

What Future for the Competitive European Pharmaceutical Sector?

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Introduction & Summary

Having reached the half-way point of the European Union's "Lisbon Strategy" the fundamentals of Europe's relative decline remain unchanged. This is nowhere more apparent than in the pharmaceutical sector, one of the most research-intensive sectors of industry and a major part of European ambitions to generate growth and employment. The President of the European Commission has acknowledged that the Lisbon Strategy, the "flagship" of EU policy, is barely out of the harbour.

Research suggests that Europe's competitors, particularly the USA, are continuing to make the most of Europe's lack of progress. Even European firms are now placing their investments, including research and operational headquarters, in the US in order to benefit from some of the "home player" advantages in a vibrant market. Data from the European Federation of Pharmaceutical Industries and Associations (EFPIA) show that more than 40 percent of R&D spending by EU companies was placed outside of Europe in 1999, compared to just 27 percent in 1990, in an almost directly inverse relationship with the global importance of the European pharmaceutical market, which declined from 37.8 percent of the world market in 1990 to 23.7 percent in 2001.

Overview of Major European Pharmaceutical Markets 2004					
	Production (€m)	Employees	Total Market Size (€m)	Generics' Market Share (%)	Trade Balance
France	31,296	98,900	21,320	5.4	5,900
Germany	21,262	119,800	22,670	26.8	2,648
UK	21,685	73,000	16,713	17.2	5,250
Switzerland	12,338	29,613	2,549	4.8	9,789
Ireland	14,293	21,000	1,130	7.1	11,444
Italy	17,989	84,088	14,606	Na	-1,023

(Source: EFPIA)

The European Union does still have a significant presence in world pharmaceuticals. Five EU countries alone have almost 400,000 jobs in the sector. Ireland has a pharmaceutical trade balance that is 10 times the size of its domestic pharmaceutical market, citing relative advantages from the youth and quality of its workforce and advantageous rates of corporate taxation. These claims are supported by analysis showing that amongst the EU15 only Ireland exceeds US levels of gross value added per employee¹. Europe will clearly remain a major pharmaceutical market, whether in research, manufacture, or consumption, but it is losing out in maintaining its share of the global growth of these activities.

Whilst the strategic goal of European policy is to support a competitive and innovative pharmaceutical industry, the evidence suggests that many individual policy actions can still have the opposite effect. Far from encouraging overseas firms to adopt Europe as an important base, governments' actions (or lack of action) are leading European firms to place their new investments elsewhere.

As can be expected given the importance of the US market in firms' profitability, and hence their ability to invest increasingly in R&D, the major European pharmaceutical firms have for some years been purposely increasing their shareholder bases in the US. Firms tend to be most successful in their "home" market, and the increasing

difference between the prospects of new medicines in the US and European markets, is leading to the ‘Americanisation’ of European firms, including their R&D activities.

“Home” US & EU15 Major Firms’ Market Shares (% 2003)				
	UK	France	Germany	US
Home	20	33	41	62
US	36	28	24	62
EU15	38	60	62	24
Source: Pammolli et al (2004). IMS data				

The European Commission has recognised that the European Union’s relative decline has continued since the launch of the Lisbon Strategy. The “G10” High Level Group on Pharmaceuticals, the subsequent Commission

Communication, and Vice-President Verheugen’s creation of a Pharmaceutical Forum, all represent valuable attempts to give direction and pace to the Strategy.

Some EU Member States too have been taking their own steps. In the UK the “PICTF” work has seen the industry working closely with the Government to find practical solutions to the challenge that they face, and more recently in France the creation of a Strategic Council for the Healthcare Industry secured some rapid improvements.

