manual 1986 and from industry federations in Europe and the and the USA; and an extensive interview programme with appropriate ministries, government agencies, industry federations and pharmaceutical companies both within and without the Community.

In all we interviewed in depth senior executives from 12 large international pharmaceutical companies with major European operations. We also interviewed five industry associations, including EFPIA (European Federation of Pharmaceutical Industries Associations). These interviews were semi-structured in nature and designed to elicit mainly qualitative information about attitudes and possible responses to official action.

We would like to thank all concerned who contributed the data, information and opinions on which this report is based. Naturally, responsibility for the report itself lies with the author.

1.3 Timing

The desk research was carried out between July and November 1987 and the interviews in August and September 1987. Our draft report was submitted 23 November 1987 and the final report in February 1988.

1.4 Currency conversion

The US dollar is commonly used as the standard yardstick for pharmaceutical sales, costs and expenditure. The bulk of the data used in this report refers to 1984, when the dollar had greatly appreciated against the ECU. All dollar figures have been converted to ECU at the value given by the International Monetary Fund (IMF) as prevailing at the end of 1984, ie 1ECU=0.71 US$.

2 THE PHARMACEUTICAL SITUATION IN THE EUROPEAN COMMUNITY

The aim of this chapter is to review the pharmaceutical market and industry of the European Community as it was in the mid-80s. In so doing, particular attention is given to the extent to which they are divided along national or regional limes and to the factors which account for this state of affairs. Certain of these factors are analysed in greater detail at later points in the report; here the object is to identify and to describe.

2.1 Patterns of demand

In 1984 the consumption of pharmaceuticals within the 12 member countries of the Community was approximately ECU26,000m. (cf. table 2.1). This was 21 per cent of the world total of ECU123,750m and made the Community market the second largest in the world, behind the USA, with nearly 28 per cent, but in front of Japan, with 15 per cent. Within the Community five large countries - France, the Federal Republic of Germany, Italy, Spain and the United Kingdom - accounted for 89 per cent of pharmaceutical sales (1).

In economic terms, the role of pharmaceuticals in health care is significant but not dominant. In 1983 pharmaceutical consumption formed between eight and 12 per cent of the health care budget in the member countries of the Community or rather less than one per cent of gross domestic product (GDP). Only in Portugal and Greece was this proportion much exceeded. Growth in the consumption of drugs has been moderate in recent years: in real terms the annual rate of increase from 1977 to 1984 was 2.6 per cent, which is less than that of health care spending in general and close to that of GDP (2).

The large majority of pharmaceuticals are available only on prescription. Over-the-counter (OTC) products generally account for ten per cent or less of total sales; only in the FRG, the Netherlands and the UK are they more significant. They consist of established remedies for minor illnesses. Their share of the market is static. Between 12 and 20 per cent of prescription drugs are used in hospitals; the remainder are prescribed by medical personnel working

TABLE 2.1 PHARMACEUTICAL CONSUMPTION WITHIN THE EUROPEAN COMMUNITY, 1984

Country	Total sales ECU (1)	Per capita ECU	As % GDP	As % health care costs (2)	By type and outlet (%)			Average price (UK=100) (4)	Relative volume Per capita (UK=100) (5)
					OTC	Ethical through retail pharmacies (3)	Ethical through hospitals		
Belgium	880	90	0.81	8.6	12	76	12	103	140
Denmark	370	74	0.50	7.0	15	70	15	154	77
France	5600	102	0.81	8.8	9	78	13	76	216
FRG	7660	125	0.89	11.0	16	66	18	164	122
Greece	449	45	0.95	20.2	83		17	73	99
Ireland	160	46	0.67	8.8	5	80	15	115	65
Italy	4440	78	0.91	12.4	8	79	13	57	221
Nether-lands	660	46	0.38	4.1		n/a		145	51
Portugal	350	35	1.08	18.9	93		7	low	n/a
Spain	1830	48	0.81	12.1	88		12	low	n/a
UK	3510	62	0.59	9.6	20	67	13	100	100
Total	25910	82	0.78	9.5	12	74	14	91	152

(1) at manufacturers' prices
(2) 1983
(3) including dispensing doctors
(4) using the 1983 indices of the EC statistical office
(5) per capita spending/average price.

Source: Author's estimates based on IMF and IMS data and OECD: Measuring Health Care 1960-1983

outside hospitals. Thus, the role of the physician, and especially the physician practising outside hospitals, has a powerful influence on the scale and nature of pharmaceutical consumption.

There are considerable variations in the demand for drugs between the various member countries of the Community. Table 2.2 presents relevant data. It is clear that these differences cannot readily be explained in economic or demographic terms. Age structures and major causes of death are similar everywhere. National consumption is sensitive to differences in per capita income and in average price levels, but these factors account for less than half the total variance. In terms of volume, demand is unusually high in France, Greece and Italy, and unusually low in the UK and and, especially, in Denmark and the Netherlands (3).

More fruitful explanations lie in the variations in attitudes towards medicines and in the institutional arrangements by which they are delivered to patients. As has already been seen, most drugs are obtained on prescription and it may be significant that countries in which doctors are paid on a capitation basis consume less than those in which they are paid for each consultation. A possible reason is that in the former, unlike the latter, the physician has no incentive to see his or her patients more than is absolutely necessary and opportunities to prescribe are thereby reduced (4).

Attitudes also differ. A belief in the prophylactic benefits of taking medicines is more common in France or Italy than in, say, the UK or the USA. This may affect both the tendency to offer drugs and the tendency to accept them. British patients are markedly less likely to receive prescriptions than their French, Italian or Spanish counterparts. As table 2.3 shows, there are also considerable national variations in patterns of diagnosis and treatment. Mental disorders are strikingly more common in Britain and France than in Italy or Spain. Conversely, the incidence of diseases of the digestive system is much higher in Italy than elsewhere.

The types of complaint with which patients present themselves are in part social constructions resulting from the underlying assumptions about health and sickness of professional and patient alike. Many

TABLE 2.2 ECONOMIC, DEMOGRAPHIC AND MEDICAL CHARACTERISTICS OF THE EUROPEAN COMMUNITY IN 1984

Country	GDP per capita ECU	Birth rate /1000	Death rate /1000	% Population aged 0-14	% Population aged 65+	Expectation of life at birth (yrs.) Men (1)	Expectation of life at birth (yrs.) Women (1)	% Deaths from Cardio-vascular disease	% Deaths from Neoplasms
Belgium	11090	11.7	11.1	18.8	13.7	70.0	76.8	38.0	23.3
Denmark	14926	10.1	11.2	18.6	14.9	71.6	77.5	44.2	24.4
France	12560	13.8	9.9	21.6	12.9	71.2	79.4	36.0	23.1
FRG	14119	9.5	11.3	15.5	14.7	70.8	77.5	50.6	22.8
Greece	4760	12.7	8.9	21.5	13.3	72.1	76.4	45.9	19.4
Ireland	7042	18.2	9.1	29.6	10.6	70.1	75.6	50.5	19.6
Italy	8611	10.3	9.3	20.2	12.8	71.0	77.8	47.3	22.7
Nether-lands	12018	12.1	8.3	20.9	11.9	73.0	79.5	44.5	27.4
Portugal	2911	14.2	9.6	24.8	10.5	68.9	75.8	44.2	16.1
Spain	5926	12.5	7.7	24.7	11.8	72.6	78.6	45.8	20.1
UK	10598	12.9	11.4	19.6	14.8	71.8	77.6	49.1	22.8
Total	10366	11.9	10.0	20.4	13.4	<---n/a--->		47.2	22.9

(1) 1980-85

Source: Eurostat Demographic Yearbook 1987, national sources.

TABLE 2.3 LEADING DIAGNOSES BY ICD CHAPTER HEADINGS IN FIVE EUROPEAN COUNTRIES IN 1982

Chapter heading	% of all top 20 diagnoses				
	France	FRG	Italy	Spain	UK
Infective, parasitic diseases	2.7		4.4	4.4	
Endocrine, nutritional and metabolic diseases	4.2	3.4	5.6	5.5	2.3
Mental disorders	16.4	10.5	7.4	4.6	16.5
Diseases of the nervous system and sense organs	2.7			2.7	2.3
Circulatory diseases	31.0	26.0	23.6	18.4	16.7
Respiratory diseases	21.4	23.9	25.6	41.9	20.0
Diseases of the digestive system	3.6	7.4	17.1	3.5	2.5
Diseases of the skin etc.	3.4	6.0	4.1	3.0	3.9
Musculoskeletal diseases	3.8	8.0	12.2	7.0	9.0
Symptoms and ill-defined conditions	10.8	11.6		9.0	22.8
Leading twenty diagnoses as % all diagnoses	36.5	46.5	42.2	36.5	46.6

TABLE 2.3 continued

LEADING TWENTY DRUG SUB-GROUPS BY ANATOMICAL GROUP

	% of all top 20 drug sub-groups				
Group	France	FRG	Italy	Spain	UK
Alimentary tract and metabolism	6.2	3.7	19.4	13.2	6.5
Blood and blood-forming organs					2.9
Cardiovascular system	26.5	29.2	25.5	16.2	16.3
Dermatological					3.6
Genito-urinary/sex hormones		2.6	3.2		3.3
Systematic anti-infectives	6.6		7.0	13.6	15.4
Musculoskeletal system	12.0	12.0	13.4	14.4	5.2
Central nervous system	25.9	20.4	13.6	14.4	28.9
Respiratory system	22.8	26.5	17.9	28.2	14.6
Leading twenty drug sub-groups as % all prescriptions	51.3	53.3	47.0	50.6	61.5

Source: O'Brien, 1984 tables 10 and 13

consultations and much treatment concerns minor illnesses, often vague in nature, and social factors play an important part in determining the outcome. This is reflected in the types of drugs consumed. There is a much higher degree of international consensus where serious illness is concerned. Even here, however, there are significant national variations in the preferred forms of pharmaceutical treatment, as table 2.4 indicates for the case of essential benign hypertension, one of the most common diagnoses in all European countries.

In fact there appear to be three broad traditions of medical practice within the Community. The first is common to Denmark, Ireland, the Netherlands and the UK. In these countries the propensity to take drugs is low. Products acting on the central nervous system are unusually important. Beta-blockers are widely used to treat cardiovascular conditions. The second is common to the Mediterranean member countries, and, to a considerable extent, to Belgium and France. Here the propensity to consume pharmaceuticals is high. Treatment of the alimentary tract is emphasised. Peripheral vasodilators are the most important class of cardiovascular drug. The use of pharmaceuticals in the FRG shows elements of both these traditions, but also peculiarities of its own (5).

This is an important conclusion. The European pharmaceutical market is not only divided by wide variations in national wealth but also by attitudes to the use of medicines. These attitudes are embodied in the training and behaviour of doctors and the expectations of patients. The product of fundamental social and psychological factors, they are slow to change and difficult to manipulate. Divisions of this kind are therefore likely to remain for many years to come, with consequences that are explored later.

2.2 Patterns of supply

The supply of pharmaceuticals to the member nations of the Community is highly internationalised. Table 2.5 shows the breakdown of 1984 sales through retail pharmacies by the nationality of the company concerned. Although an approximate measure - only 74 per cent of the

TABLE 2.4 THE DIAGNOSIS AND TREATMENT OF ESSENTIAL BENIGN HYPERTENSION IN FIVE EUROPEAN COUNTRIES IN 1982

	France	FRG	Italy	Spain	UK
Number of diagnoses (000)	21651	22260	24780	9157	18622
Number receiving drug treatment (000)	20059	n/a	24373	8593	15641
Total no. of prescriptions (000)	37254	25568	33421	10754	22335
Diagnoses/1000 population	401	360	433	244	333
Drug treatment/diagnosis	0.93	n/a	0.98	0.94	0.84
Prescriptions/drug treatment	1.85	n/a	1.37	1.22	1.43
Five leading prescriptions as % total prescriptions in each country					
Beta-blockers	12.7	13.6	10.9	7.2	26.1
Beta-blocker + combinations		9.7			8.1
Synthetic hypotensives	19.8	9.9	20.2	11.3	18.8
Hypotensives + diuretics		37.9	21.5	38.3	
Thiazide combinations	17.4	8.3	11.3	8.0	31.1
Other diuretics	11.0		14.5	18.6	7.8
Peripheral vasodilators	8.6				

Source: O'Brien, 1984

TABLE 2.5 SALES OF DRUGS THROUGH RETAIL PHARMACIES BY COMPANIES OF VARIOUS NATIONALITIES IN 1984

ECUm (1)

Origin of company --> / SALES IN	Bel	Den	Fra	FRG	Gre	Irl	Ita	Net	Por	Spa	UK	USA	Swi	Swe	Total
Belgium	58	7	65	59			10	17			72	237	73	10	608
Denmark	11	169	20	45			4	7			30	7	28	20	349
France	113	24	2500	346			15	79			220	1023	342		4662
FRG	99	26	248	2730			45	97			241	962	534	82	5064
Greece	4	6	13	44	42			4			34	70	52		269
Ireland	1	4	4	7		1					31	42	11	2	103
Italy	13	15	176	520			1494	39	23		311	720	393	38	3742
Netherlands	11	14	35	56			4	56			107	163	66	23	535
Portugal	6		10	28			4		44		18	86	46		242
Spain	20	13	68	227			44	8		508	120	248	196		1452
UK	28	46	85	232			8	20			723	865	187	39	2233
Total	364	324	3224	4294	42	1	1628	327	67	508	1915	4423	1925	214	19259
% Of European market held	1.8	1.7	16.8	22.4	<1	<1	8.5	1.7	<1	2.6	10.0	23.0	10.0	1.1	100.0
% Local market held	10	48	54	63	16	1	40	17	18	35	32				
Home sale as % European sales	16	45	78	63	100	1	92	17	66	100	38				

(1) At manufacturers' prices

Source : Author's estimates based on IMS data - see text.

total market is covered - it indicates the general pattern clearly enough (6).

Taking the Community as a whole, 43 per cent of sales are by indigenous companies to their own national market. In every member country the locally-owned industry has a disproportionately large share of the local market, although only in France and FRG does this amount to more than 50 per cent. In the case of the smaller member nations the proportion is usually much lower; in Belgium, Ireland and the Netherlands it is ten per cent or less.

Supplies from companies based in other Community countries make up a further 23 per cent of the total. German, British and French firms, in that order, are most important sources, although the very strong international orientation of Belgian, Danish and Dutch companies is apparent. Geography and national attitudes to medicine play an obvious part in determining the strength or otherwise of particular suppliers in particular countries.

Approximately 34 per cent comes from firms based outside the Community. US companies account for 23 per cent; they are especially strong in the UK and in the smaller Community nations. Swiss firms have ten per cent of the total market, showing strength in every country. Of the remainder, only Sweden is a significant source of drugs for the Community. Japanese and third world companies are as yet conspicuous by their absence.

This situation has not greatly changed since 1980, although British firms appear to be gaining ground in Europe and French and Italian ones losing it. This reflects the stability of the industry as a whole in recent years, and the measured pace at which the international distribution of strengths and weaknesses changes. This latter area is explored in section 2.5 below (7).

Companies can supply foreign markets by trade or through local manufacture. In the case of pharmaceuticals the latter is the more important. Community trade in finished drugs in 1984 is shown in table 2.6. Total imports from outside the Community amounted to ECU1,176m or about four per cent of total sales. A comparison of individual

TABLE 2.6 TRADE IN FINISHED DRUGS IN THE EUROPEAN COMMUNITY IN 1984

ECUm

From:	Bel	Den	Fra	FRG	Gre	Irl	Ita	Net	Spa	UK	USA	Swi	Swe	Oth	Total
To:															
Belgium	-	13	100	145	1	3	20	59	7	41	23	65	18	8	503
Denmark	14	-	17	21	-	14	3	13	1	37	4	23	23	11	181
France	44	1	-	21	-	7	24	31	1	77	23	30	8	13	280
FRG	128	34	182	-	1	11	69	59	24	96	55	182	58	82	981
Greece	8	6	11	24	-	1	4	3	-	13	6	17	1	1	95
Ireland	4	3	4	10	-	-	1	8	4	120	4	4	1	4	167
Italy	25	10	41	128	-	-	-	13	1	75	35	108	4	30	474
Nether-lands	131	24	72	75	-	7	13	-	4	75	3	68	11	8	491
Portugal	7	4	4	24	-	-	1	4	1	20	7	30	1	1	103
Spain	1	14	1	4	-	-	1	-	-	8	13	4	4	4	54
UK	54	51	86	189	4	39	27	59	3	-	58	54	42	27	693
Total	416	164	518	641	6	82	163	249	46	562	231	585	171	189	4022

Source : OECD: Trade by Commodities, Imports, category 5417, 1984

trade figures with the market shares held by companies of particular nationality (table 2.5) suggests that production in the Community by US firms amounted to about ECU4,200 and by Swiss firms to about ECU1,450m.

It is more difficult to decide how much foreign production there is within the Community by firms based there. Trade returns do not differentiate between companies according to their ownership. A figure of ECU2,500m seems probable, which would give a grand total of about ECU8,000m or about 40 per cent of all sales through retail pharmacies. If this proportion were to apply to all pharmaceutical sales, then the foreign production within the Community might be as high as ECU11,000m (8).

Estimates of the distribution of this capacity, based on a variety of sources, are given in table 2.7. Local production by the affiliates of foreign multinationals is most common in large countries, especially where restrictive attitudes towards imports formerly existed. France, Italy and Spain fall into this category. The UK is popular with US firms for cultural reasons and Germany because prices are high and the industrial milieu attractive.

Among the smaller countries, Greece and Portugal have encouraged the development of local production facilities by a variety of means. Although their local markets are dominated by foreign companies, most of the products consumed are made locally. Denmark, Ireland and the Netherlands, however, are supplied largely by imports, even though Ireland is a favourite site for the manufacture and export of active ingredients.

Once again, this situation has changed little in recent years. Multinational operation within Europe developed in the period 1950-1975 as a response to then prevelant non-tariff barriers. As these have been reduced, the drive to penetrate local markets through local production has abated somewhat, although other arguments favouring such activities have taken its place. Much recent expansion has involved the purchase of existing companies by foreign interests (9).

TABLE 2.7 SUPPLIES OF FINISHED DRUGS THROUGH RETAIL PHARMACIES BY LOCAL AFFILIATES OF FOREIGN COMPANIES IN EUROPE

ECUm (1)

Origin of company--> / Host country	France	FRG	UK	USA	Switzerland	Other	Total
Belgium			30	210			240
France		350	170	1000	320	40	1880
Germany	110	-	170	920	400	30	1630
Greece		30	30	70	40		170
Italy	140	420	250	700	300	70	1880
Nether-lands				110			110
Portugal		15		80	30		125
Spain	70	210	110	240	210	70	910
UK	30	110	-	850	140		1130
Total	350	1135	760	4180	1440	210	8075

(1) At manufacturers' prices

Sources: Author's estimates

Other aspects of multinational operation are discussed in later parts of this report. It is clear that a large minority of the drugs consumed within the Community are made outside the country of origin of the companies selling them. US and Swiss firms are overwhelmingly dependent on local production of this kind, while British and German firms also have substantial foreign facilities. French and, still more Italian firms are more centralised.

2.3 The structure of the European pharmaceutical industry

In 1984 pharmaceutical production within the European Community amounted to ECU39,300 (table 2.8). The largest national producer was the FRG, followed by France, the UK, Italy and Spain in that order (10).

Size by itself, however, means little. A nation's drug industry may very largely consist of foreign-owned firms; equally it may be limited to turning active ingredients into dosage forms. At the present time, competition between companies is primarily through the introduction of new and better products. The capacity for product innovation is therefore critical, and this capacity is very largely embodied in a limited number of large firms with the necessary resources, which now require minimum annual sales of ECU150m. It is companies of this kind which dominate the world production of and the world trade in pharmaceuticals (11).

In 1985/6 there were approximately 100 such firms in the world, of which 60 were operating in the European Community. They are identified in table 2.9. They include all but a handful of the companies with a serious research capability; conversely, all of them but a handful are research-oriented firms. Of this total, 20 were American in origin, 10 German, eight British, five French, four Swiss, four Italian, three Swedish, and two each Belgian, Danish and Dutch. No Greek, Portugese or Spanish company had sales of as much as ECU75m. The predominance of the USA was even more marked in the select group of firms with annual sales of more than ECU750m.

These companies have a strong international orientation. Their products are developed for world-wide markets; the costs of innovation

TABLE 2.8 PHARMACEUTICAL OUTPUT IN EUROPEAN MEMBER COUNTRIES, 1984

COUNTRY	PHARMA COMPANIES NUMBER (1)	PHARMACEUTICAL PRODUCTION				R&D EXPENDITURE		EMPLOYMENT (000)
		TOTAL ECUm	VALUE ADDED % (2)	TRADING PROFIT AS % SALES (3)	AS % CHEMICAL SALES (2)	TOTAL $m	AS % PHARMA SALES	
Belgium	80	1290	49	17	9.4	125	10	10
Denmark	39	870	44	19	36.4	65	7	8
France	331	8530	30	5	19.6	1090	13	66
FRG	308	10140	46	11	12.4	1430	14	87
Greece	90	405	20				<1	3
Ireland	153	1040	69		52.4	15	5	4
Italy	365	6300	41	10	21.0	380	6	64
Nether-lands	47	1050				110	11	10
Portugal	96	410					<1	3
Spain	370	2570	42	12	19.3	40	2	32
UK	333	6700	52	29	16.8	910	14	66
Total	2212	39300	43	13	16.8	4165	11	353

(1) Manufacturers only

(2) 1983

(3) Author's estimates based on 1983 Eurostat data.

Source: IMS, Eurostat, National sources

TABLE 2.9 PHARMACEUTICAL COMPANIES SELLING MORE THAN ECU150M IN 1985/6 AND ACTIVE IN THE EEC MARKET

Company	Nationality	Pharma sales ECUm (1)	Main therapeutic areas	Other interests
SOLVAY	Belgian	428	Antispasmodics, vaccines	Chemicals
UCB	Belgian	152	CNS	Chemicals
BENZON	Danish	207		
NOVO	Danish	322	Antidiabetic	
RHONE-POULENC	French	1178	Cardiovascular, antibiotic	Chemicals
ROUSSEL	French	887	Cardiovascular, CNS, NSAI	(1)
SANOFI	French	707	Varied	
SERVIER	French	282	Cardiovascular, CNS, other	
SYNTHELABO	French	300	Cardiovascular, digestive	
ALTANA	German	413	Antiasthmatic, other	
BASF	German	459	Cardiovascular, other	Chemicals
BAYER	German	3193	Cardiovascular, CNS, other	Chemicals
BOEHRINGER-INGELHEIM	German	1843	Antiasthmatic, cardiovascular CNS	
BOEHRINGER-MANNHEIM	German	n/a	Antidiabetic, cardiovascular	Diagnostics
DEGUSSA	German			
E MERCK	German	600	Varied	
NATTERMAN	German	183	OTC, generic	
SCHERING	German	1018	Sex hormones, digestive	Agrochemicals
SCHWARZ	German	150	Cardiovascular	
ERBAMONT	Italian	606	Antibiotics, anti-cancer	Chemicals, fibres
MENARINI	Italian	362	Anti-ulcer, other	
SERONO	Italian	175	Immunological, hormones	
SIGMA TAU	Italian	170	Cardiovascular, other	
AKZO	Netherlands	907	Sex hormones, CNS, other	Chemicals, fibres
GISTBROCADES	Netherlands	207	Antibiotics, cardiovascular	Chemicals

TABLE 2.9 Continued

BEECHAM	British	1290	Antibiotics, cardiovascular	Consumer products
BOOTS	British	360	Anti-rheumatic	Consumer products
FISONS	British	403	Anti-allergy	Scientific equipment
GLAXO	British	2408	Anti-ulcer, anti-asthmatic, dermatological, other	
ICI	British	1707	Cardiovascular, anti-cancer	Chemicals
RECKITT & COLEMAN	British	218	Analgesic, OTC	Consumer products
SMITH & NEPHEW	British	342	OTC	
WELLCOME	British	1316	Anti-gout, anti-infective, other	
CIBA-GEIGY	Swiss	3208	Anti-reumatic, cardiovascular other	Chemicals
HOFFMANN-LAROCHE	Swiss	2179	CNS, vitamins	Fine chemicals
SANDOZ	Swiss	2242	Cardiovascular, analgestic, other	Chemicals
NESTLE	Swiss	480	Opthalmological, special foods	Food
ASTRA	Swedish	727	Cardiovascular, anti-asthmatic	
PHARMACIA	Swedish	383	Digestive	
KABIVITRIUM	Swedish	201	Urological	
ABBOTT	US	2628	Antibiotics, cardiovascular	Hospital supplies
AMERICAN CYANAMID	US	1646	Antibiotics, antirheumatics	Chemicals
AMERICAN HOME PRODUCTS	US	3570	CNS, hormones, OTC	Consumer products
BRISTOL-MEYERS	US	2469	Antibiotics, anti-cancer, other	Toiletries
DOW	US	1068	Various	Chemicals
JOHNSON & JOHNSON	US	1606	Antifungal, CNS, digestive	Consumer products Hospital supplies
ELI LILLY	US	2515	Antibiotics, other	Agrochemicals
MERCK & CO	US	3977	Cardiovascular, antirheumatics, opthalmological	

TABLE 2.9 Continued

MONSANTO	US	369	Cardiovascular	Chemicals
PFIZER	US	3762	Antibiotics, antirheumatics, cardiovascular	Agrochemicals
PROCTER & GAMBLE	US	413	Cardiovascular, urological	Consumer products
ROBINS	US	521	Anti-rheumatics, OTC	
RORER	US	476	Digestive, OTC	
SCHERING-PLOUGH	US	1580	Dermatological, hormones	Consumer products
SMITHKLINE BECKMANN	US	2330	Anti-ulcer, cardiovascular	Scientific equipment
SQUIBB	US	1686	Cardiovascular, antibiotics, Anti-rheumatics	Consumer products
STERLING	US	814	Analgesics, OTC	Consumer products
SYNTEX	US	1131	Anti-rheumatics, hormones	
UPJOHN	US	2243	Antibiotics, anti-cancer, CNS	Agrochemicals
WARNER-LAMBERT	US	2637	Cardiovascular, dermatological, OTC	Toiletries, foods

(1) World wide sales

are too high to permit any other strategy. They are usually organised on multinational lines. The extent to which operations are decentralised depends on the function in question. Marketing is always organised on a nation-by-nation basis. The formulation of active ingredients into bulk drugs and their conversation into dosage forms may be carried out in many countries, but the manufacture of the active ingredients themselves is usually confined to limited number of sites. Clinical and other development work is often dispersed, but basic and commercially sensitive research tends to be centralised (12).

As would be expected from section 2.2 above, the multinational form of organisation is especially favoured by the largest companies and by those of American and Swiss origin. British and German firms also decentralise their operations but the French and Italians do so to a much more limited extent. Britain is a particularly popular site for fundamental research and Ireland for the manufacture of active materials. Downstream manufacturing is widely dispersed, especially among the member nations of Southern Europe (13).

These major research-oriented companies form, as it were, the first division within the industry. Below them are a much larger number of independent firms of more limited capacity. Some are on the fringes of the research-oriented group, although their continued ability to stay there must be increasingly in question. Others specialise in particular areas, such as diagnostic aids. Yet others concentrate on generics and OTC products, or exploit local markets with well-established remedies. Their focus is national rather than international, and their strategies opportunistic rather than dynamic (14).

Companies of this type with annual sales of ECU5-75m, are important in most European countries. Among the larger Community nations they retain 20-30 per cent of the retail market in France, Germany, Italy and Spain. Only in the UK have they largely disappeared. Their continued importance is an important element in the fragmentation of the European pharmaceutical market. International firms have international attitudes to medicine; national ones have national attitudes (15).

2.4 National strengths and weaknesses

There is no one yardstick of national competitive strength in pharmaceuticals. The number of new active materials developed in a country is a measure of innovative activity but not all new compounds are successful. Trade balances lose some of their meaning in an industry which is organised on multinational lines. World sales are a better measure, but may reflect the successes of the recent past rather than the present. In any case, some markets are more attractive than others from a commercial standpoint.

In practice, however, most indicators point in the same direction. A number are listed in table 2.10. Most of them are self-explanatory, but several call for explanation. Estimates of sales in the various national and regional markets and in total are based on a mixture of market and company data which are not entirely comparable. Innovative strength is particularly difficult to measure, and several different scales are therefore presented (16).

The USA industry is clearly hors concours. With more than one-third of world sales outside the command economies it is everywhere strong, continuing to dominate its own exceptionally competitive domestic market. It remains the major source of new products and, in particular, of those which attain world-wide sales. The Swiss industry, although much smaller, is also in the first rank. As has already been seen, both hold substantial proportions of the Community market, and have extensive manufacturing and research facilities there.

The position of the European member countries is more complex. The research-oriented German companies are clearly competitive at the world level; the German industry also contains, however, a considerable number of smaller firms whose viability is less certain. The UK-owned pharmaceutical companies hold only a minor part of their home market, but they are both large and have excellent records of research and a markedly international outlook. The appreciable share of sales in the USA and the rest of the EEC held by UK firms is highly significant.

TABLE 2.10 MEASURES OF COMPETITIVE STRENGTH AMONG NATIONS

Country	Measures of innovative capacity			Share of 1984 markets (%)				Overall ranking
	% of new chemical entities introduced (1)		No of top 100 products in 1980 (2)	EEC (3)	USA	Japan	World	
	1971-80	1981-5		<-------(4)------>				
Belgium	2.1	5.0	2	4	<1	<1	2	Medium
France	15.0	6.5	3	17	<1	<1	7	See text
FRG	13.5	14.0	14	22	4	4	11	High
Italy	10.8	5.5	2	8	<1	<1	3	Medium
UK	4.4	8.0	14	10	5	2	6	High
Other EEC	0.5	0.5	1	5	<1	<1	2	Generally low
Switzerland	6.7	6.0	12	10	8	3	9	High
USA	22.9	13.0	35	23	80	10	35	High
Japan	11.7	26.0	8	<1	<1	80	19	Medium
Other	12.4	14.5	9	1	<1	<1	6	Generally low

(1) 1971-80, Reis-Arndt: Die Pharmazeutische Industrie, 1982, 44, 415, 1981-5: Scrip, various issues

(2) EFPIA, 1984

(3) Table 2.5 above

(4) Author's estimates based on IMS data

France is less well placed. The French industry is still heavily dependent on sales within France and to the Franc zone. French companies have made little impact in the USA or Japan, and only a relatively modest one in the European Community. The sector still contains a large number of small firms with limited resources. The situation in Italy is broadly similar. The Italian industry is excessively fragmented and bears the marks of the long period during which patent protection for pharmaceuticals was not permitted.

The industries of Belgium, Denmark and the Netherlands show elements of competitive strength. They are strongly export-oriented, but suffer from their moderate size. With one exception, their major companies lack a fully developed international structure. Ireland is in a curious position: supplied almost entirely by imports, it is a centre for the manufacture of active ingredients by foreign, especially American firms, for reasons which are discussed in section 2.5 below. A notable Irish-owned research-only firm has recently emerged (17).

The indigenous pharmaceutical industries of Greece, Portugal and Spain are weak. Their main activity is the conversion of active ingredients into dosage forms; they are still heavily dependent on imports of the former. Research is limited. The local companies are small by international standards and concentrate on the local markets, which are dominated by foreign multinationals.

2.5 The role of governments

The pharmaceutical industry is subject to a very considerable degree of government regulation. The ways in which certain of these regulations work, and their role in dividing the European market is the subject of later chapters in this report; at this point our aim is to identify the activities controlled and to examine the explicit and latent objectives of official direction.

The main areas of regulation are shown in table 2.11. A major objective is to make sure that pharmaceutical are effective and safe to use (cf chapter 3 below). The admission of new products to national markets is strictly controlled. Proof of safety, efficacy and quality is universally required. This process of registration applies not only

TABLE 2.11 GOVERNMENT REGULATION AND OTHER SPECIFICATION INVOLVING THE COMMUNITY PHARMACEUTICAL INDUSTRY

Country	Admission of new products controlled	Price of individual drugs controlled	Other measures to limit pharma expenditure	Subsidies and tax concessions	Tariff and non-tariff barriers to trade	National pharma company	Qualification of patent protection
Belgium		Yes					
Denmark		Yes				No	No
France		Yes		No			
FRG		No					
Greece	Yes	Yes	Yes	Limited	No	Yes	Yes
Ireland		No		Yes			
Italy		Yes		Limited		No	
Netherlands		No					
Portugal		Yes		No	Being phased out		No
Spain		Yes			Being phased out		
UK		No			No		

Source: EAG

to genuinely novel products but also to those based on existing ingredients, although the requirements are generally less stringent for the latter. The packages, labels and patient information leaflets to be used must be approved. Post marketing surveillance is now standard in all member countries. Manufacturing requires a licence and the periodic inspection of production facilities is normal. The methods used to market drugs are also regulated to a greater or lesser extent.

A second important aim is to limit pharmaceutical expenditure. In all member nations the state is heavily committed to the provision of health care, whether directly or through national insurance agencies. Expenditure for this purpose has greatly increased during the past 25 years and economy measures have become necessary. Controls over pharmaceutical expenditure are therefore normal (cf chapter 4 below). Most member countries prefer to fix the prices of individual drugs, usually on a cost-plus. The UK limits the profitability of companies. The FRG, unusually, has no formal price controls but strongly encourages generic competition. Positive lists, which confine reimbursement to approved products, and negative lists, which exclude certain drugs or categories of drugs, are common. As a result of these measures, there are large variations in pharmaceutical prices between one European country and another, even when they have many economic and demographic characteristics in common (cf. table 2.1)(18).

A third objective is to encourage the development of the local pharmaceutical industry for strategic reasons, as a source of income and employment, or in order to economise on foreign exchange. Measures to this end may be positive or negative. In the former category are subsidies and tax concessions. They have been used successfully in Ireland to build up a substantial capacity for the production of active ingredients, almost all of which is owned by foreign companies. Elsewhere they have been little employed. Negative measures include tariffs and restrictions on imports. Important in the past, they have largely disappeared except in Spain and Portugal, which are phasing them out. The abrogation of patent rights in the interests of local producers is likewise of significance only in these countries, which, once again, are in a transitional stage following their adherence to the Treaty of Rome (19).

In practice most regulation is carried out at the national level. Progress towards a fully unified European system has been considerable but is not yet complete. Obvious barriers to trade, such as tariffs, quotas and specific restrictions on pharmaceutical imports have been eliminated. A European Patent Convention has been in operation since 1978. The registration of new products, however, remains a national responsibility, as do price controls. To a substantial extent, the criteria of safety, quality and efficiency employed within the Community have been harmonised, as have certain of the procedures for marketing authorisation and for manufacture. An agreed method for multistate applications has existed since 1977 and was revised in 1985. In practice, however, there are still substantial differences in the decisions made by the various national authorities. Little progress has been made in the harmonisation of pricing systems (20).

A further point may be made. Regulations can be used for more than one purpose. The registration of new products may be delayed in order to control pharmaceutical expenditure. Negotiations about price may be the occasion to press a foreign company to expand its local activities. National controls may be used to discriminate in favour of the national industry. There is much anecdotal evidence, some of which was collected in the course of the enquiry, to suggest that such practices are common (chapter 4.4 below).

2.6 The place of the pharmaceutical industry in national politics

Government regulation of the pharmaceutical industry means that official policies are a permanent if minor part of the political agenda. Every administration faces the same dilemma.

As we have seen, health care expenditure has grown rapidly in the recent past. There is now a general, if unspoken consensus that it should not increase at more than the growth of national income. At the same time, high-technology medicine and aging populations put intense pressures on existing budgets. Economies are unavoidable and spending on drugs is an obvious target. Labour may be 70 per cent of health care costs but medical and paramedical personnel are well organised and enjoy high standing. On the whole, pharmaceutical

companies do not. Drug prices should therefore be kept low, limited lists imposed and generics encouraged. Patent protection should be reduced on the Canadian model.

The research-based pharmaceutical sector, however, is a model of the commercially successful high-technology industry. For some countries it is a significant part of the national economy. It should therefore be supported. Prices should be kept sufficiently high to maintain or increase current levels of R&D spending. Patent protection should be improved. There is therefore a clash between the interests of consumers and producers. The outcome must depend on official perceptions of the strength or weakness of the local industry. Four questions may be posed:

- do we have an innovative local industry ?
- is it an important national asset ?
- does it need official support ?
- is our local market vital to it ?

If the answer to the first question is 'no', then absolute priority may be given to the interests of consumers. If the answers to the second, third or forth questions are 'no', then the interests of consumers may be weighted more heavily than would otherwise be the case.

The answers implied by the behaviour of European governments are indicated in table 2.12. Belgium, Greece, the Netherlands, Portugal and Spain may be expected to favour consumers unambiguously. They either do not have a research-based industry, or where they do, attach only secondary importance to it. The FRG values its major companies but is strongly committed to a hands-off attitude to all types of industry. Denmark and the UK have a supportive attitude towards their own firms, which, however, make most of their sales abroad. The governments of France and Spain might experience a severe conflict of aims.

TABLE 2.12 GOVERNMENT ATTITUDES TO THEIR INDIGENOUS RESEARCH-BASED PHARMACEUTICAL INDUSTRY WITHIN THE EUROPEAN COMMUNITY

Country	Do we have an indigenous research-based industry?	Is it an important national asset?	Does it need official support?	Is our national market vital to it?	Outcome
Belgium	Yes	Perhaps	No	No	Consumers prevail
Denmark	Yes	Yes	Yes	No	Balance of interests sought
France	Yes	Yes	Yes	Yes	Conflict of interest
FRG	Yes	Yes	No	Yes	Market prevails
Italy	Yes	Yes	Yes	Yes	Conflict of interests
Netherlands	Yes	No	No	No	Consumers prevail
Spain	No	◄——	some official concern	——►	Consumers prevail
UK	Yes	Yes	Yes	No	Balance of interests sought

Source: EAG

Once again, this is a conclusion of considerable importance. The interests of the various nations of the Community are not identical. Any course of action to unify the market will therefore produce gains and losses which will be different for each country and will be received accordingly.