European health systems’ antipathy towards pharmaceutical innovation lies at the heart of much of the challenge in achieving the Lisbon Strategy. Recently-imposed price, reimbursement or budget cuts in France, Germany, the UK, Spain and Denmark continue to demonstrate this point. Whilst the worst performing health systems in terms of delays to making new medicines available to patients have improved in recent years, some of the best performing systems have been going in the opposite direction. In the UK, the record of poor adoption of new medicines is now compounded by the introduction of significant delays whilst prescribers await guidance from the National Institute for Health and Clinical Excellence (NICE)

Price regulations, and parallel trade resulting from the interplay of each country’s

Europe: Slowly Following the US Lead		
	Implementation Date	
<i>Legislation</i>	<i>US</i>	<i>Europe</i>
Patent Term Restoration	1984	1992
Orphan Drug Incentives	1984	2000
Biotech Patents	1983	2000+
Paediatric Incentives	1998	2006?

pricing actions, continue to affect pharmaceutical companies’ expectations of returns on their European R&D investments. As yet the consequences for R&D from new or recent regulations on clinical trials, paediatric research and financial penalties are largely unknown. Europe is too often a slow and reluctant follower of an American lead, whether in incentives for biotech patenting, orphan drugs or paediatric research

incentives, fast track licensing, or the use of fiscal incentives to R&D.

The longer that action to reverse this situation is delayed, the greater is the challenge facing the European Union. The new EU “Pharmaceutical Forum” is proposed to meet once each year and is unlikely, therefore, to meet more than four times by the 2010 target.

Clear and immediate direction, accompanied by specific actions to improve the environment for pharmaceutical R&D and manufacturing, is needed. Participants in

the UK Presidency roundtable discussion on 1st December 2005 in London
“Delivering Patient-Centered Innovation in Medicines - The Role of a Competitive European Pharmaceutical Industry”, could take the opportunity to turn five years of analysis and good intentions into concerted action.

Much of the change that would be necessary in order to try to regain lost leadership in pharmaceuticals is cultural, and requires a change of attitudes towards pharmaceutical innovation and the use of new medicines.

The “Lisbon Strategy”

It is now more than five years since the Member States of the European Union committed themselves to the enterprise goals now known as the “Lisbon Strategy”. At the Lisbon European Council in March 2000 ministers set themselves the 10-year target of making Europe the most competitive and dynamic knowledge-based economy in the world, capable of sustained economic growth with more and better jobs and greater social cohesion. Immediately following the Council meeting the European Commission set out the strategy to meet the target.

G10 Medicines: In 2001 the European Commission established a High Level Group on Innovation and Access, known as “G10 Medicines”. Its 2002 report, with 14 recommendations, was followed by a Commission Communication the following year, entitled: “*A Stronger European-based Pharmaceutical Industry for the Benefit of the Patient - A Call for Action*”.

For all this activity in Brussels, it is clear that at the half-way stage for the Lisbon Strategy little progress has been made. Meanwhile, new global competitors, particularly China, are adding to the challenge facing Europe. In March 2005 the Commission President, José Manuel Barroso, confirmed that the Lisbon Strategy remains the “flagship” of European policy, whilst adding that: “*We have barely sailed out of the harbour*”².

Pharmaceutical Forum: The formation of a new European Commission and European Parliament has provided an opportunity to renew the European commitment to the Lisbon Strategy, following a mid-term review that amply demonstrated the lack of progress. With regard to pharmaceuticals, the Vice-President of the new Commission, Günter Verheugen, has noted that:

“In 1992, six out of the top ten medicines were developed in Europe; by 2002, this had fallen to only two. Europe, the Commission, and the Member States, must decide whether we want to continue to be a leading player in pharmaceutical innovation or whether we simply step aside and let others overtake this job. You will not be surprised to hear that I have no intention of stepping aside”³.

To support this ambition, Vice-President Verheugen announced the creation of a Pharmaceutical Forum, to meet annually to monitor and guide progress in re-establishing Europe’s role as a global leader in pharmaceutical innovation. Around the same time the Research Directorate-General of the European Commission announced its 7th Framework Programme for Research, with a considerably strengthened commitment to supporting innovation and public-private partnerships in health research.

Pharmaceutical Industry Competitiveness Task Force: Following serious concerns expressed by industry representatives with regard to Britain’s competitive position in pharmaceuticals, in 2000 the UK Government created the Pharmaceutical Industry Competitiveness Task Force (PICTF), co-chaired by the junior health minister, Lord Hunt and the chief executive of AstraZeneca, Sir Tom McKillop. The Task Force published its report in 2001, and a work programme and annual system of performance indicators was set in place.