2.7 Conclusions

Both the European pharmaceutical market and the European pharmaceutical industry are extensively fragmented. There are widely differing traditions of medical practice and corresponding variations in diagnosis and prescription. Levels of consumption differ markedly between one country and another. The industry is also fragmented. A high proportion of the products consumed are made by the local affiliates of foreign companies. In addition to the large research-based international firms there are may locally-oriented small and medium-sized companies in most countries. US and Swiss firms are prominent in the European industry.

Despite progress towards the harmonisation of government regulations, there remain considerable differences in the operation of registration procedures and, especially, in pricing systems. National capabilities for pharmaceuticals vary greatly. National objectives for the industry differ.

NOTES

1 Throughout this report the European Community is taken to include Portugal and Spain, even when, as here, the time to which reference is made is before 1986.

2 See also Burstall and Senior: The Community's Pharmaceutical Industry, 1985, Brussels: Commission of the European Community, table 4.1, p.30.

3 For the nine member countries in 1983, the relationship between per capita income, relative drug prices, using the EEC estimates, and per capita pharmaceutical consumption was Consumption = 0.3 (income(exp 0.83)(price(exp - 0.48)) with r = 0.69.

4 See Able-Smith and Grandjeat, Pharmaceutical Consumption in the Community,1978, EEC, p26. The number of diagnoses per capita is usually low in the UK by the standards of the other major European countries (O'Brien: Patterns of European Diagnosis and Prescription, 1984, London: Office of Health Economics, table 4, p. 25).

5 O'Brien, op, cit, tables 5-9, 14-18. IMS data concerning the national sales of particular products strongly supports this conclusion. The FRG is unusual inter alia in its high consumption of antidiabetic drugs and its preference for sulphonamides over antibiotics.

6 Based on IMS retail pharmacy audits, except for Denmark, for which national sources have been used. The coverage is only 93 per cent complete since company sales below a minimum level are not reported. The use of sales through pharmacies discriminates against Italy in that a high proportion of the sales of Erbamont, its largest firm, are cytostatic drugs used mainly in hospitals.

7 For the situation in 1982 see Burstall and Senior, op. cit., table 9.1, p. 108.

8 The figure of ECU8,075 was derived by reducing the 1984 import figures for each country in proportion to the ratio of sales through retail pharmacies (table 2.6) to total sales (table 2.1). If the import figures are taken at face value, the estimate is reduced to ECU7,000m. There are, unfortunately, no figures for sales to hospitals comparable to those for retail sales, and there is reason to suppose that the patterns of consumption are markedly different.

9 Thus, for example, Zambeletti (Italy) was taken over by Beecham (UK), Abello (Spain) by Merck and Co. (USA) and Almirall (Spain) by Erbamont (Italy).

10 These figures comprise all pharmaceutical production within national borders. The manufacture of active ingredients is usually included; since some of these will later be used to make finished medicines, there is an obvious element of double counting.

11 For a discussion of this point, see Burstall and Senior, op. cit, pp. 105-6. Firms with annual sales of more than ECU750m accounted for 58 per cent of world sales excluding the command economies; those with sales of more than ECU150m for 80 per cent.

12 Burstall, Dunning and Lake: Governments, Technology and Multinational Enterprises - The Pharmaceutical Industry, 1981, Paris: Organisation for Economic Cooperation and Development, chapter 3, pp.

13 Estimates of R&D spending within the European Community in 1982 by firms of various nationality are presented by Burstall and Dunning: International Investment in Innovation, in Pharmaceuticals among the Sunrise Industries, edited by N. Wells, 1985, London: Croom Helm, pp.185-198. At that time total spending was about ECU3,350m, of which ECU2,450m was spent by companies in their country of origin. The main recipients of foreign money were the UK, with ECU270m and France, with ECU240m. The main donor was the USA with ECU270m, of which ECU170m was spent in the UK.

14 This generalisation does not, of course, apply to the research-only companies which are developing rapidly, but rather to those firms which are engaged in manufacturing and marketing their own products.

15 Independent companies with annual sales of less than ECU75m have 19 per cent of the French retail market, 23 per cent of the German, 28 per cent of the Italian and 35 per cent of the Spanish (authors' estimates based on IMS data). In the UK firms of this size are usually the local affiliates of foreign multinationals, although a few are generic or other specialists.

16 For more extended discussions of the problems of assessing competitive strength, see Burstall and Senior, op. cit., pp. 105-127, and Burstall, Dunning and Lake, op. cit., pp.

17 Two American multinationals have major research centres in Belgium and a third has one in Italy.

18 Thus, for example, between France and the FRG.

19 In both Portugal and Spain, only process patents were available before 1986 and enforcement was difficult. Both countries have been given a transitional period lasting until 1992 to bring their patent and other institutions into line with those prevailing in the Community.

20 The transparency directive is discussed in chapter 4.6 below.

3 REGISTRATION AND ITS PROBLEMS

If a pharmaceutical product is to be admitted to a particular national market it must first be approved by the national registration authority (cf chapter 2.5 above). In principle that body is autonomous: it is free to make its own decision and is not obliged to consider what has happened elsewhere. Registration is therefore a potential barrier to the unification of the Community pharmaceutical market. The object of this chapter is to describe the process of registration, to estimate the extra costs due to registration being on a national rather than a pan-European basis, and to review the advantages and disadvantages of alternative arrangements.

3.1 The process of registration

The purpose of registration is to make sure that a drug is safe, effective and of adequate quality before it is put on sale. The onus is on the applicant to satisfy the authority; the role of the latter is to evaluate the evidence produced by the former and come to a decision. It is not to carry out experimental work itself. It is judge, not advocate. Alternatives to this system have been suggested but nowhere have they been put into effect.

Registration authorities have always provided guidance about the evidence that they need. During the past 20 years these requirements have gradually converged as a result of directives by the European Commission and a high degree of uniformity within the Community is now apparent. Common standards concerning pharmacological and toxicological tests in animals and the conduct of clinical trials have been adopted, as have common forms of documentation. All Community countries accept evidence obtained abroad. All now provide abbreviated forms of registration for products based on known ingredients. The formal differences between the requirements of one Community nation and another are now small. Equally, the stated grounds on which a product may be rejected, other than safety, efficacy and quality, show only minor variations. A uniform 120-day

decision period - plus 90 days if the medicine is referred to an advisory committee - has been agreed. The current position is summarised in table 3.1 (1).

In practice registration procedures are less harmonised than this account might suggest. Interviews undertaken in the course of this enquiry show that there are substantial differences between one country and another. To some extent this reflects different administrative arrangements. The UK carries out all its evaluations in-house, as does the US Food and Drug Administration (FDA), whereas Belgium, Denmark, France and Italy rely very largely on outside experts directed by small official organisations. Germany and the Netherlands use mixed systems. To rely entirely on in-house expertise is clearly to favour a more formal and standardised approach. The major problem, however, is the element of judgment that is involved in making the decision to approve or to reject an application. This cannot but involve the local traditions of medical practice already discussed in chapter 2.1 and the local perceptions of what sorts of evidence carries the most weight.

Thus, in one country the emphasis may be on the pharmacology of a new substance, whereas in another the main stress is on the controlled large-scale clinical trial. Significantly, the FDA looks with particular favour on British and Scandinavian data. This reflects both the general perception that these countries have rigorous standards, and also the fact that they share a medical culture common with that of the USA. Similarly, local clinical trials, although not required in theory, are often advisable in practice. Carried out by well-known local experts, they are the more acceptable to the registration agency for that reason. Differences of opinion between one European authority and another rarely occur over major discoveries, about which a high degree of consensus usually exists. They are more common in the case of products which represent a modest improvement or are intended for the treatment of minor illnesses, where, inevitably, differences of opinion play a greater part (2).

Delays in processing applications are common. At the present time no country can meet the official 120-day limit, although France has approached it on occasion. Some estimates from various points in the

TABLE 3.1 REGISTRATION PROCEDURES FOR PHARMACEUTICAL PRODUCTS IN MEMBER COUNTRIES OF THE EUROPEAN COMMUNITY 1985-86

Country	Evaluation system	Special local requirements	Grounds for rejection (1)	Abbreviated procedure for copy products
Belgium	Outside experts	Analytical data	None	
Denmark	do	Extra clinical data may be required	Poor safety/efficacy balance	
France	do	Local clinical trials advisable	Combinations must be justified	
FRG	Mainly in-house		None	
Greece	Outside experts	None	None	Yes
Ireland	In-house		None	
Italy	Outside experts	Mutagenicity tests; clinical trial certificates required. Local clinical trials advisable	Poor safety/efficacy balance	
Netherlands	Mainly in-house	None	do	
Portugal	Outside experts	Currently in transition	Price, no therapeutic advantage	
Spain	do	do		
UK	In-house	None	Comparative safety	

Source: IMS, national sources, interviews

recent past are shown in table 3.2. At the present moment, the European average appears to be 18-24 months, with France and Belgium rather quicker and Italy, Spain and Portugal substantially slower. The FDA takes 30-36 months to deal with a New Drug Application. Delays have tended to increase in recent years. One major reason is under-staffing, coupled with a rise in the work-load in certain countries due to the growth of applications for generic products.

Registration procedures do not appear to be used in a discriminatory manner. In reporting variations in the ways in which particular countries dealt with particular products, the companies interviewed explained them in terms of the differing national attitudes to medicine mentioned previously. They did not consider that local firms were at an advantage except in so far as they might be especially attuned to the preferences of the local market.

3.2 The response of companies

Given that there exist both the need to apply for marketing authorisation in a number of countries and substantial variations in the approaches of registration authorities, how do the large research-oriented multinational companies cope?

The development of a new chemical entity (NCE) is a prolonged and expensive process. Much of the time and money is occupied in establishing that the product is both safe and efficacious. After preclinical studies in rodents and in larger mammals come tests in healthy human volunteers. If the compound maintains its promise it is then used in steadily larger numbers of patients suffering from the condition which it is intended to remedy. These are referred to as phase 1, 2 and 3 clinical trials. Meanwhile, work on animals continues in order to detect possible carcinogenic and other long-term effects. The dossier presented to a registration authority will typically contain results from up to 3-4,000 patients together with exhaustive pharmacological and toxicological data. Even after a product is marketed studies will normally continue in order to develop new uses for it and additional line extensions.

TABLE 3.2 ESTIMATES OF THE TIME TAKEN TO OBTAIN MARKETING AUTHORISATION WITHIN THE COMMUNITY

months

Country	Source and dates of estimates		
	IMS 1984/5	FDA 1985	Present study 1987
Belgium	12	19	12
Denmark	12	12-18	
France	4	12	6-12
FRG	6-10	12-15	18-24
Greece	12-24	18	"lengthy"
Ireland	<12	12-18	
Italy	24-36	16	24-36
Netherlands	9-24	18-24	
Portugal	6-24	24-30	
Spain	12-48	24-30	36-
UK	10-12	12-18	18-24
Average (1)	15,3	14,4	18-24

(1) Weighted for sales

Source: Information obtained from IMS, the FDA and major multinational companies interviewed during this study

Much animal testing is sub-contracted to outside specialists as is all clinical testing. In the latter case the company selects an established clinical investigator working in the appropriate area with whom to cooperate. A protocol for the study is developed jointly, after which the investigator carries it out with the company providing the resources. Since so many patients must be studied, the dossier will contain the results from a number of such trials, which may well have been conducted in several countries. Within broad limits, therefore, the company has a considerable element of discretion as to where and with whom it carries out its clinical work. The UK and Scandinavia are favoured on technical grounds but other factors, discussed below, enter into the equation (3).

Research-oriented companies work to high standards. Many of them explicitly follow FDA procedures. The USA is the largest single national market, and a potential world-class product must be able to sell there. Moreover, given the severity of American regulations, a drug that can satisfy the FDA has an excellent chance of satisfying other regulatory authorities. A dossier prepared with the FDA in mind is therefore often used as the basis for all applications. If it is thought necessary or desirable to include local clinical testing, then this is done as part of the total programme on which the dossier is based. As far as possible other special requirements are dealt with in the same day. This central document is then translated, rearranged and modified to suit the needs of each regulatory authority. In this way the work associated with multiple applications is minimised.

Meeting local requirements could be more of a burden for a small firm, but small firms rarely develop new chemical entities. They are more interested in new products based on known ingredients, for which, however, abbreviated applications are normally sufficient. The latter are much more sterotyped in nature and vary little from one country to another. Clinical studies are not required and evidence of purity and adequate bioavailability is enough.

3.3 The costs of multiple registration

The direct costs of multiple registration are limited.

A study of the costs of the UK regulatory system carried out in 1980 estimated that pharmaceutical firms operating in the UK, British and foreign, employed an extra 350 people in meeting the requirements of overseas regulation. Extending these figures to the rest of the Community would suggest a total of about 2000 extra staff. However, this figure is probably high, as it included those dealing with countries outside Europe and, of course, somewhat predates the systematic approach to registration described in the previous section. Interviews conducted in the course of this study revealed that a large research-oriented company typically employs 3-5 people in each major European country to deal with local registration and related problems. For the 50 such companies operating in the Community this gives a total of 750-1250 people, and, assuming an average annual salary of ECU40,000m an extra expenditure of ECU30-50m per year.

To this figure should be added the cost of those extra operations, such as translation, which are carried out centrally and that of total requirements such as clinical trials. Both of these appear to be quite small. A figure of ECU10-15m seems reasonable for the former item. As regards the latter, it has already been seen that local testing usually forms part of the overall clinical programme, and so the extra costs are negligible. It might also be noted that such testing is designed in part to familiarise local opinion leaders with the product and its advantages. To this extent it has a positive function and should be seen as a form of marketing. Taking these findings into consideration, and allowing for the fact that many of the staff identified have more than one duty, the extra costs of multiple registration are most probably about ECU40-55m per year (4).

The potential cost of delays in approval is higher. During the 1970s expenditure per NCE introduced, inclusive of failures but exclusive of interest foregone, was around ECU85-100m, spread over 8-10 years. Patent protection is normally obtained at the beginning of - or even before - the main testing programme, which now lasts between eight and ten years. The effective life of the patent, which only starts when the product reaches the market, is correspondingly reduced, and is now no more than 8-12 years, depending on country in question. Thus, to delay approval is to impose a double burden on the discoverer. The money already committed to the development of the new product is tied

up for a further period, while the sales within the period of patent protection are lost (5).

The development of a new pharmaceutical product immobilises funds which might otherwise be invested in interest-producing ventures. The sums involved are large because lead times are long. FDA estimates based on data from the 1970s show that the direct cost of developing a single NCE up to the point of marketing, inclusive of the failures, was approximately ECU96m in 1987 dollars. When the opportunity costs were charged, this sum becomes between ECU130 and 250m, depending on the discount rate used. The cost of a year's delay in approval may then be readily calculated, since it is the income that might have been earned by investing the money used in the development for a further year. It lies in the range ECU6.5-37.7m. These figures, however refer to the world as a whole; since the EEC market is 24 per cent of the market economy total, the pro-rata sums are between ECU1.6 and 9.0m, per NCE per year (6).

In 1986 24 NCEs were launched by European or North American companies in Europe or elsewhere. It may be assumed that they will all eventually be marketed within the Community. Taking the FDA estimate that the average time taken to approve an NCE in the Community was 15 months in 1985 (cf, table 3.2), then the opportunity cost due to the failure to observe the 120 day limit was between ECU34 and 199m, the most probable range being ECU58-83m, which correspond to discount rates of eight and ten per cent respectively. The opportunity costs due to the fact that the market is not unified and approval times differ must obviously be less. Assuming that the minimum time required for approval is one year, then taking each country in turn and weighting its contribution by its total sales a figure of between ECU20 and 28m, is obtained (7).

These sums are trivial. Much more important is the loss of revenue during the period of patent protection due to delays in approval. As yet, there is no patent restoration within the Community, and effective patent lives, weighted by sales, average nine years. The average sales per NCE per year in the Community market may be estimated in several approximate ways:

1 If the average cost of developing an NCE is ECU96m, and R & D is between 10 and 15 per cent of sales for a research-oriented company (cf table 2), then during its lifetime it should realise between ECU630 and 960m. Assuming that this lifetime ends with patent protection, then the average revenue per year is between ECU70 and 105m, and the proportion to be assigned to the European Community pro rata between ECU17 and 25m.

2 Estimates of sales by age structure in six Community countries in 1982 showed that the 208 NCEs introduced in Europe and North America between 1976 and 1980 had by then attained average Community sales of between ECU18 and 24m (8).

3 An extrapolation of FDA data suggests that the 135 NCEs introduced into the US market between 1980 and 1985 accounted for between 134 and 175m US prescriptions in the latter year. Estimates of the cost per prescription on various assumptions yield total sales of between ECU4590 and 5210m, or sales per NCE of between ECU34 and 38m. Since the US market is approximately 30 per cent larger than that of the Community, the corresponding figure for the latter would be between ECU25 and 30m (9).

These figures are surprisingly comparable, especially when it is remembered that US prices are on the whole higher than the European average.

It is now possible to determine, at least approximately, the loss of sales due to delays in registration. Failure to observe the 120 day limit means that there was a delay of approximately eleven months and a loss of sales to the innovators of ECU370-650m, in 1985. The costs due to the market not being unified may be estimated in the same way as between ECU100m and 175m. From a practical standpoint, however, these figures should be qualified in one important particular. There is no such thing as an average NCE, and the distribution of penalties is therefore very uneven. A major discovery might sell ECU150m or more per year within the Community, and the loss of sales could be correspondingly more serious for its inventor (10).

Who suffers from the loss of sales? The research-based companies clearly do. The average value added in the European pharmaceutical industry is approximately 40 per cent of revenue; for an NCE it is certainly higher. Where a new and clearly superior product is involved, the losses may be serious, as has already been noted. However, important as this is for the innovator, it must be offset for the industry as a whole by the continued sales of product which would otherwise be made obsolete. This effect is difficult to quantify. Given, though, that new products command higher prices and are more attractive to doctors (chapter 4.5), it appears certain that the overall income of the sector is appreciably reduced by delays in registration (11).

There is also a definite loss in consumer welfare, in that the patient is denied the new medicine. Here again, much turns on its therapeutic advantages: a "breakthrough" product is in a different category to a "me-too" one. It is however, often difficult to decide a priori which is which in particular cases; reduced side-effects or improved convenience of administration may not greatly affect the outcome but can make the process of recovery much more agreeable. Once again, therefore, the losses are real, although exceedingly difficult to estimate in monetary terms (12).

Thus, as far as registration is concerned, the costs of "Non-Europe" to the pharmaceutical industry are between ECU160m and 260m, about 25 per cent of which is represented by direct costs and the bulk of the remainder by loss of sales due to differential delays in approval. Given that only a part of the latter falls on the industry, these figures must be taken as an upper bound. Probably more serious are the penalties imposed by the general failure to observe the 120 day decision period, which cause losses of sales amounting to ECU360-650m. These sums are respectively 0.5-0.8 per cent and 1.1-1.9 per cent of total industry cost incurred within the Community (13).

3.4 Alternatives to present institutional arrangements

The possibility of replacing the present methods of national

registration by some more convenient system have been repeatedly discussed in recent years. Two main alternatives have emerged: mutual recognition of registrations by all member countries and a pan-European registration agency.

The companies interviewed saw considerable difficulties with both of these proposals. There are doubts about the equality of the countries involved. Some respondents felt that the approval of north European agencies carries more weight than that of south European ones, even though it was generally agreed that technical standards had been harmonised upwards to a very considerable extent during the past decade. The differences in medical culture and therefore in the subjective elements of assessment were thought to present serious problems. Several companies commented that mutual recognition would imply both the mutual acceptance and the mutual rejection of products, which would have negative as well as positive effects. They did not consider that their registration policies would be affected by a policy of mutual recognition, since they followed a world-wide strategy in any case.

There would also be problems with a single European registration agency. Technically possible, it was thought that it could offer real gains in principle to both producers and consumers. It would be impartial and it could be rapid. There was much anxiety, however, about the procedures that might be used. Several respondents commented that the most likely outcome was a combination of the most severe elements of each national agency. There would also be political difficulties. How could it be staffed and to whom would it be responsible? A rigid, elaborate and bureaucratic system would be unwelcome but was perhaps unavoidable. The precedent of the FDA was not felt to be encouraging. Doubts were also expressed as to whether such an organisation could entirely replace national agencies, which currently deal with many minor as well as major issues.

The costs of operating the present registration agencies are not large. They are difficult to compute with accuracy since much of the work is carried out by outside personnel (cf chapter 3.1 above). If, however, the manning levels of the Medicines Division of the UK Department of Health and Social Security, which carries out all its

evaluations in-house, are typical, then the equivalent of 1500 staff are employed. At an average annual salary of ECU40,000 this suggests a total budget of ECU60m to which the expenses of accommodation and other overheads should be added. The Drugs and Biologics Division of the FDA employs 1500 staff at its centre in Maryland, about one third of them qualified at the PhD level, at a total cost of ECU150m. They also have about 900 personnel in the field, which adds a further ECU60m. Allowing for the higher rates of pay in the USA, these figures are not very different. Both the FDA and the majority of European registration agencies are understaffed for their work-load. Possible economies resulting from either mutual recognition or a pan-European agency would seem to be limited.

From the standpoint of the large research-oriented company the key issue is the speed of registration. Any change which shortened the time required would be welcomed, any change which increased it would be opposed. The welfare of the consumer would also benefit from more rapid registration provided that this did not result in a reduction in standards of safety. As we have seen, the average time taken is more important than the differences between nations. The direct costs of multiple registration are not negligible but they are of relatively minor importance. Enforcement of the 120-day decision period might well represent a larger gain than the further integration of the national registration procedures.

3.5 The impact of EEC initiatives

The companies interviewed considered that the measures already taken to harmonise data requirements had been helpful and had had a considerable effect in raising as well as standardising national requirements.

The original multistate application procedure, which operated from 1978 until the end of 1985, was used for 41 applications. Few of them involved products or companies of the first importance. The procedure was known to all respondents, whose general attitude was cautious. In their opinion the resources committed to the development of an NCE were so large that a new registration procedure would have

to have very striking advantages over those already established before they would consider it seriously. The revised multistate procedure, however, aroused considerably more enthusiasm, as did that for high-technology and biotechnology products. By the middle of 1987 14 applications under the former had already been made.

NOTES

1 The relevant directives of the Commission are 65/65, 75/318, 83/570 and 87/19. To the 120-day limit, 90 days are to be added if the application is referred by the licensing authority to an advisory committee.

2 The comments in the last two paragraphs are drawn from interviews with large multinational companies and national registration authorities.

3 This account is based on discussions with the clinical testing manager of a major firm.

4 This estimate is confirmed by the qualitative comments of executives interviewed in the course of this study, who considered the direct costs of multiple registration to be minor.

5 J Thesing: Industrielle Arzneimittelforschung Heute, 1983, Mainz: Medizinisch Pharmazeutische Studiengesellschaft, pp 24-9, gives an estimate of 155m DM per NCE introduced by the seven research-oriented German firms between 1972 and 1981. The period currently required for testing in the USA is given as 10 years by the Pharmaceutical Manufacturers Association of the USA (Facts at a Glance, 1987, p 21); this was confirmed by the FDA. For the UK, see NEDO: Pharmaceuticals: Focus on research, 1987, London; HMSO, pp15-16, which suggests a time of eight years. Estimated of effective patent lives in 1983 are given by R Chew , G Teeling-Smith and N Wells: Pharmaceuticals in seven nations, 1985, London; Office of Health Economics, p 39. They suggest 13 years for France, 6,5 for the FRG, 8-10 for Italy and 8,7 for the UK.

6 Data supplied by the FDA, based on R W Hansen: The Pharmaceutical Development Process-Estimation of Current Development Costs and Times, 1977, Rochester; University Graduate School of Management, up-dated and expressed in 1987 US dollars.

7 Scrip, 1986, 1176/8, 8. NCEs developed by Japanese companies were excluded because of uncertainties about the extent to which they would be marketed outside Japan. During the period 1960-1985 Japanese NCEs were not widely introduced into the Community market.

8 The number of NCEs introduced between 1976 and 1980 was 208, excluding those introduced in the Command Economies, in Japan (see note 8 above) and in unspecified countries (Reis-Arndt, quoted in Pharma Data 83, 1984, Frankfurt/Main: Bundesverband der Pharmazeutische Industrie, p23. Sales of these products in 1982 were estimated from the age-distributions given in Indicatori Pharmaceutici 1984, 1984, Table 27, p50. The lower figure for annual sales per NCE is calculated on the basis of sales through retail pharmacies and the higher on the basis of total sales, since it is not clear which applies.

9 FDA: Drug Utilisation in the US-1985, Seventh Annual Review, 1986, Washington DC, gives numbers of NCEs introduced 1980-85 and cumulative and 1985 prescription figures for the first 52 of these. By the use of the Pareto distribution (H A Wittcoff and B G Reuben: The Pharmaceutical Industry-Chemistry and Concepts, 1987, Washington: American Chemical Society) it was possible to estimate the total number of prescriptions of these compounds graphically. The average price per prescription, weighted by sales, was calculated from the histogram of wholesale prices as given by the 1987 Red Book (Dradel, NJ: Medical Economics Press) and adjusted to manufacturers' prices.

10 In 1982 there were three products selling $100m or more, 16 selling between $50 and 100 m, and 36 selling between $25 and 50m, in the Community of the time. Not all of these were in patent (M L Burstall and I S Senior: The Community's Pharmaceutical Industry - Evolution of Concentration, Competition and Competitivity, 1985, Brussels: European Commission, Table 7.4, p83).

11 At the European average level, the loss in value added would be ECU147-259m; as noted in the text a higher figure is probable. Anecdotal evidence suggests that the introduction of a new product is not a zero-sum game; the total market often expands, as appears to be the case with H2-antagonist anti-ulcer drugs (comment of several industrial respondents).

12 A study of several therapeutic markets suggests strongly that advantages that are minor in medical terms may be critical in commercial terms. This point was made strongly by the FDA, who remarked that their own classification of drugs was entirely medical in its basis. The importance of convenience and low side-effects may be expected to increase as incomes rise, in line with Maslow's concept of the hierarchy of needs.

13 For the estimation of industry costs see appendix B.

4 PRICING SYSTEMS, PRICES AND PRICE COMPETITION

National controls over pharmaceutical expenditure also serve to divide the European pharmaceutical market. As has already been seen (chapter 2.5 above), all member nations take steps to limit the health care budget, of which drugs form a minor but significant part. Each has its own objectives for the pharmaceutical industry (chapter 2.6) and its own views about the best way to attain them. In consequence there are large differences between countries, both in average price levels and in the prices of individual products. These are increased by variations in the incidence of VAT and of the margins permitted to pharmaceutical wholesalers and retailers.

4.1 Price control systems

The methods employed to control pharmaceutical expenditure in the member nations of the Community are shown in table 4.1. They vary greatly, the only common features being an element of patient copayment and the exemption of OTC products from any form of price regulation.

At one extreme, the FRG does not control prices at all. Total pharmaceutical expenditure, however, is regulated by a variety of means. A negative list excludes all products in four therapeutic categories from reimbursement. Since 1981 the members of the national pharmaceutical manufacturers association (the BPI) have operated a voluntary price restraint scheme. The health insurance agencies exert pressure on physicians to economise in prescribing. These measures have had considerable success. Prices are also uncontrolled in the Netherlands, where the situation is broadly similar to that in the FRG. The government is, however, currently examining a markedly more restrictive system based on fixed reimbursement for identical or equivalent products (1).

The UK controls pharmaceutical expenditure through limits on profitability based on sales to the National Health Service. An overall rate of return on capital for the industry is fixed; that

TABLE 4.1 METHODS USED BY EUROPEAN GOVERNMENTS TO CONTROL PHARMACEUTICALS COSTS, 1984/5

Country	Drug expenditure directly controlled?	Individual drug prices controlled	Basis for allowed price	Positive or negative list
Belgium	Yes	Yes	Novelty, therapeutic value, local activities	Positive
Denmark	Yes	Yes	Costs, "reasonable" profit	Positive
France	Yes	Yes	Therapeutic value, cost, local activities	Positive
Germany	No	No	Not applicable	Negative
Greece	Yes	Yes	Costs	Positive
Ireland	Yes	No	Tied to UK prices	Neither
Italy	Yes	Yes	Costs	Positive
Netherlands	No	No	Not applicable	Negative
Portugal	Yes	Yes	Costs, comparative prices-	Positive
Spain	Yes	Yes	Costs	Positive
UK	Yes	No	Control of global profits	Negative

Source: National and IMS information

TABEL 4.1 (contd) METHODS USED BY EUROPEAN GOVERNMENTS TO CONTROL PHARMACEUTICALS, 1984

Country	Manufacturers' price level	Wholesalers' average price (3)	Retailers' average price (3)	VAT %	Patient copayment scheme[1]	% prescription drug bill met by patients[2]
Belgium	Low	113	131	6	25, 50 or 100% of price	50
Denmark	High	109	182	22	25, 50 or 100% of price	40
France	Low	110	175	7	0, 30, 60, or 100% of price	30
FRG	High	112 - 121	130 - 168	14	Flat fee	10
Greece	Low	111	148		10-20% of costs	15
Ireland	Medium	115	173	Up to 23	Depends on income	
Italy	Low	112	149	8.25	Flat fee & 15% of cost	20
Nehterlands	High	120	192	5	Flat fee	20
Portugal	Low	111	139		Flat fee & 35-40% of price	30
Spain	Low	119	167	6	40% of price	30
UK	Medium	114	152	15	Flat fee	108

1 For out-of-hospital prescriptions

2 Author's estimates

3 Manufacturers' price = 100

Source: IMS, national sources

permitted to individual companies varies according to their activities, and in particular to their innovative efforts. Allowance is made for expenditure on research and development and for the promotion of new chemical entities. Within these limits companies are free to set the prices of individual new products. A negative list excludes all but the generic forms of certain specified drugs from reimbursement; unlike the FRG, however, the UK does not ban entire therapeutic classes. Prices in the Republic of Ireland are tied to those prevailing in the UK (2).

Seven member states - Belgium, Denmark, France, Greece, Italy, Portugal and Spain - control the prices of individual products, but use widely differing methods to do so. Denmark, Greece, Italy, Portugal and Spain use plus-cost systems of one kind or another, accompanied with positive lists which confine reimbursement to specified products. In France, companies are in principle free to set their own prices but admission to the reimbursement system is strictly controlled. An acceptable price, based on the therapeutic advantages of the product and on cost data must be negotiated. Since four ministries are involved, prolonged delays are common. In Belgium a maximum selling price is fixed at registration by the Ministry of Economic Affairs, taking both economic and therapeutic considerations into account. The health insurance agency (INAMI) then sets a reimbursement price (3).

A further point deserves emphasis. In every member nation except the FRG the price of drug is in effect fixed at the time when it first enters the national market. This is as true of such countries as the Netherlands or the UK in which it is set by the company as in countries such as Italy or Spain where it is set by negotiation with an official body. Any increase in price necessary to offset, say, inflation or rises in the cost of raw materials, requires permission, which may or may not be forthcoming. Since a product may be marketed for many years, price increases for existing products are often as important to pharmaceutical firms as the prices that they obtain for new ones. In consequence, it is open to a government to use pricing

as a means to more than one end. Admission to a reimbursement list, a better price for a new product or more frequent and extensive price increases for an existing one, may all depend on the behaviour of the company in question. Information obtained in the course of this enquiry leaves no doubt that this is a fact of life on most member countries. The ways in which these opportunities are exploited and the consequences for the Community are discussed in chapters 4.4 and 5.4 below.

4.2 Price levels within the Community: the industry's standpoint

Price levels differ greatly between member countries.

The comparison of average pharmaceutical prices is not easy. Not only do exchange rates vary but much turns on the basket of drugs common to all national markets which must be used for this purpose. Some recent estimates, adjusted to 1985 exchange rates, are presented in table 4.2. It is clear that by all measures prices are high in Denmark, the FRG and the UK occupying an intermediate position. The state of affairs in Belgium appears less certain but the consensus view is that prices there are comparatively depressed. Those prevailing in Portugal and Spain are very low; a recent estimate suggests that they are only 60 per cent of the European average (4).

The evolution of prices has been a complex process. The relative positions of particular nations have changed considerably over the past decade. In pharmaceutical terms, Belgium was an expensive country in 1974 and Britain a cheap one, whereas most estimates suggest that the reverse is now true. It is also obvious that, relative to the UK, German prices have dropped considerably, although they remain high by European standards. The decisive effect of official action on average price levels is clear. In most member countries of the Community, however, pharmaceutical prices remained constant in real terms between 1980 and 1984 (table 4.3), the main exceptions being Belgium and France, where they fell.

TABLE 4.2 PHARMACEUTICAL PRICE COMPARISONS IN COMMUNITY NATIONS 1974 - 1985

UK = 100

COUNTRY	RELATIVE PRICES (1)					
	COOPER	PROGNOS	HEALTH ECON	EEC	DUKES	EFPIA
DATE	1974	1981	1982	1983	1984	1985
Belgium	143	73	66	103	69	70
Denmark			143	154	99	
France	80	69	57	76	52	77
FRG	288	128	159	164	124	120
Greece				73		
Italy	85	65	62	57	58	73
Netherlands			140	145	114	113
UK	<----------100---------->					

(1) Adjusted to 1985 exchange rates.
Source: see note (4).

TABLE 4.3 REAL PHARMACEUTICAL PRICES IN EEC COUNTRIES 1980-1984
1980 = 100

	1980	1981	1982	1983	1984
Belgium	100	93	87	78	79
Denmark	100	102	105	103	104
France	100	98	93	87	84
FRG	100	100	97	99	99
Netherlands	100	96	96	97	101
Spain	100	100	100	99	97
UK	100	100	100	99	97

Source: IMS, based on national data.

How reasonable are European prices? The opinions of producers and consumers naturally differ. The view of the research-oriented pharmaceutical sector is clear: prices in Denmark, the FRG and the Netherlands are "satisfactory"; those in Ireland and the UK are "adequate"; but those in the other nations of the Community are "unsatisfactory". These judgments are based on the view that each market should make a proportionate contribution to overhead costs and in particular to the cost of innovation. At the same time, however, it is significant that international firms rarely withdraw from or even run down their operations in a low-price country. Within the Community, only Greece has suffered from such action, and other factors besides price were involved.

The key to such behaviour lies in the cost structure of the research-based industry. Manufacturing costs, inclusive of raw materials, are normally considerably less than half the selling price (cf table 4.4). At the margin total variable costs may be as low as one-third of the whole or even less. A high proportion of the balance is fixed in the short run. In such circumstances, it is rational for an international company to sell in any market in which the prices available cover direct costs and make some contribution to overheads. This appears to be the case in all the member countries of the Community. That this contribution is always adequate from the standpoint of the firm is less certain (5).

It is not easy to relate the pharmaceutical prices prevailing within a nation to the costs incurred by the national pharmaceutical industry. Most significant companies operate on a world-wide basis. Within Europe national markets are supplied not only from the production of indigenous firms but also from abroad and from the output of the local affiliates of foreign companies (chapter 2.2 and tables 2.5-2.7). Production may include active materials that are subsequently converted into dosage forms. The position in 1984 is shown in table 4.5, from which it is apparent that among the larger countries the national market absorbs a minimum of between 40 and 70 per cent of local production. The balance is exported or consumed in the later stages of production.

4.4 COST STRUCTURE OF THE EUROPEAN PHARMACEUTICAL INDUSTRY IN 1983

ECUm

	Belgium	Denmark	France	FRG	Italy	Spain	UK	Total
Employees (000)	10.0	7.7	64.8	86.9	64.0	32.1	66.6	332.1
Turnover	1205	740	7290	8205	6578	2380	5377	31775
Production value (1)	1015	752	7042	7433	5865	1965	5163	29235
Raw materials etc	348	273	2998	2098	2297		1866	
Services	181	136	2363	1739	1179		636	
Value added (2)	502	330	2111	3448	2388	819	2660	12258
Salaries and wages	184	154	1061	1816	1064	345	925	5549
Total labour costs	262	167	1539	2313	1511	459	933	7184
Gross margin (3)	240	163	572	1135	877	360	1727	5074
Capital employed (4)	1050	700	6100	6870	5520	2050	4550	26500
Depreciation (5)	40	25	245	275	220	80	180	1065
Trading profit (6)	200	140	330	860	660	280	1550	4020
Investment	70	59	164	360	250		398	
R&D expenditure	109	55	943	1233	326	36	786	3488
Value added as % value of production	49.4	44.0	30.0	46.4	40.7	41.7	51.5	41.9
Value of production per capita (000 ECU)	101.6	97.5	108.7	85.5	91.7	61.2	77,5	88.0
Value added per capita (000) ECU	50.2	43.0	32.6	39.7	37.4	25.4	39.9	36.9
Salaries and wages per capita (000 ECU)	18.4	20.1	16.3	20.9	16.7	10.8	13.9	16.7
Labour costs per capita (000 ECU)	26.2	21.6	23.7	26.6	23.6	14.3	14.0	21.6
Labour costs as % value added	52.2	50.5	72.9	67.1	63.3	56.1	35.0	58.6
Gross margin as % production value	23.6	21.7	8.1	15.3	14.9	18.3	33.5	17.4
Gross margin as % value added	47.8	49.5	27.1	32.9	36.7	43.0	65.0	41.4
Profit margin (7)	16.6	18.9	4.5	10.5	10.0	11.8	28.8	12.7

TABLE 4.4 (contd) COST STRUCTURE OF THE EUROPEAN PHARMACEUTICAL INDUSTRY IN 1983

ECUm

	Belgium	Denmark	France	FRG	Italy	Spain	UK	Total
Profitability (8)	19.0	20.0	5.4	12.6	12.0	13.7	34.4	15.1

(1) Excluding VAT
(2) At factor cost
(3) Value added less labour costs
(4) Calculated from the equation (capital employed) = 0.828 (turnover) + 76 and rounded up to three significant figures; see Appendix B.
(5) Taken as 1/30 of turnover; see Appendix B.
(6) Gross margin less depreciation
(7) Trading profit/turnover
(8) Trading profit/capital employed.