Strategic Council for the Healthcare Industry: More recently, in September 2004, the French Prime Minister took similar steps, through the creation of the Strategic Council for the Healthcare Industry which he personally chaired. It is an indicator of the French Government's desire to boost pharmaceutical employment and investment in France, that specific steps were agreed and acted upon within months of the creation of this new group.

The French Government's active support for the merger that created Sanofi-Aventis, also served to demonstrate the Government's renewed commitment to strengthening the country's role as one of Europe's leading bases for research-based pharmaceuticals. Hourly unit labour costs⁴ in France have fallen slightly from a peak of £12.26 in 1995 to £11.62 in 2002, and in Germany from £19.18 to £16.73, whilst they rose in the UK from £8.73 to £11.66 over the same period. Whilst labour costs are just one element of competitiveness, the data show that the wide differentials of the past, upon which the UK often relied for its competitiveness, are narrowing. If the renewed focus on growth and employment within the Lisbon Strategy is pursued by France and the other EU Member States, then competition within the EU for new investment will continue to intensify, particularly with the inclusion of the new Member States.

The European Decline

Studies during the time of the Lisbon Strategy have consistently demonstrated that Europe is suffering a relative decline in the research, development, and manufacture of pharmaceuticals.

Two authoritative reports for the European Commission have amply demonstrated the problems that Europe faces.

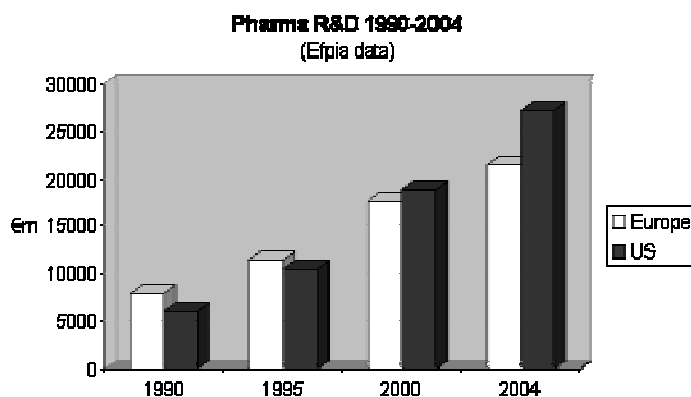
Share of Patent Citations (by HQ Location of Assignee) ⁵				
Country	Pharma %		Biotech %	
	1978-88	1987-97	1978-88	1987-97
France	5.48	6.85	4.77	5.18
Germany	12.86	8.59	7.58	6.87
Switzerland ⁶	4.02	2.98	4.17	5.12
UK ⁶	9.48	10.98	8.08	8.57
USA	44.33	51.02	54.16	55.61

In November 2000 the study “*Global Competitiveness in Pharmaceuticals: A European Perspective*”⁷ found that Europe was not only experiencing a

quantitative decline as a location for innovation in pharmaceuticals and biotechnology, but also a decline in the quality of innovation in Europe.

The authors highlighted the European industry’s failure to keep pace with the consistently strong rate of growth in US R&D spending during the 1990s, and the increasing dominance of the US in terms of the share of patent citations (i.e. a measure of patents that are sufficiently important for citation in subsequent patent applications). The best growth in the share of patent citations for a major European market was 1.5 percentage points, compared to almost 5 points added to the US share,

and 4 points lost by Germany. The authors of the 2000 report concluded that:



“*In the 1980s the European industry has grown less than the US industry. This stems from a deceleration of the growth of the industry in Europe, and an acceleration of US industry growth. The restructuring of pharmaceutical*

demand, and particularly of the health care system, in the US, seems to have translated into demand growth, which has benefited mainly the US firms”

Four years later Charles River Associates produced a further study for the European Commission on *Innovation in the Pharmaceutical Sector*⁸, following a significant decline in new applications to the medicines licensing authorities in both the EU and the USA between 1999 and 2003. The authors identified a fall in innovative productivity, with increasing spending on R&D failing to produce similar increases in the number of new products. They noted that: “*There is also a clear trend with a higher proportion of R&D expenditures being spent in the US at the expense of*

*Europe and Japan*⁹. They identified several factors that may have contributed to a five-fold increase in the costs of clinical development and a 60 percent increase in the real costs of preclinical development in ten years¹⁰ including:

- Increasing complexity of clinical trials, for increasingly intricate products, although the authors suggest that this applies to few products.
- Increasing numbers of clinical trials required, due to the need for comparative studies for pricing and reimbursement negotiations, and marketing.
- The costs of several high-profile product withdrawals.
- Costs of introducing new technology into R&D.