Source: Eurostat: Structure and Activity of Industry 1982/3, 1987; author's estimates based on national sources.

TABLE 4.5 DEPENDENCE OF NATIONAL INDUSTRIES ON NATIONAL MARKETS IN 1984.

ECUm

	Belgium	Denmark	France	FRG	Greece	Ireland	Italy	Netherl	Portugal	Spain	UK	Total
Total pharmaceutical sales	890	379	5634	7705	448	166	4465	665	353	1845	3535	26090
Imports of finished pharmaceuticals (1)	503	180	280	980	96	166	475	490	105	56	691	4022
Sales supplied from local production	387	199	5354	6724	352		3990	175	248	1789	2843	22068
Total pharmaceutical production	1296	873	8577	10197	408	1042	6338	1056	415	2585	6648	39435
Local sales as % production	38	22	62	66	86	<1	63	17	70	69	42	56

(1) SITC 5417

Source: Table 2.1, 2.5, 2.8

A conflation of the data in tables 4.4 and 4.5 leads, however, to certain definite if tentative conclusions. Comparing those countries for which the local market forms the major outlet for the local industry - France, the FRG, Italy and Spain - it seems very probable that high prices are offset to some extent by high costs in the FRG and low prices by low costs in Italy and Spain. The UK industry is in the fortunate position of having low costs and selling its products at generous prices. France suffers from a combination of high costs, especially for non-industrial services, and low prices within France. This is aggravated by the fact that French exports of pharmaceuticals are mainly to low-price countries. Value added is therefore unusually low in relation to sales; to bring it up to the European average would require an increase in the prices received of about 16 per cent (6).

The financial experience of the research-oriented companies of France tend to support this finding. Of these firms, Rhone-Poulenc, with a profit margin of 18 per cent and a return on capital of 16 per cent in 1985, showed profits comparable with those of British and American firms. It is, of course, the French company that most closely approximates to the world-wide type. The other French firms had profit margins below 10 per cent and generally below five per cent. This state of affairs has prevailed for a number of years. Significantly, a recent estimate of the profitability of national pharmaceutical industries suggested a pre-tax figure of 4.0 per cent for France in 1982, compared with 8.7 per cent for the FRG, 13.6 for the UK and 18.8 per cent for the USA (7).

The evidence therefore confirms the view, general in the industry, that French prices are uncomfortably low. The same is true of those in Greece. The position in the other low-price countries is much less certain; as a proportion of sales value added is only marginally below the European average in both Italy and Spain. The same is true of the gross margin. It is also clear that the high prices that prevail in the FRG might be seen as a necessity imposed by high costs rather than an opportunity to reap large profits. These conclusions refer, of course, to national industries as a whole, and do not necessarily apply to individual companies. They are nevertheless suggestive.

4.3 Prices within the Community: the consumer's standpoint

Spokesmen for the consumer start from a different position. When the major pharmaceutical firms argue that the fixed costs incurred in their world-wide operations are unavoidable if the industry is to continue as at present, consumer advocates deny that premise. In their view central costs are inflated and conceal much unnecessary activity, especially in marketing and administration. Innovation is desirable but too much R & D is directed towards the development of "me-too" products. Because entry barriers are high, the industry tends towards monopoly. Price controls should be maintained and extended. Alternatively, freer competition would reduce prices, force costs down and improve efficiency.

Some of these arguments presuppose an extensive restructuring of the industry and, indeed, of national social security and health care systems. Scenarios of this kind are discussed in chapter 6. At this point we are concerned to explore the present situation, and, in particular, to examine current price levels from the consumers' point of view. The consumers' interest is both to have ready access to effective chemotherapy now and to have continued access to it in years to come. In a sector characterised by continuous innovation, this would imply that the consumer should be willing to pay a premium over the minimum price for current products in order that the products of the future should actually be developed.

Reasonable as this statement may be, it raises a number of questions. How large should this premium be? Is it not already adequate for the purposes of innovation, if not, as some might say, too large? Moreover, there are problems of equity: should consumers in countries where prices are high subsidise those in which they are low? Alternatively, should not those better able to pay carry a heavier burden than others? To an extent such questions are too simple: as has just been seen, low prices do not necessarily mean low margins, nor high prices high margins. Some further light is thrown on them by an examination of two specific issues.

The first concerns the impact of current pharmaceutical expenditure on consumers in member countries of the Community. Some relevant information is summarised in table 4.6. It is clear that in relation to per capita income, pharmaceutical spending is high - between 0.8 and 1.1 per cent - in France, the FRG, Greece, Italy, Portugal and Spain. Apart from the FRG, these countries share a common medical culture, which emphasises the benefits of pharmaceuticals, both in curing illness and in maintaining health (chapter 2.1). However, it is also that, compared to prices in general, drugs are very cheap in France and Italy but by no means so in the other mediterranean countries.

At the other extreme, it is notable that expenditure is low by all measures in Denmark and the Netherlands. Once again, this appears to be due to social factors rather than to the relatively high prices which prevail: patients in these countries see their doctors relatively infrequently, and when they do, are less likely to receive a prescription than their counterparts in the mediterranean nations. Prices can then be high without an intolerable burden being imposed on the patient or on the insurance system. The same is true, though to a lesser extent, in Britain and Ireland. In the FRG, consumption is moderate in terms of volume but, because prices-like costs-are high, spending is substantial (8).

It appears, therefore, that, in terms of volume, pharmaceutical expenditure is determined in the main by the attitudes of doctors and of patients. In the mediterranean medical culture, the consumption of pharmaceuticals is seen as an unequivocal benefit; in that of northern Europe as a sometimes avoidable necessity. Attitudes in the FRG are intermediate. Economic factors are of lesser significance, the more so in that the direct charge to the patient is limited: it may indeed be suspected that prices are kept low in France and Italy because consumption is high rather than the latter resulting from the former. The use of economic measures to control the burden of expenditure must depend on the elasticity of demand with price. This is discussed in chapter 4.5 below.

TABLE 4.6 PHARMACEUTICAL CONSUMPTION, PHARMACEUTICAL PRICES AND THE ABILITY TO PAY, 1984

	BEL	DEN	FRA	FRG	GRE	IRL	ITA	NET	POR	SPA	UK
GDP per capita (ECU)	11040	14927	12561	14120	4761	7042	8611	12018	2911	5927	10599
Pharmaceutical consumption per capita											
- ECU	90	74	102	125	45	46	78	46	35	48	62
- AS % GDP	0.81	0.50	0.81	0.89	0.95	0.67	0.91	0.38	1.08	0.81	0.59
- relative volume (1)	140	77	216	122	99	65	221	51	103	129	100
Relative prices (1)											
- pharmaceuticals	103	154	76	164	73	115	57	145	60	65	100
- consumer prices	97	122	105	115	79	101	86	103	63	75	100
- ratio	106	126	72	143	92	114	66	141	95	87	100

(1) UK = 100

Source: Tables 2.1, 2.2; Social Trends 17, 1987, London: HMSO, Table 6.6, p104.

The second point concerns the efficiency or otherwise of the national pharmaceutical industries. Some relevant evidence is presented in table 4.7. There are obvious difficulties in comparing one industry with another and the pharmaceutical sector may fairly be described as sui generis in certain aspects. Production value per employee is lower than the average for the chemical industry, though generally higher than that for manufacturing as a whole. This reflects the nature of the pharmaceutical sector, in which the use of large-stream plants with their attendant economies in the use of labour is generally not feasible. Value added per employee, however, is close to the average for the chemical industry.

More significantly, labour costs per employee are very similar to those prevailing in other parts of the chemical industry, except in the UK, where they are strikingly lower. Thus, it does not appear that manpower is used in an inefficient way or that it is rewarded in a disproportionately generous manner. Comparisons of the efficiency with which capital is used is not feasible, since different sectors differ very markedly in their technologies and therefore in their need for capital. It is, however, probable that the pharmaceutical industry is in general rather less capital-intensive than most parts of the chemical industry, although it has become more so during the past decade.

A reasonable conclusion would seem to be that, in so far as comparison is possible, the pharmaceutical sector is as efficient as other parts of the chemical industry in it use of resources, but that it is distinctly more profitable than the latter in most member countries. The gross margin is generally higher than elsewhere, especially in the UK. The main exception is France. Some implications of this finding are discussed later (cf chapter 6.3).

TABLE 4.7 COMPARISON OF PHARMACEUTICAL SECTOR WITH OTHER PARTS OF MANUFACTURING INDUSTRY 1983

	Belgium	France	FRG	Italy	Spain	UK
Value of production per employee 000 ECU						
Pharmaceuticals (1)	101.6	108.7	85.5	91.7	61.2	77.5
Chemical industry (2)	139.3	125.4	104.7	102.2	90.7	106.5
Manufacturing industry	84.7	81.6	76.3	65.8		65.9
Value added per employee 000 ECU						
Pharmaceuticals	50.2	32.6	39.7	37.4	25.4	39.9
Chemical industry	44.0	33.7	36.9	26.4	29.7	38.5
Manufacturing industry	25.8	24.7	27.0	20.0		23.5
Labour costs per employee 000 ECU						
Pharmaceuticals	26.2	23.7	26.6	23.6	14.3	14.0
Chemical industry	24.7	23.9	26.8	21.3	13.9	21.3
Manufacturing industry	18.5	19.3	21.4	14.3		14.0
Gross margin (3) per employee 000 ECU						
Pharmaceuticals	24.0	8.9	13.1	13.8	11.1	25.9
Chemical industry	19.3	9.8	10.1	5.1	15.8	17.2
Manufacturing industry	7.3	5.4	5.6	5.7		9.5
Investment per employee 000 ECU						
Pharmaceuticals	6.8	3.5	4.1	5.0		6.0
Chemical industry	5.8	3.7	4.7	4.4		8.7
Manufacturing industry	4.7	3.4	4.2	3.7		3.3

(1) NACE 258

(2) NACE 25

(3) Value added less labour costs

Source: Eurostat: Structure and Activity of Industry 1982-3, 1984;
Author's estimates based on national sources

4.4 Distortions of the Community market due to the regulation of prices

Price controls and the variations in national price levels which they cause give rise to appreciable distortions in the Community pharmaceutical market and industry.

The most obvious symptom is parallel importing, in which products exported from a country where prices are high are bought in a country in which they are low and re-exported to their nation of origin. A series of cases heard before the European Court of Justice in the 1970s established that this practice is legal even when the differences in price arise from official regulation. The main sources of parallel-imported products are currently France and Italy and the main destinations the FRG, the Netherlands and the UK (9).

In practice parallel imports have not developed to the extent that was originally expected. In 1985, they amounted to about ECU150m in value or about 0.5 per cent of European sales. They are most prominent in the FRG and the UK but even there do not have more than two per cent of the market. Information gathered in the course of this study shows that since 1983 they have receded as a cause for alarm among the research-based pharmaceutical industry.

There are several reasons for this situation. The countries in which parallel imports are significant have taken steps to control their admission to their national markets; although requiring a minimum of formalities, such regulations may act as a disincentive to the importer. The companies who make the products have also defensive measures. Since it is commonly believed that a margin of 20-25 per cent in price is required to make parallel importing worthwhile, and any steps which add significantly to costs will therefore have a discouraging effect.

Both public and private attitudes have hardened in other ways. There are increased doubts about the benefits of parallel imports to those who pay the bills. At first, the gain went entirely to the pharmacist, who bought at a reduced price but who was reimbursed by

the state or the insurance agency at the standard rate. This practice has now been brought under control but at the expense of reducing the incentive to the retailer. Enthusiasm for parallel imports among consumer spokesmen has waned.

A more serious problem is the use of pricing regulations to influence decisions about the location of industry facilities. As has been pointed out already (chapter 4.1 above) to control prices is to create opportunities for official pressure to be brought to bear on international companies. In exchange for admission to a reimbursement list, a better price for a new product or permission to raise an existing one, a firm may be expected to create or expand local facilities. Such opportunities are frequently exploited.

Interviews carried out in the present study suggest that pressures of this kind are most common in Belgium, France, Italy and Spain. In Belgium they are embodied in the Oleffe law, introduced in 1975 and extended for a further five years in 1983. This permits discretionary price increases in return for company commitments on local investment, R & D and exports. The French system of contracts, introduced in 1983, works in the same way, and is reported to be applied vigorously. Italy follows a less formal, but broadly similar policy of favours for favours.

Elsewhere the use of price controls to promote the local industry is less common. Under the system used in the UK up to 1986, the profitability permitted to individual companies depended on the scale and nature of their British activities, but this element has been somewhat diluted in the new regulations. There are no direct controls over prices in the FRG and the Netherlands and so they cannot be used as instruments of pressure. Denmark has never attempted to do so. In Ireland, the government has actively fostered a local industry exclusively oriented to the export of active materials. The chosen instruments, however, have been tax concessions and subsidies, and differential pricing has played no part.

The use of price controls to build up local pharmaceutical capacity has two effects. The first is to force international companies to expand their facilities beyond what they would otherwise choose. This increases their costs, in that economies of scale cannot be realised. Estimates of these additional costs are presented in chapter 5 below. The second is to favour indigenous firms, since all pharmaceutical companies carry out a large proportion of their manufacturing and research in their country of origin. This is especially important in France and Italy, where the national firms are heavily dependent on their national markets.

From the standpoint of a unified market both these outcomes are undesirable. They increase costs and limit competition. In terms of national objectives for the pharmaceutical industry, however, they can make sense (chapter 2.6). A conflict of aims is therefore unavoidable.

4.5 The role of prices in the pharmaceutical market

The unified market is expected to reduce costs, increase competition, and lower prices. This implies that demand is sensitive to price. To what extent is this true of the pharmaceutical sector?

The traditional answer is that prices play a very limited part there. Within a therapeutic sub-market, demand is determined by the incidence of the particular disease. Most drugs are available only on prescription and doctors are therefore the customers. Their training emphasises the well-being of the individual patient and medicines are chosen on that basis. Price is at most secondary consideration. Moreover, in every member country state or the insurance agency meets all or most of the cost and so neither the doctor nor the patient has a direct interest in economising. There is much truth in this view. The importance of social attitudes and medical traditions have already been emphasised. At the same time, there is evidence to suggest that prices have a significant and increasing role in the pharmaceutical market.

It is generally agreed within the industry that the price set for a new medicine must take into consideration those of competitive products. This is true of countries where the prices of individual drugs are not controlled. A premium may be charged if it has substantial therapeutic advantages but this cannot be very large. Several respondents mentioned a maximum of 25 per cent for a "breakthrough" product and smaller figures for those showing lesser gains over existing medicines. Within these limits arguments which justify a relatively high price on medical grounds were often accepted by regulatory authorities. The importance of economic as well as therapeutic considerations in pricing new pharmaceuticals is considered to be on the increase everywhere.

Price competition is considerably more vigorous in the out-of-patent sector, which now makes up more than 50 per cent of the Community market by value. A substantial generic sector has emerged in those member countries in which average prices are relatively high. In 1984 generic products had approximately three per cent by value of the entire European market, four per cent of that in the FRG, six per cent in the UK and ten per cent in the Netherlands. Since they have made further advances, especially in the FRG where, by some estimates, they have more than ten per cent of the national market. As yet they have had little impact in France or the mediterranean countries.

This market is, however, by no means perfect. The generic companies have only achieved their share of the market by severe price reductions, sometimes amounting to 50 per cent or more of that charged by the originator. Moreover, it is normal for the latter to retain a substantial proportion of the total sales despite charging a premium price. The advantages of size and reputation are sufficient in the eyes of many doctors to justify a conservative attitude towards new suppliers. Significantly, most generic companies in the FRG have found it necessary to promote their products directly to the medical profession rather than relying on price alone.

The role of official agencies has also been crucial. Within the Community, a generic sector has developed only where they are commercially attractive and where there has been action, direct or indirect, from governments or insurance organisations to encourage their use. Thus in the FRG, the combination of high prices and vigorous action by the Krankenkassen to control pharmaceutical spending has favoured generics. In all member nations they are used extensively in hospitals, which, as readily identified cost centres are under constant pressure to economise. The development of the European generic market is a result of paymaster-led demand rather than customer-led demand, and, given the constraints imposed by current social security systems, this seems likely to be the case in the foreseeable future (10).

More general evidence from several countries confirms that there is an element of price sensitivity in demand. When in 1983 the FRG excluded products for certain minor illnesses from reimbursement, their sales fell substantially and had not fully recovered by 1986. The UK negative list had a similar impact on the demand for branded tranquillisers and minor analgesics. More recently, increases in the levels of patient copayment in France and Italy are reported to have reduced pharmaceutical consumption appreciably. The overall picture is one of a market characterised by a low - probably below unity - but not zero elasticity of demand with price (11).

At present, then, price has an appreciable but not critical role in the competition between in-patent products. Therapeutic advantage is still the major factor. Among out-of-patent medicines, price could in principle be much more significant element, but much turns on the willingness or otherwise of official bodies to emphasise its importance. From the standpoint of the unified market, the central consideration will be the balance between in-patent and out-of-patent products. Unification could reduce costs without leading to a reduction in the prices of the former (cf chapter 3.3). As already indicated, the prices of out-of-patent drugs are much more likely to fall as costs drop and new producers enter the market.

4.6 The impact of Community initiatives

There is a consensus common to both industry and government that the harmonisation of prices will be a slow process. The political difficulties are seen as formidable. In the eyes of many respondents a considerable degree of harmonisation between social security systems would be a necessary prerequisite. There are also problems of equity: how could the same price be charged in the FRG and in Portugal, given that per capita real incomes differ by a factor of nearly three?

The industry would ideally prefer unrestricted free pricing but sees little hope of this happening. Given the political realities, the major companies accept, if reluctantly, the existence of national price controls with all their disadvantages. Cost-plus methods are seen as complex, time-consuming and unrealistic; the British system is preferable but might not work outside the UK. As has already been seen (cf chapter 4.4) they are not especially worried by parallel imports, which are seen as an irritant rather than a major threat. In their foreign operations they resent discrimination in favour of indigenous firms, but have bowed, again reluctantly, to pressures to expand their local activities, which are seen as the necessary cost of a licence to operate in many countries (cf chapter 5.4). Price freezes are particularly disliked because of their unpredictability and their long-term effects.

As far as prices are concerned the industry view of the Commission is a broadly favourable one. There is appreciation of what is has done on occasion to bring about price increases, notably in Italy, and to limit blatantly discriminatory practices. Such approval is, however, tempered by a feeling, particularly common among Swiss and American firms, that more might have been done. The proposed transparency directive is generally welcome. If the 120-day limit for decision were to be generally observed there would be a saving in time; as was shown in chapter 3.3 this would be economically significant. Discrimination between companies would be, as one industrial respondent put it, "smoked out" and thereby made more difficult. It is also hoped that pressures to expand local facilities unnecessarily would be abated.

On the general issue of the unification of the market the attitude of the major firms is more reserved. Fear was expressed that it would lead in the longer run to generally lower prices. Pressures to harmonise prices downwards would become irresistible. Consumer groups and at least some governments, of course, tend to fear the reverse. At the same time, some degree of harmonisation of prices was seen as part of an irreversible trend. Some scenarios which involve a degree of price convergence are explored in chapter 6.3 below.

NOTES

1 The categories excluded are products for coughs and colds, those for mouth and throat infections, laxatives and medicines for motion sickness. Very recently it has been proposed to restore cough and cold remedies to the reimbursement list but to exclude tranquillisers.

2 The British PPRS was extensively modified in 1986. Until then the permitted rate of return was explicitly based on value added, investment, exports and R & D expenditure in the UK.

3 The French authorities have now (October 1987) set up an economic commission with which companies will now negotiate. At the time that this step was announced it was admitted that under the previous system it took an average on one year to agree a price (Scrip, 1987, 1247, 1). The Belgian pricing mechanisms are also under review, following pressure from the European Commission (Ibid, 1987, 1249, 2-3).

4 Data from the following sources: 1974, M H Cooper: European Pharmaceutical Prices, 1975, London; Croom Helm; 1981: Prognos, quoted in R Chew, G Teeling-Smith and N Wells: Pharmaceuticals in Seven Nations, 1985, London: Office of Health Economics, 47; 1982, Health Economics, private communication; EEC 1983 and EFPIA 1985, European Commission, COM (86) 765 final, table 1, p18; 1983, M N Dukes: Drugs and Money, 1985, Copenhagen: WHO, table 2, p8, Price levels in Portugal and Spain were estimated by an industrial source to be 40 per cent of those of the FRG in 1987. Those in Italy, previously low, have risen sharply during the past two years.

5 Eurostat: Structure and Activity of Industry 1982/3, 1987. Information from the Association of the British Pharmaceutical Industry indicated that in 1982 manufacturing costs amounted to 46% of total costs; the Bundesverband der Pharmazeutische Industrie gave a 1984 figure of 43% for the FRG. Senior executives of large research-oriented companies interviewed in the course of the study suggested a marginal cost of 30-35%.

6 In 1984 French exports of pharmaceuticals (SITC 541) to the developed world outside the European Community were ECU256m compared to exports of ECU1000m to the developing world. Burstall and Senior: The Community's pharmaceutical Industry, 1985, Brussels: European Commission, table 9.4, p115, estimated that French-based companies made only 3.5 per cent of their 1982 sales to the USA and Japan; the corresponding figures for the FRG and the UK were 15.5 and 24.0 per cent respectively. The position of the UK in these markets has improved considerably since that date.

7 Profit margins calculated from Scrip's Pharmaceutical League Tables 1985/6, 1987 Richmond: PJB Publications, Profitabilities are from Teeling-Smith and Wells: Pharmaceuticals in Seven Nations, 1985, London: Office of Health Economics, table 11, p17.

8 Based on B O'Brien: Patterns of European Diagnoses and Prescribing, 1984, London: Office of Health Economics, Table 4 p25. According to the Dutch pharmaceutical industry organisation NEFARMA, no drugs are prescribed in 44 per cent of consultations in the Netherlands; the corresponding figures for other countries are USA 37, UK 26, France 22, Spain 16, and Italy and Belgium 8 per cent each (Scrip, 1986, 1107, 3)

9 See Burstall and Senior, op cit, chapter 8.3, pp98-101.

10 This discussion is based on M L Burstall: Generic Pharmaceuticals in Europe - Blessing or Threat?, 1986, London: Economists Advisory Group, Especially chapter 4, pp 47-70.

11 Explicit calculations of the elasticity of pharmaceutical demand with price are rare, in part because the product mix is constantly changing, in part because a variety of factors enter into the equation, and in part because prices in most member nations of the Community are set by administrative action. A simple model relating per capita consumption to price and real per capita income in the USA, where prices are not controlled, suggested an elasticity of 0.67 with price and one of 1.25 with income for the period 1960-1984.

5 THE MULTINATIONAL SYSTEM AND ITS COSTS

5.1 The origins of the system

To a large extent the Community pharmaceutical industry is organised on multinational lines (chapter 2.2, 2.3). Companies make and sell drugs and carry out research in a number of countries. In principle this must add to operating costs in that economies of scale cannot be fully realised, and that extra capital and labour are required.

The multinational system predates the second world war. German, Swiss and American pharmaceutical firms began to create networks of local subsidiaries in European countries from the turn of the century onwards. Until the 1950s, however, most of these affiliates were purely marketing organisations. Local manufacturing became widespread in the aftermath of the war, mainly in response to restrictions on imports imposed by governments anxious to economise on foreign currency and to encourage the indigenous pharmaceutical sector. Thus, the majority of US companies began to make drugs in the UK at the time of the dollar shortage of the immediate postwar era, later expanding their operations to other member countries (1).

Such considerations have remained important. As tables 2.5-2.6 indicate, imports of finished drugs are still remarkably small in France and Italy, although foreign firms have a large share of the market in both countries. Until Spain acceded to the Treaty of Rome, the official policy was to exclude such products altogether as far as this was possible. The process of integration within the Community has removed many of the obvious barriers to freer trade, but, as has been shown in chapter 4.4, others still remain. In any case the past cannot be repealed. Institutional inertia means that local facilities, once created, acquire a life of their own. Good reasons appear why they should expand rather than contract. Public relations may make it awkward to withdraw; political factors may make it impossible.

The multinational system has therefore continued to develop within the Community. As already noted, the American and Swiss firms supply the large majority of their European markets by local production. This form of operation is also important for British and German companies,

though less so for those of France and Italy. These local affiliates often export a substantial proportion of their output. R&D is also carried out by foreign firms, sometimes on a considerable scale; in this field the favourite host is the UK and guest the US. Local sales organisations of almost every significant company are to be found in almost every member country (2).

5.2 Where do potential economies exist?

In a truly unified pharmaceutical market there would be less need for local production. Nations could be supplied from fewer, perhaps even a single source, which might be outside the Community. There are few technical difficulties: pharmaceuticals are small in volume and cheap to transport.

Costs could therefore be reduced. In part the savings would arise from economies of scale and in part from a simplified organisational structure. The problems of coordinating a complex and geographically diffuse empire would be much decreased. The scale and nature of such savings, however, is more difficult to predict. Thus, economies of scale may exist in some operations and not in others. They may already have been realised. There may be diminishing returns to size above a certain point. A careful inspection of the evidence is therefore a necessary pre-requisite to attempts to calculate the possible reductions in operating costs.

There are substantial economies of scale in basic research. Below a certain size - often said to be 2-3000 personnel - it is impossible to provide special facilities such as libraries, animal testing, analytical services etc - on the necessary scale. Moreover, drug discovery is a multidisciplinary activity and it is desirable to bring together scientists from widely different backgrounds. Research teams interact in productive ways. For these reasons, a large centre is more productive than a small one. However, there are also limits to the size of a research establishment. Above perhaps 1000 personnel - many would say well below this number - management problems become intractable and output falls. In addition, many companies wish to 'tap into another research culture' in order to improve their efficacy.

Such factors favour dispersion rather than concentration (3).

The multinational firms interviewed in the course of this study considered that they had, broadly speaking, realised the possible economies of scale in this field. All of them had a large research centre or centres in their country of origin where they did the bulk of their fundamental work. Establishments in other nations were relatively few in number, usually, though not always, on a smaller scale, and often worked in specialised areas in which there was local expertise. The availability of such staff is an important factor. 'We go for the best people. If they can do the job, we go to them' was a typical explanation. Cost was very much a secondary consideration. None of these firms thought that their policies concerning the location of research would be altered by the emergence of a unified market (4).

Similar considerations apply to the later stages of innovation. Apart from clinical testing (cf. chapter 3.2) development is concentrated at a single or at most a very few centres. Indeed, several respondents thought this was more true of such work than of basic research, in that it was more suited to systematic organisation. However, the adaptation of existing products to local needs is usually carried out in a local laboratory. To do so facilitates cooperation between the research, manufacturing and marketing divisions of a company. Once again, the firms approached were unanimous in thinking that further economies of scale were very limited and that their own practices would not be changed by unification of the European market.

Manufacturing is in a different position. There are two basic stages in the production of pharmaceuticals - the preparation of the active ingredients and their conversion into dosage forms. The first involves chemical or microbiological technologies in which there are large economies of scale. The square/cube law relating capital costs to output applies very generally; labour is also used more efficiently in a large plant than in a small one. The only limiting factor is the need to preserve flexibility of production. Both Community and non-Community multinationals reported that economies of scale at this stage were largely realised. They owned a limited number of plants for the production of active ingredients - often only one within the

Community - which were frequently of a near-optimum size (5).

The same companies, however, agreed that there were large and unrealised economies of scale in the stage at which the active ingredients are formulated into dosage forms. Because of pressures of various kinds from governments they had been obliged to build local plants to turn imported active materials into dosage forms. The main cost of such factories is the building, together with the air-conditioning and ultra-clean facilities required; the machines themselves are relatively cheap and have a very large output (cf. chapter 5.3 below). All firms reported that many of these plants ran at well under capacity; several of them suggested that in a unified market their number could be reduced by a factor of between one-half and two-thirds (6).

The situation in marketing is different again. Here, it is generally agreed, economies of scale exist within a country. A large company can offer a bigger range of products through its sales force and can promote its drugs more effectively in other ways. However, it is absolutely necessary to organise marketing along national lines. The main cost is the sales force, which must be composed of local personnel familiar with local traditions of medical practice and, of course, speaking the local language. Some respondents thought that it was possible that there might be potential economies in a unified market-through, for example, the adoption of common strategies, but this was a minority view. In any case, such practices do not necessarily require a single Community market (7).

Few firms found it difficult to coordinate their European activities. The numbers of staff involved were modest and largely informal procedures were thought to bè adequate. It is clear that the major pharmaceutical companies are thoroughly accustomed to the multinational form of operation and have adjusted their modes of control accordingly.

Thus, it is clear that in most fields of activity within the industry, the economies of scale that might result from a unified market do not exist, as in the case of marketing, are relatively trivial, as with

coordination, or have already been realised as far as is desirable, as in the R&D and probably the production of active materials. The area which shows real scope for cost reduction is formulation and it is to the scale of these economies that we now turn.

5.3 How large are the potential economies?

A reduction in the number of formulation plants would save fixed capital and labour costs.

The first step is to determine the amount of excess capacity. In 1982 the number of prescriptions written by doctors practising outside hospitals in the member countries of the Community was approximately three billion (three thousand million). Allowing for in-hospital prescription the grand total might be four billion. At an average of 100 tablets per prescription, consumption would be 400 billion tablets (8).

A medium-sized compression tabletting machine has an output of 250,000 tablets per hour, and an annual output of about two billion on a three-shift basis. It could be used to make 10-12 products in fairly long runs. Thus, the entire European consumption of tablets could be made on 200 machines. The output of equipment to make vials or capsules is much lower but still very considerable. In practice a formulation plant will contain a number of machines in order to ensure operating flexibility. As already noted its main cost is the building and the specialised facilities required by the product mix. The formulation equipment itself is relatively cheap: the tabletting machine mentioned previously costs about ECU200,000 (6).

The Community pharmaceutical market is highly fragmented. No company holds as much as five per cent of the total and the typical figure for a large multinational is below two per cent. It therefore appears that on purely technical grounds no company needs more than a single European formulation plant. As table 5.1 shows, however, foreign manufacturing facilities within the Community number approximately 250. If it is assumed that all Community-based companies locate their single plant in their country of origin, and that every non-Community

TABLE 5.1 FOREIGN COMPANIES WITH PRODUCTION FACILITIES IN EEC COUNTRIES

Location of facility --	Bel	Fra	FRG	Gre	Ita	Neth	Por	Spa	UK	Total
Nationality of companies										
Belgium		2	1		1	1		1		6
France	5		4	3	7		2	6	2	29
FRG	1	5		2	10	1	2	10	5	36
Italy	1	1	1					4	1	8
Netherlands	1	1	1	1	2			1	1	8
Portugal					1					1
UK	4	6	3	3	5		1	5		27
USA	9	18	14	7	19	2	5	17	19	110
Switzerland	4	3	3	2	4	1		4	3	24
Other			1			1		2	1	5
Total	25	36	28	18	49	6	10	50	28	254

Source: see note (9).

multinational needs a single plant within the Community, then there are 225 surplus plants (cf table 2.9). Such a conclusion is undoubtedly over-simple. Special factories may be needed for special products. To centralise production completely carries obvious risks. It does, however, lend force to the comment of several companies, mentioned above, that in a unified market the number of formulation plants could be reduced by one-half to two-thirds (9).

The total cost of a formulation plant depends on the technology employed. A state 'state of the art' facility containing 10-20 machines and making 40-50 products would cost ECU35m and employ 150-200 staff. At the other extreme, a factory making straightforward generic or OTC drugs on a large scale would use 3-6 dedicated machines and cost perhaps ECU10m. Since there are no data about the age distribution of these plants, for the purposes of calculation of conservative figures of ECU10 and 20m will be assumed. This suggests that the book value of the foreign formulation plants in the Community is between ECU2500 and 5000m. If one half of them are surplus to requirements, then the extra capital involved is ECU2500m; if two-thirds, the sum is ECU1650-3333m. Assuming a life of 10 years, the corresponding annual depreciation payments are in the range ECU125-333m (6, 10).

The magnitude of these figures can be checked to some extent from company data. From UK returns the fixed capital required by foreign subsidiaries operating in the UK during 1985/86 was equal to 35 per cent of their annual sales. Firms described as marketing pharmaceuticals rather than making them reported fixed capital averaging 12 per cent of their sales. There was no systematic variation in these ratios with the size of the company. If total sales by the local affiliates of foreign multinationals operating in the Community, including exports to destinations outside the Community, are taken as ECU12,500m, then the fixed capital used by them for purpose other than marketing is ECU2875m at book value. This figure includes, of course, the value of R&D facilities and of plant for making active ingredients. Given the uncertainties involved,

however, the agreement with the earlier estimate is surprisingly good (11).

The saving in labour must now be considered. Here much turns on the mode of operation: to replace three factories working single shifts with one working three shifts is to reduce total employment but not by a factor of two-thirds. A rough estimate, based on the interviews undertaken, is that 30 per cent of all personnel or a total of 105,000 for the whole of the Community (table 2.8) are involved in production. Pro rata about 35,000 work for the subsidiaries of foreign companies, of whom perhaps 25,000 work in formulation. Assuming once again that in a unified market between one-half and two-thirds of the plants could be closed down, then the maximum saving in labour would be between 12,500 and 15,500 or between 3.5 and 2.5 per cent of the total. At European average labour costs (table 4.4) this would represent a saving of between ECU270 and 356m. The actual saving is likely to be less, however, partly for the reason already mentioned and partly because production workers receive below-average pay.

5.4 Why are these economies not realised?

These calculations are very approximate, but they suggest that savings of several hundred millions of ECUs would be possible in a unified market. Why, then, has the concentration of production not already taken place?

The main reason is that the prices a company receives for its products depends in many countries on the scale and nature of its local activities (chapter 4.4). This is especially true of price increases for drugs already on the national market. 'If we were to close down our plant in ------, we'd never get another price increase there. This would outweigh any possible savings' was one entirely typical comment. Thus the funds invested in local facilities are in effect the price of a licence to operate in the local market. As previously remarked, pressures of this kind are most intense in France, Italy and Spain, among the larger member nations, and Belgium, Greece and Portugal among the smaller ones. They are much resented but equally seen as an inescapable fact of life.

When pressed on possible courses of action if the market were to unified in 1982 all respondents took a cautious attitude. Much would depend on national pricing systems: if the present situation continued, then little change was foreseen. If, however, the transparency directive were to inhibit or remove pressures towards local investment there would be a greater degree of concentration. This would, however, be limited and would take place at a measured pace. Most thought that they would retain manufacturing facilities in the main European markets, although not necessarily in the smaller member nations. The production of individual products might be concentrated at a single European centre but radical policies would not be pursued. Strategies would rather be of a selective 'horses for courses' type.

Several reasons were offered for this considered approach. Companies wish to present a favourable image in the countries in which they operate. 'We wish to be good corporate citizens' as several respondents commented. There is some feeling that products seen to be locally made are preferred to imports in many countries. To close a plant invariably create hostility. There are also very practical considerations. To have a local plant is to facilitate the process of product development for the local market. There is greater flexibility and speed of response. Opportunities can be more readily seized and problems averted. Financial factors play a part. The FRG is a popular host country even though the attitude of the federal government is one of strict non-involvement in the industry's affairs. German prices are high, though, and in many parts of the world the permitted price is tied to that in the country of origin. Accordingly, the FRG is an attractive centre from which to export. The same is true of the UK.

It should also be remembered that for most companies the decision to invest in a particular European country was made in the past when circumstances were substantially different. The money has been spent; it is 'water over the dam'. In many cases the local subsidiary is now of appreciable size, and, of course, it will be manned almost entirely by local personnel. Such an organisation is both part of the country and part of the larger company. To dispose of it would not be easy. Most commonly it is not a free-standing entity, capable of carrying out all functions, but is relatively specialised in its operations. If

so, then it could not readily be sold to local operator, while to shut it down may well be politically unacceptable. Therefore it is better to treat it as an asset and make the best use of it.

NOTES

1. For a general account, see M L Burstall, J H Dunning and A Lake: Governments, Technology and Multinational Enterprises - the Pharmaceutical Industry, 1961, Paris: OECD, especially chapters 3 and 9.

2. Comparing tables 2.5 and 2.7 local production supplies 95 per cent of the Community market for US firms, 75 per cent for those of Switzerland, 73 per cent for those of Germany, 64 per cent for those of the UK and 49 per cent for those of France. Information is lacking for Italian firms but interviews suggest that their production outside Italy is limited. Approximately 28 per cent of all 1982 R&D spending in the Community was by foreign companies, and about 17 per cent by firms from outside it (M L Burstall and J H Dunning: International Investment in Innovation in ed N Wells: Pharmaceuticals among the Sunrise Industries, 1985, London: Croom Helm, pp 185-197).

3. Burstall, Dunning and Lake, op cit pp 69-72; Burstall and Dunning, op cit.

4. Of the major companies identified in table 2.9 only two have their principal basic research centre outside their country of origin, although a much larger number have important establishments abroad.

5. Where companies have several plants for making active materials this is often the result of acquiring an existing local company, Respondents reported that pressure from governments to set up such facilities, although existing, was not as intense as that to set up formulation plants.

6. This statement is based on interviews with the tabletting manager of a large multinational and with a leading firm of tablet machine manufacturers.

7. Some examples of the economies of scale possible within a

national market are given is Gaps in Technology - Pharmaceuticals, 1969, Paris: OECD.

8. Figures of prescriptions from B O'Brien: Patterns of Diagnosis and Prescription in Five European Countries, 1984, London: Office of Health Economics, table 4, p 25. Doctors practising outside hospitals in France, the FRG, Italy, Spain and the UK wrote 2603m prescriptions; these countries account for 89 per cent by value of all 1984 pharmaceutical sales within the Community (cf table 2.1), so a total of 3000m for all member nations seems reasonable.