The report expressed serious concern that, against this background of increasing R&D costs, the EU has suffered a relative decline in pharmaceutical R&D with regard to the US¹¹ despite having lower costs than the US, and that it now faces increasingly strong global competition, in addition to increasing transatlantic competition. This new challenge is most severe in global manufacturing. India, for example, now has the second largest number of pharmaceutical manufacturing facilities approved by the US Food & Drug Administration (FDA) and is also experiencing a surge in scientific activity¹². Between 1994 and 2000 American firms increased their R&D investments in Singapore from \$167m to \$548m, in China from \$7m to \$506m, and in South Korea from \$17m to \$131m, and the European share of US firms' R&D declined¹³.

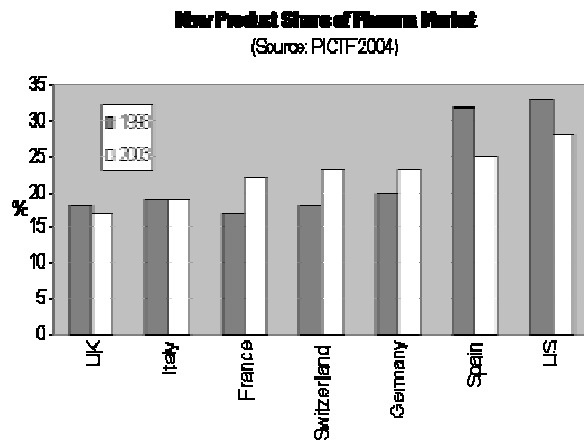
Firms' expectations of future returns within European markets appear to have a significant and understandable impact on the location of innovative and manufacturing activity. Price regulation, parallel trade, generic substitution, therapeutic reference pricing, and differences in data exclusivity provisions are all cited as aspects of the European market that affect company expectations. Other researchers have estimated that the US lead over Europe in pharmaceutical R&D will grow from a margin of 20 percent in 2002, to being double the European level in 2012, based on current trends¹⁴.

The main recommendations from the Charles River report were that there should be measures that support faster market access, particularly for the most innovative products, and streamlined regulation.

Research by Europe Economics into the delays between an important new medicine being authorised for use and actually being available on prescription showed that during the 1990s patients in Portugal had to wait almost three years on average, and those in France waited around two and a half years, whereas in the UK the wait was a little over 6 months¹⁵. The most substantial delays were largely due to issues relating to pricing and reimbursement requirements. Subsequent research by Cambridge Pharma Consultancy, covering 78 products authorised between 1997 and 2001, showed that the average delay in Portugal and France had decreased to a little over a year, but that in several other European countries the situation was worsening¹⁶.

The UK: Lost Leadership in Europe?

In many ways the UK has been going through a convergence with its European partners. Not only have labour costs been rising towards the European average, due particularly to an increase in National Insurance Contributions and rising pension costs, but the imposition in 2005 of a 7 percent price cut has similarities with arbitrary



systems that have long existed in many other European countries. Prior to the 7 percent cut, medicines already comprised a relatively small share of UK health spending, and in 2004 are estimated to have fallen to the lowest proportion of health spending for a decade, at 11.2 percent¹⁷. The 7 percent price cut in the 2005 PPRS continues a trend of UK price cuts and

freezes that began with a 2.5 percent cut at the time of the 1993 PPRS, followed by a 4.5 percent cut in 1999, increasing to 7 percent in 2005.