9. The number of plants was estimated primarily form the World Drug Marketing Manual 1986, London: IMS. All branches of firms outside their country of origin which were described as 'manufacturers' rather than 'marketers' were included. The list was then revised in the light of information from individual companies and national sources. It is in broad agreement with information from the major multinationals operating in the Community, most of whom had between four and eight formulation plants apiece, but is more likely to be an under- rather than an-overestimate.

10. A 10-year lifetime is suggested by the depreciation figures given for foreign subsidiaries operating in the UK in 1985/6 (Business Ratios-Pharmaceuticals, 1987, London: ICC-Business Ratios). This figure may be rather low, particularly for the simpler type of plant.

11. See Appendix B. Chapter 2.2 suggested that pharmaceuticals made by the local affiliates of foreign firms were 42% of sales through retail pharmacies. If this ratio applies to all sales then the total made in this way is ECU11,000m. To this figure must be added exports by such companies. These are considerable in some cases, thus, it is known that US companies operating in the UK account for 30% of all UK drug exports. A figure of ECU1,500-2,000, seems reasonable, suggesting a total output of ECU12,500-13,000m.

6 THE RESULTS OF UNIFICATION

What will be the outcome of measures to unify the Community market for pharmaceuticals?

In a political industry much will turn on the nature of the political actions taken by member countries and by the Commission. Since the dynamic part of the sector is organised on a world-wide basis the impact of such measures on the international competition and competitive strength must also be considered. Finally the distribution of benefits resulting from particular strategies should be examined; as has already been seen, at a number of points there is a degree of conflict between the interests of producers and consumers. These areas will be explored in the course of answering the following questions:

- what savings are possible through unification of the market under various assumptions?

- how would this affect patterns of competition within and without the Community?

- what would be the effects of moves towards common pricing within the Community?

- what further steps are needed - if any - to unify the market completely?

6.1 Possible reductions in operating costs

The main savings in the operation of pharmaceutical companies through the unification of the Community market have already been identified and their magnitude tentatively estimated (chapters 3 and 5). It remains to consider the extent to which the possible savings might be realised. Here the critical factor is the effect of the transparency directive on the locational policies of multinational firms (chapters 4.5, 5.4). Three scenarios will be examined:

- the directive has no effect. Prices continue to be linked to

local activities in most countries. Cost savings are limited to those possible through unified registration procedures.

- the directive is effective. Pressures on companies to maintain or increase their local activities ceases. For the reasons outlined in chapter 5.4, however, companies withdraw manufacturing facilities only from marginal areas.

- the directive is effective. Companies follow policies of maximum practicable concentration.

In all cases it is assumed that relative prices remain unchanged.

In the first scenario the annual savings are small. They probably amount at the most to ECU160-260m or 0.5-0.8 per cent of total industry costs within the Community (chapter 3.3) These savings accrue to large innovative multinational companies; if they are divided in proportion to their Community sales outside their own country, then US firms would benefit the most (table 6.1), followed by those of Switzerland, the FRG and the UK. Changes in employment would be negligible and there would be none in patterns of trade. Member countries would save a maximum of perhaps ECU5m apiece from a pan-European registration agency, although this is doubtful (chapter 3.4). (1).

In the second scenario thes savings would be maintained. To them would be added the reductions in cost from a limited concentration of production. The most probable targets for economy would be Greece and Portugal. In both countries prices are low and the local market small. Of the other smaller member nations Belgium is a bad place to sell drugs but quite a good place to make them (cf table 4.4); the Netherlands has attracted a relatively small amount of foreign investment and Denmark hardly any (cf table 2.7). Both countries have high pharmaceutical prices and are therefore potentially attractive centres from which to export (2).

If it is assumed that international companies withdraw from Greece and Portugal and that they supply those countries by exports, then a number of consequences may be identified. The international companies

would ultimately save the capital-related costs of their operations in those countries. On a book-value basis (cf chapter 5.3) these might be in the range ECU28-42m per year (table 6.2). Foreign firms would also save in labour provided that there was excess capacity elsewhere which could be used instead, which seems probable. The reduction in labour costs would be 700-1000 in Greece and 400-600 in Portugal and in annual labout costs ECU15-25m. The total savings, inclusive of those estimated in the first scenario, would therefore rise to ECU204-235m. (3).

Trivial as such decisions might seem from a European or world standpoint they are quite serious from those of Greece or Portugal. In both countries the industry is small and oriented towards the local market (tables 2.1, 2.5, 2.8). If the multinationals were to withdraw, employment in the industry would drop by up to one-third and the balance of payments on pharmaceuticals, already markedly negative, would deteriorate further. The additional loss would be approximately ECU170m in the case of Greece and 125m in the case of Portugal. These consequences might not be acceptable to the national governments, both of whom have followed active policies towards the industry in recent years (4).

The third scenario is much more speculative. It assumes that international companies might withdraw, not only from Greece and Portugal, but also from one or more major European markets and concentrate their facilities in a very small number of member countries. Who might be chosen? Both economic and subjective factors are likely to enter into the decision. Among the more likely candidates are the FRG and the UK. The FRG is viewed with some enthusiasm by most foreign companies. Although local costs are high, local prices are both high and largely free, and the government allows the industry unusual freedom of action. Moreover, the technical and educational infrastructure is excellent, and the German official culture is felt to be markedly sympathetic. The UK has relatively low costs, research personnel of the highest calibre, and a reasonable pricing system. Both have strong indigenous pharmacuetical sectors.

Other large European countries are less well placed. France couples high costs with low prices. Industry-government relations are

consistently frigid and foreign firms resent strongly the continuous pressure on them to expand their local activities. Italy and Spain suffer from the latter problem, but, although their prices are generally low - in the case of Spain very markedly so - so are their costs. Accordingly, as a proportion of output value added and gross margins are close to the European average in these nations (table 4.4). It is therefore difficult not to feel that France would suffer most in a search for economies on the part of companies based elsewhere. The only countervailing factor is feeling that French biomedical science is of good and rising quality. For a variety of reasons international firms prefer to combine R&D with production and this consideration might act in favour of France as a location.

For purposes of illustration, therefore, this scenario assumes a 50 per cent reduction in foreign involvement in France and a 25 per cent reduction in both Italy and Spain. The lost production is transferred by European firms to their country of origin and by American companies in equal amounts to the FRG and the UK. The annual savings in capital in these three countries would be in the range ECU38-76m (table 6.3). The savings in labour costs have been estimated using two alternative sets of assumptions. In the first, two-thirds of those originally employed are replaced in the new sites. In the second, the reserve capacity is such that no replacements are needed. The savings realised in this scenario are the ECU65-208m, and taking into account those estimated for the earlier scenarios, ECU269-533m. Unit costs in the Community industry would be reduced by 0.8-1.6 per cent. US firms would realise the largest savings, followed by those based in the UK, Switzerland and the FRG.

These calculations are highly approximate and are subject to a large margin of error. Nevertheless, they suggest that the potential direct savings from the unification of the European market are relatively limited. Even the most sweeping reorganisation envisaged by the major companies (cf chapter 5.3), in which between one-half and two-thirds of their local plants were shut down, would reduce their European costs unit by no more than ECU555-960m or 1.6-2.8 per cent. This is not negligible: if prices remained unchanged, the average profit margin would be increased by between 14 and 24 per cent (table 4.4). This figure is, however, in the nature of an upper bound, and might

not in any case be sufficient reward for what would be a distinctly fraught transitional period. Alternatively, if passed on in their entirity to the consumer they would reduce pharmaceutical costs by between 2.1 and 3.7 per cent.

The balance of power within the European pharmaceutical sector would be changed substantially by such policies of concentration. The countries from which the multinational companies withdrew would be affected in negative ways. Employment would be lost, though only marginally. Perhaps more important, balances of payments in pharmaceuticals would drop sharply. In the most extreme case it is probable that France would move from a large to a small positive balance and that Italy and Spain would be in substantial deficit rather than only marginally so as at present. Conversely the position of the FRG and the UK, already strong, would be further improved (table 2.11).

6.2 Costs and competition

If costs fall, will competition increase? if so, what are the possible results for the industry and for the consumers?

As we have just seen, the likely reductions in costs are relatively small. They could be used to raise profits appreciably or reduce prices marginally. They would accrue to relatively large research-based companies operating on a multinational basis. The overall elasticity of demand for pharmaceuticals, although not zero, is unquestionably low, for reasons which are unlikely to change. In the in-patent sector there is some trade-off between price and therapeutic efficacy. In the out-of-patent sector there is increasing price competition between different makes of the same product but the market is still highly imperfect (cf chapter 4.5).

The main barrier to entry in the innovation part of the industry is the high cost of product innovation, which consists largely of the expenditure needed to establish that the new product is both safe and efficacious. Currently the cost per NCE, including failures but excluding interest forgone is approximately ECU100m, corresponding to

TABLE 6.1 SAVINGS IN DIRECT COSTS OF OPERATION TO COMPANIES AND COUNTRIES THROUGH THE UNIFICATION OF REGISTRATION PROCEDURES (SCENARIO 1)

Origin of firms --->	France	FRG	UK	USA	Switzerland	Other	Total
Savings to firms							
- ECUm:							
lower value	10.7	23.4	17.6	65.6	28.6	14.4	160
upper value	17.2	37.7	28.3	105.6	46.0	25.3	260
- As % unit costs:							
lower value	0.19	0.26	0.51	0.91	1.34	0.22	0.47
upper value	0.30	0.40	0.82	1.47	2.10	0.29	0.77
Savings to countries							
- ECUm:							
lower value	<----------0---------->						
upper value	<----------5---------->						

Source: see chapter 3.3 and the Appendix B

TABLE 6.2 OUTCOME OF LIMITED CONCENTRATION OF PRODUCTION FACILITIES (SCENARIO 2)

A Annual savings (ECUm) to companies from economies in Greece and Portugal

	France	FRG	UK	USA	Switzer-land	Other	Total
Capital costs:							
lower value	5.0	4.0	4.0	12.0	2.0	1.0	28
upper value	7.5	6.0	6.0	18.0	3.0	1.5	42
labour costs:							
lower value	2.8	2.2	2.2	6.7	1.1	0.6	15.6
upper value	4.2	3.3	3.3	10.0	1.7	0.9	23.4
total savings:							
lower value	7.8	6.2	6.2	18.7	3.1	1.6	44
upper value	11.7	9.3	9.3	28	4.7	2.4	65
as % total European unit costs:							
lower value	0.14	0.07	0.19	0.26	0.14	0.02	0.13
upper value	0.20	0.10	0.29	0.39	0.22	0.03	0.19
plus savings from scenario 1:							
lower value	0.32	0.34	0.70	1.17	1.43	0.24	0.61
upper value	0.50	0.50	1.11	1.86	2.32	0.32	0.96

B Annual losses (ECUm) to Greece and Portugal

	Greece	Portugal
Output	170	125
as % output	42	30
Employment (000)	0.7 - 1.0	0.4 - 0.6
as % total	23 - 33	13 - 20
Balance of payments in finished drugs		
current	-31	-62
after concentration	-231	-202

TABLE 6.2 (contd)

C Annual gains (ECUm) to current guest countries

	France	FRG	UK	Switzer-land	Other
Output	25	100	90	65	15
as % output	0.30	1.08	1.36	n/d	4
Employment	<---------- 0 ---------->				
Balance of payment in finished drugs					
1984	1140	631	692	877	17
after concentration	1170	731	782	942	32

Sources: Tables 5.1, 6.1, chapter 6.1.

TABLE 6.3 OUTCOME OF EXTENSIVE CONCENTRATION OF PRODUCTION FACILITIES (SCENARIO 3)

A Annual savings (ECUm) to companies from economies in France, Italy and Spain

Origin of companies -------->		France	FRG	UK	USA	Switzer-land	Other	Total
In capital costs:	low	3	7	4	18	3	3	38
	high	6	14	8	36	6	6	76
In labour costs:	low	1.3	2.7	6.6	14.1	1.1	1.1	27
	high	11.3	27.6	16.3	58.1	9.1	9.1	132
Total savings:	low	4.3	9.7	10.6	32.1	4.1	4.1	65
	high	17.3	41.6	24.3	94.1	15.1	15.1	208
As % unit costs:	low	0.07	0.11	0.31	0.44	0.20	0.06	0.19
	high	0.30	0.48	0.71	1.30	0.71	0.24	0.61
plus savings from scenarios 1 and 2:								
As % unit costs:	low	0.40	0.44	1.00	1.62	1.68	0.30	0.79
	high	0.81	1.00	1.81	3.17	3.03	0.56	1.57

B Annual losses (mECU) to current host countries

	France	Italy	Spain
Output	1250	600	300
- as % output	14.8	9.6	11.8
Employment (000)	1.8-2.7	1.2-1.8	1.2-1.8
- as % employment	2.8-4.2	1.9-2.8	3.8-5.6
Balance of payments in finished drugs: 1984	1140	39	-6
after concentration	-110	-560	-300

TABLE 6.3 OUTCOME OF EXTENSIVE CONCENTRATION OF PRODUCTION FACILITIES (SCENARIO £)

C Annual gains (ECUm) to countries of current guests

	FRG	UK	Switzer-land	Other
Output	845	655	350	300
- as % output	8.4	9.9	n/d	9.4
Employment (000)	0-1.4	0-1.4	0-0.3	0-0.3
Balance of payments in finished drugs:				
1984	631	692	877	382
after concentration	1476	1347	1227	682

Source: chapter 6.1, tables 5.1, 6.1.

annual world-wide sales of ECU150m (chapter 3.3). As noted earlier (chapter 2.3) the number of companies with such sales is limited. Only 60 are operating within the Community. This group of major research-based firms has remained remarkably stable in composition over the years, with few companies entering the circle and few leaving (6).

Cost reductions of the type discussed in chapter 6.1 might be of significance here. Supposing prices to be unchanged, they could help to support a larger research programme. In 1984 R&D expenditure in Europe was approximately ECU4200m (table 2.8). The scale of savings envisaged in scenario 3 above could increase this sum by between 6 and 13 per cent. However, a large part of the savings would be realised by US firms and might well not be spent in Europe. Alternatively, firms could shade the prices of their less striking new products with greater comfort. Both outcomes would serve merely to entrench the position of existing companies.

Seriously to increase competition in the research-based sector of the industry would require a drastic reduction in the cost of innovation, so permitting the entry of large number of new contenders. To do so the time and money needed for safety and efficiacy testing would have to be cut. At the present stage of technological development this would seem to present insuperable difficulties. There is no alternative to the use of long-drawn-out trials in animal and human subjects. While this remains the case, however, the possibilities of increased competition through purely economic measures seem to limited.

In the out-of-patent sector the prospects for increased competition are apparently brighter. The barriers to entry are relatively low. Many small generic companies have appeared in recent years. However, a note of caution is appropriate. As the number of major products coming out of patent rises the generic market may be expected to grow, but it is far from clear that it will be supplied by new entrants. When margins are low, costs savings are critical, and large firms are in a better position to realise economies of scale than small ones. In this connection it is significant that the savings due to the unification of the Community market already identified in this report all benefit the major international firm rather than the small local one.

American experience shows that it is quite feasible for a research-based company to enter the generic market itself. Although there are often problems of management style, these can be overcome. The American generic market, which is much larger than that of any Community country, is dominated by the generic arms of the major American multinationals. The situation in the UK is not dissimilar. Generic does not mean small, nor are there any insuperable difficulties in running both kinds of operation in tandem.

A further point has already been made in chapter 4.5. The market for copy products of all kinds is imperfect. The originator is usually able to retain a substantial share of his market after patent protection expires, often at a premium price. For a variety of reasons, discussed earlier, doctors do not necessarily welcome cheaper equivalents and official pressure is often needed to encourage their use. Even in the USA, where most patients pay for their own drugs, administrative action - maximum allowable cost regulations, generic substitution - has been required. In Europe, where drugs form part of national health care provision, this is even more the case. Measures to promote price competition are likely to be necessary; in this sector it is unlikely to happen automatically.

The implications of unifying the market for competition are therefore clear. By themselves the measures taken will do little. The potential cost savings are too small to encourage new entrants; in any case, their benefits are concentrated on large established firms. Thus, they are likely, if anything, to reduce rather than to promote competition. Further and different measures would have to be taken if this were not to happen.

6.3 Towards common prices within Europe?

A genuine common market implies a convergence of prices between member nations. The transparency directive was thought by a number of industrial repondents to be a first step in that direction. The political obstacles to complete harmonisation are both well-known and formidable (chapter 2.5-6) above). It is nevertheless instructive to explore the outcome of moves towards common pricing in order to

identify, if only qualitatively, the possible consequences for both industry and consumers.

Table 6.4 shows what might happen if 1984 prices were equalised at the Community average as weighted by sales. Spain and Portugal are omitted because directly comparable data about the average price levels which prevailed in those countries are not available. Much depends on the elasticity of demand with price which is assumed. It was suggested in chapter 4.5 that this was low - below unity in all probability - but not zero; accordingly, the results obtained when e = 0.5 are the most likely. To unify prices on this basis would lead to a large increase in pharmaceutical expenditure in Italy and a proportionately large decrease in the FRG, the Netherlands and Denmark. Elsewhere the changes would be small. The overall result would be a drop in expenditure of less than two per cent.

Such an outcome would have considerable disadvantages for consumers in Italy and Greece, and almost certainly for those in Portugal and Spain as well. Although incomes are relatively low in these countries the proportion of national income spent on pharmaceuticals is already high (Table 4.6). This state of affairs results from social factors which are difficult to change in the short run. To equalise prices completely would therefore be to transfer income from the poor to the rich.

Offsetting these losses, however, would be changes in the cost structure of the industry, which could affect policies of location. As we already seen (chapter 4.2 and table 4.4), high prices in the FRG are accompanied by high costs, and low prices in Italy and Spain by relatively low costs. To unify prices in the manner indicated would be to make the FRG less attractive as a place to make drugs and Italy and especially Spain more attractive. A conflation of the data of tables 4.4 and 6.4 suggests, for example, that in a unified market the German pharmaceutical industry would actually lose money unless its costs were reduced, whereas that of Italy would become notably more profitable than it is at present. France would benefit from such changes: the increase in local pharmaceutical expenditure would be less than 10 per cent, while the cost structure would be shifted in favour of the industry, which is very probably under-funded. The UK would experience little change (7).

TABLE 6.4 CHANGES IN THE CONSUMPTION OF PHARMACEUTICALS IF ALL PRICES WERE EQUALISED AT THE PRESENT AVERAGE LEVEL

Country	Sales in 1984 (ECUm)				% Change over actual		
	Actual	On unified basis					
		e = 0	e = 0.5	e = 1.5	e = 0	e = 0.5	e = 1.5
Belgium	880	790	834	929	-4.0	-5.2	+5.6
Denmark	370	222	296	463	-40.0	-20.0	+25.1
France	5600	6815	6178	5076	+21.7	+10.3	-9.4
FRG	7660	4320	5753	10199	-43.6	-24.9	+33.1
Greece	450	569	496	400	+26.4	+10.2	-11.1
Ireland	160	130	143	166	-18.8	-10.6	+3.8
Italy	4440	7205	5656	3485	+62.3	+27.4	-21.5
Netherlands	660	421	527	826	-36.2	-20.2	+25.2
UK	3510	3247	3376	3650	-7.5	-3.8	+4.0
Total	23730	23730	23259	25194	0.0	-2.0	+6.2

Source: table 2.1 and chapter 6.3

Thus, to unify prices would be to transfer resources between industry and consumer with the outcome varying sharply from one nation to another. A more limited equalisation would produce similar but more limited changes. Scenarios of this type, however, are largely neutral with respect to the Community as a whole: they assume that the average European price level is satisfactory from the standpoint of the actors involved. This is not necessarily the case. The industry considers, if implicitly rather than explicitly, that is too low as a whole and that prices are certainly much too low in some countries. Consumer representatives take the reverse position. Such conclusions merit a closer examination.

A comparison with other parts of the chemical industry is instructive. Both sectors are capital-intensive in nature; both employ a relatively low labour force with a bias towards highly trained non-manual grades. Much of the chemical market proper, however, is characeterised by multiple suppliers and intense competition. Buyers are relatively few in number, highly informed and extremely sensitive to prices. In these ways it differs from the pharmaceutical market. It has already been suggested (chapter 4.3 and table 4.7) that the pharmaceutical industry compares quite closely with the chemical industry in the efficiency with which it uses its resources. It is, however, notably more profitable that the rest of the chemical sector. Arguably, this results from features in the arrangements by which drugs reach patients, which reduce competition and sensitivity to price and permit an element of rent. Suppose, then, that the profit margin obtained from sales of pharmaceuticals was no higher than that from other chemical products. What would be the effect on pharmaceutical prices in Europe?

Although directly comparable figures for total costs and products are not available an approximate calculation is possible. The 1983 gross margins-value added less labour costs for pharmaceuticals and for other chemicals are shown in table 6.5. They refer to all sales, including those of intermediates, by companies of all nationalities operating within a given nation, and include receipts from exports as well as from sales to local markets. They must therefore be interpreted with caution. Nevertheless, it is clear that margins are generally higher for pharmaceuticals. They suggest that the element of

TABLE 6.5 PHARMACEUTICAL PROFIT MARGINS IN 1983 COMPARED TO THOSE FOR OTHER BRANCHES OF THE CHEMICAL INDUSTRY

	Gross margin (1) as per cent turnover		
	Pharmaceuticals (2)	Other chemical (3)	Difference
Belgium	19.9	11.1	8.8
Denmark	22.0	10.6	11.4
France	7.8	6.1	1.7
FRG	13.8	7.7	6.1
Italy	13.3	6.3	7.0
Spain	15.1	17.3	-2.2
UK	32.1	14.7	17.4
All	16.0	9.2	7.8

(1) See table 4.4, note (3) (2) NACE 257 (3) NACE 25 - NACE 257

Source: Eurostat: Structure and Activity of Industry 1982/3, 1987.

rent identified previously might raise Community prices by an average of about eight per cent. Were this fully realised, the saving in 1984 would have been approximately ECU2000m or one per cent of health care expenditure. There are large variations between one member nation and another, but the differences in national chemical and pharmaceutical industries are so considerable as to make further analysis unprofitable (8).

Such an estimate assumes, of course, that the operations and therefore the costs of the pharmaceutical industry would remain essentially unchanged under such a price regime. The sector as a whole would suffer a reduction in profits but would maintain, for example, its European research effort. This might not happen. Lower profits would certainly handicap companies in their efforts to profitability. Non-European firms might be tempted to run down their activities. More severe reductions in price levels have been discussed on many occasions. Here much turns on the extent to which substantial economies in operation are possible. These may exist - large successful firms ususally have room for improvement in this respect - but to identify them and to estimate their extent is difficult. The pharmaceutical industries of all countries are remarkably similar in nature. To compare what already exists with radical alternatives which do not is no easier than to hear the sound of one hand clapping.

Thus, it may be concluded that current arrangements for delivering drugs to patients may raise prices above what is strictly justifiable in a truly competitive market. There might therefore be room for limited downward movement in average price levels without greatly affecting the operations of the industry. The room for such manoevres, however, is small, and they could prove counter-productive. There is no prima facie case that the industry is inefficient in its use of resources, although alternative systems might be more effective. Only a very different - and much severe environment - would test this point and it remains to be seen if this is either possible or desirable.

6.4 Competitive strength in Europe and in the world

What will be the effect of unification of the Community market on the competitive position of Community pharmaceutical industry?

To answer this question it is necessary to separate the effects on companies based within the Community and on individual countries within the Community. The two are not identical. For example, if unification of the market led to reduced prices in Germany and increased prices in Spain (cf chapter 6.3), German companies might move their production facilities to the latter country. By doing so they would maintain or increase their profits and thereby their recources for competition in the future. Spain would gain in terms of employment. The FRG would lose one kind of economic activitity but would be strengthened in so far as German-owned companies were strengthened. German patients would receive cheaper drugs.

Some possible outcomes are indicated in table 6.6. The harmonisation of registration achieved through mutual recognition or a pan-European registration agency would primarily benefit the research-oriented multinational companies. The reduction in their costs would be small but perceptible (chapter 3.3). There might also be a modest saving to individual member countries. The transparency directive should reduce and possibly eliminate pressures to expand local activities beyond what is desirable on commercial grounds. In the longer run poroduction facilities would be concentrated. In the absence of changes in relative national price levels, this would benefit US comapnies most of all, followed by those of Swizerland, the UK and the FRG, but all multinationals would gain. In terms of countries France, Greece, Italy, Portugal and Spain would suffer and the FRG and the UK would benefit (chapter 6.1). As has already been seen (chapter 6.3), a convergence of price levels would favour the movement of production facilities to low-cost nations. The FRG and the Netherlands would become less attractive as manufacturing sites and Italy, Spain and the UK more attractive. Since relocation takes time and money to accomplish, the multinationals already strong in low-cost areas - those based in the FRG, the UK and the USA (table 2.7) - would be the first to benefit.

TABLE 6.6 OUTCOME OF MOVES TOWARDS UNIFICATION OF THE EUROPEAN MARKET FOR MEMBER COUNTRIES AND FOR COMPANIES OF PARTICULAR NATIONALITIES

Action --> Unified registration procedure

	For country	For company based there
Belgium		Small saving in costs
Demark		do
France		Saving in costs
FRG		Significant saving in costs
Greece	Small saving in expenditure	No saving in costs - no research-based industry
Ireland		do
Italy		Saving in costs
Netherland		do
Portugal		No saving in costs - no research-based industry
Spain		do
UK		Signigicant saving in costs
USA		Substantial saving in costs
Switzerland		Significant saving in costs

Action --> Concentration of facilities

	For country	For company based there
Belgium	No change	Limited reduction in costs
Denmark	No change	No change
France	Output declines	Reduction in costs
FRG	Output increases	do
Greece	Output declines sharply	No change

TABLE 6.6 OUTCOME OF MOVES TOWARDS UNIFICATION OF THE EUROPEAN MARKET FOR MEMBER COUNTRIES AND FOR COMPANIES OF PARTICULAR NATIONANALITIES (continued)

Action --> Concentration of facilities

	For country	For company based there
Ireland	No change	No change
Italy	Limited decline in output	Limited reduction in costs
Netherlands	Increase in output	do
Portugal	Sharp decline in output	No change
Spain	Limited decline in output	No change
UK	Output increases	Signigicant reduction in cost
USA	No change	Substantial saving in costs
Switzerland	Output increases	Significant saving in costs

Action --> Equalisation of prices on a 'neutral' basis

	For country	For company based there
Belgium	Drug bill cut	No change
Denmark	Drug bill sharply cut	do
France	Drug bill raised	Increase in profits
FRG	Drug bill sharply cut	Sharp reduction in profits
Greece	Drug bill raised	No change
Ireland	Drug bill cut	No change
Italy	Drug bill sharply raised	Sharp increase in profits
Netherlands	Drug bill sharply cut	No change
Portugal	Drug bill raised	No change
Spain	do	Increase in profits
UK	Drug bill cut somewhat	No change
USA	Not relevant	No change
Switzerland	do	No change

Source: see text

Thus, the results of unification are complex in nature. The outcome for firms is indeed not the same as that for nations. Much depends on the particular measures taken. Certain points may nevertheless be made. Among the member nations, the UK is in a favourable position. It is a low-cost country, but has a highly developed technical infrastructure, and a scientific community of high quality. For many years it has been favoured by foreign - and particularly American - investors. It is therefore likely to benefit under alsmost all circumstances. France is in the opposite position. A nation which combines high pharmaceutical costs with low prices, it is viewed coolly by most foreign companies. The considerable investment which it has attracted has largely been the result of continued official pressure, which is much resented. It is a prime target for economies if they become possible (chapter 6.1). The position of the other major member countries in their role as producers is less clear-cut.

From the standpoint of the research-oriented companies the changes from unification are unequivocally favourable as far as registration and the concentration of production are concerned. Their costs would be reduced and their resources for the future thereby increased (chapter 6.2). The effects of common price levels within the Community are more difficult to predict. A conflation of the data presented in tables 2.5 and 6.4 suggests that on the 'neutral' basis discussed in chapter 6.3 there would be a small gain in income for the French companies and larger loss for those of the FRG. UK, US and Swiss firms would break even. A reduction in average prices would be unambigiously unfavourable. The effect would be especially severe for Community-based companies; in 1982 sales within the Community were estimated to be more than 80 per cent of those of Italian firms, more than 70 per cent of French, more than 50 per cent of Dutch and German, and nearly 40 per cent of those of British companies. In contrast the Community represented only 30 per cent of Swiss sales and 18 per cent of those based in the USA (9).

In the longer run, the effect of unifying the European market will be to make the strong stronger and the weak weaker. The steps so far will benefit all firms but, as has been seen, those of the UK, the US and Switzerland will benefit the most. The industry itself is in a period of rapid technical change in which the scientific basis of innovation

is moving from organic chemistry to biochemistry and cell biology. Large resources are needed if the transition is to be made smoothly and rapidly and without losing ground to, for instance, the Japanese. New skills have to be acquired and new personnel employed. Even more important, novel approaches inevitably carry an enhanced risk of failure. For the sake of the future these risks must be accepted. For the research-oriented company, this requires that cash flow be maximised. The unification of the market presents a variety of opportunities to do so. These opportunities, however, will favour the companies who already have the resources to exploit them - those which are large, have diversified markets, are organised on multinational lines and are successful innnovators. Such firms are British and American, less certainly German or Swiss, and very doubtfully French or Italian.

6.5 Further action by the Community

To what extent might the Community assist the process of unification by further action?

Based on the analysis presented above, a number of directly relevant steps may be envisaged. In rising order of political complexity they are:

- establishment of a pan-Euorpean registration agency. Subject to the qualifications expressed earlier (chapter 3.4), such an agency would seem to have appreciable advantages over a system of mutual recognition;

- vigorous prosecution of those provisions in the transparency directive which might tend to reduce the unnecessary multiplication of company facilities within the Community (chapter 5.2-5.4);

- further action to reduce price differentials between member nations. A first priority should be to harmonise VAT rates and distributors' margins on pharmaceuticals (table 4.1). In the

longer run an agreement to move over a period of years towards a band of prices sufficiently narrow to make parallel importing no longer worthwhile (chapter 4.4) might be encouraged.

As has previously been emphasised, though, such measures would most probably increase the dominance of the existing major firms and in particular those based outside the Community. It might therefore be thought desirable to stimulate competition by assisting the emergence of new research-based companies on the one hand, and a generic sector on the other. Measures to these ends might include:

- promotion of research into less time-consuming ways to establish the safety and efficacy of new products (chapter 6.2 above);

- the arrangements for prescribing and dispensing drugs within the Community should be harmonised in order to remove artificial barriers. National regulations which discourage the use of generics should be a prime target (10).

A further aim might be to promote the well-being of the Community-based industry. Such an objective would call for:

- stimulation of biomedical and biotechnological research within the Community;

- arrangements parallel to the directive on patent protection for novel research-based pharmaceuticals to ensure adequate prices for such products.

These measures are not mutually exclusive, but represent a menu of possible steps which might help to reconcile divergent aims. The steps already taken are likely to have a considerable impact during the next decade and those who interests are affected negatively may well call for concessions in return. An approach which leads to an optimal compromise would probably be the most productive.

NOTES

1. A similar order is obtained if the number of NCEs introduced is used except that the FRG is now the runner-up to the USA.

2. Relations between the international companies and Greece are cool for a number of reasons and several of them have already withdrawn.

3. Average labour costs in both countries are taken as ECU14,000 per capita; the plants are assumed to be relatively simple and at the bottom of the cost range (cf chapter 5.3).

4. These figures suppose that the indigenous industry is unable to adjust in the short run.

5. The actual net saving will be lower since direct costs in the FRG are unusually high (cf table 4.4).

6. Variations in exchange rates makes comparison difficult, but among the top 50 research-based firms operating in the Community the only new entrants have been the Swedish company Astra, the French firms Sanofi and Sythelabo, both formed by amalgamations in the 1970s, and the British company Boots. The only one to disappear from the ranks of the research-oriented was the Anglo-Australian Nicolas.

7. An approximate calculation is possible. In 1984 the total output of the pharmaceutical industry in the FRG was ECU10,140m of which ECU3040m were exports. Assuming the cost structure of 1983 (table 4.4), then total costs were ECU9,075m. Taking the situation where e = 0.5 in table 6.4, sales within the FRG fall by 34.7 per cent to ECU5.350m, the change in the value of exports to the Community being small. Total output is now approximately ECU8,400m and, if costs remain unchanged, an overall loss of ECU675m would result. Since, however, the volume of production for the German market would have increased by 33%, a substantial increase in total costs is almost certain and the loss would be correspondingly higher. In the same way, increased prices in France and Italy would increase revenues and reduce volume and therefore costs.

8. See table 2.1. The very large difference between the margins in the case of the UK arises in part from UK sales to high-price areas such as the USA.

9. The changes calculated - for sales through retail pharmacies only - were ECU -400m for German companies, 143m for French ones, -40m for those of the USA, -16m for British firms and -12m for those of Switzerland. For the importance of particular national markets to companies of particular nationalities in 1982 see M L Burstall and I S Senior; The Community's pharmaceutical Industry-Evolution of Concentration, Competition and Competitive Strength, 1985, Brussels; European Commission, table 9.4, p115.

10. M L Burstall: Generic Pharmaceuticals in Europe - Blessing or Threat?, 1986, London; Economists Advisory Group, chapter 4, pp 47-70.

APPENDIX A

APPENDIX A

THE MEASUREMENT OF ECONOMIC ACTIVITY IN THE EUROPEAN PHARMACEUTICAL INDUSTRY

There are considerable difficulties in measuring production, consumption and trade in the pharmaceutical industry. Because there are many products, economic activity must be expressed in monetary terms.

1 CONSUMPTION

The data available are only approximate. The statistics of total national consumption used in, for instance, table 2.1, were supplied by IMS Ltd, and refer to human pharmaceuticals only. They have been compiled from national sources and cover all drugs, whether supplied through retail pharmacies, hospitals or other outlets. They are expressed at manufacturers' selling prices.

A larger number of tables, including most of those in chapters 2, are based on the regular audits of retail pharmacies carried out by IMS Ltd. They are somewhat less accurate than the national figures for the following reasons:

- except in the case of the Netherlands, no data about sales through other outlets is given. Typically, retail sales are about 80 per cent of the total in the European Community.

- coverage of retail sales is not quite complete, although it is normally about 90 per cent. Sales by companies with only small proportion of the market are often omitted.

In total, therefore, about 70-75 per cent of national sales are identified. It is possible that these figures under-estimate the share of small local firms in national markets. The IMS audit service covers all member countries of the European Community except Denmark.

2 PRODUCTION

Production statistics are compiled on bases which vary from nation to nation. They may or may not include veterinary as well as human drugs, and, again, may or may not include intermediates and active compounds that are later converted into dosage forms. For these reasons, production normally exceeds consumption by an appreciable margin.

3 TRADE

Trade statistics are gathered on a uniform basis. They differentiate between medicinal etc products (SITC 541) and various sub-categories, of which medicaments (SITC 5417) is the most important. This latter includes all products made up ready for retail sales, together with bulk mixtures requiring conversion into dosage forms. In this report category 5417 is referred to as 'finished drugs'.

APPENDIX B

APPENDIX B

Two problems arise in the estimation of costs.

The first concerns the capital employed. A sample of 23 mainly American multinational firms, extracted from Scrip's Pharmaceutical Company League Tables 1985/6, 1987, Richmond: PJB Publications, generated ECU1.12 of turnover per ECU of capital employed in their world-wide pharmaceutical operations, with marginal productivity of ECU1.21. The relationship was:

(capital employed) = 0.828 (turnover) + 100 ($r = 0.89$)

The average ratio of fixed capital to turnover was found from UK company data (Business Ratios - Pharmaceuticals, 1987) to be between 1:2.8 and 1:3.5 for firms involved mainly or entirely in pharmaceuticals. This was no systematic variation with turnover. This ratio was therefore taken as 1:3. The same source suggested that the ratio of depreciation to fixed capital was between 1:8 and 1:13. Accordingly, it was taken to be 1:10.

These relationships were assumed to hold for all member nations and are the basis for the estimates of capital employed and depreciation given in table 4.4. Although they are highly approximate, it may be noted that the profit margins and profitability figures which result are in reasonable agreement with the quantitative judgements of informed observers. Profit margins are in any case relatively insensitive to errors in estimating depreciation payments, since the latter are in comparatively small proportion of total costs.

The second problem concerns the estimation of the costs incurred within the Community by firms of particular nationality. In an industry dominated by multinational companies this is difficult: our enquiries show that such firms operate on a world-wide basis and that the allocation of costs between countries is largely arbitrary. In this report we have nevertheless attempted to do so in the following way:

a. The total turnover of the Community industry was taken from tables 4.4: allowing for production in Greece, the Netherlands and Portugal, a figure of ECU34,000m for the total costs of the Community pharmaceutical industry was obtained.

b. Production in each country by firms of particular nationality was calculated from the data of tables 2.5-2.7 and grossed up to cover all pharmaceuticals from that of table 2.1. To the resulting were added estimates of the exports by such firms from each country; these are based on fragmentary sources and are open to a large element of error. The totals obtained were then multiplied by the cost ratios of table 4.4 to yield the corresponding costs.

The total cost found in (a) above was then apportioned among the companies of particular nationality in proportion to the estimates of (b). This suggests that German firms bore 26.2 per cent of the total cost, US 21.2, French 16.8, British 10.1, Swiss 6.3 and those of other nationalities 19.4 per cent.

These estimates were used in chapter 6.1 of the report. It should be emphasised that they are highly tentative. In addition to the obvious problems of allocation already indicated, the cost structures taken are unavoidably national averages, which do not allow for differences between the operations of firms which are based in particular country and those which, say, have only a formulation plant there. It is probable that the costs attributable to US companies have therefore been overstated and those attributable to those of 'other nationalities' have been understated. This does not, however, alter the sense of the main conclusion of chapter 6.1 ie that the reductions in unit costs would be concentrated disproportionately on American firms.

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