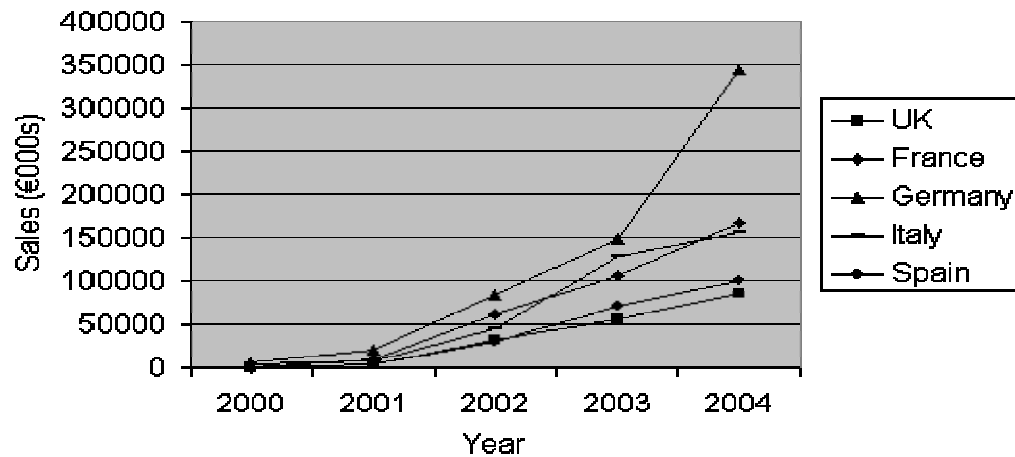
The low share of UK health spending on pharmaceuticals is partly explained by very restrictive use of new medicines and very high use of off-patent generics. Uptake of new medicines in the UK is particularly poor, taking around five years to reach even half of the average Europe level of usage¹⁸.

The *de jure* ability to supply a new medicine is only half of the picture on delays in providing patients with access to new medicines. In recent years in the UK the very slow adoption of newly-licensed medicines by the NHS has worsened, as prescribers face new limitations on their ability to determine the treatment of their patients.

The 2004 PICTF performance indicators showed that the UK continued to fall well behind most of its main competitors for pharmaceutical R&D and manufacturing, in terms of the use of medicines launched within the previous five years¹⁹. Research on access to new cancer medicines, for example, has shown that the UK has a particularly poor record in making these medicines available to cancer patients, even in the context of significant delays in other EU Member States²⁰. This research has provided a disease-specific demonstration of the poor UK record in making modern medicines available to patients.

The chart below shows the sales value of five cancer medicines launched in Europe between 1999 and 2004. The number of new cases of cancer each year in the UK, at around 275,000, is similar to the numbers for France and Italy, and substantially higher than those in Spain. UK patients' survival rates at one and five years are below the levels of all four of the other countries listed.

Access to New Cancer Medicines



During the PICTF analysis the UK Government expressed a belief that the creation of NICE would promote the uptake of cost-effective medicines²¹. The UK's continuing poor uptake of new medicines suggests that this prediction has not been borne out in practice.

The poor prospects for innovative medicines in the UK market inevitably affect decisions on the location of company investments in R&D and manufacturing. Research has shown that companies enjoy distinct sales advantages in their home market. The rapid adoption of new medicines in the US is giving firms, whose major bases are within the US, a global advantage. Delays incurred by an innovative product, particularly a first-in-class product, whether due to price negotiations or NICE-type assessments, can further reduce the time between the first to launch and subsequent competitors, thus penalising the most innovative firms.

Several studies have demonstrated the link between the strength of the local market and decisions on the location of R&D. Ramirez and Tylecote found that:

“There is evidence that European (much less US) pharmaceutical firms are increasingly globalizing their innovative efforts. This is particularly true in the UK. The two major ‘UK’ pharmaceutical firms, GlaxoSmithKline and AstraZeneca ... both have most of their R&D effort outside of the UK, and they both now have R&D headquarters in other countries (the US and Sweden respectively) which appear to be somewhat more attractive in terms of science base – as well as, in the US case, market attractiveness.”²²

Policies and their Effects

The G10 process highlighted the complexity of the pharmaceutical industry's place in Europe. The industry is probably the most heavily regulated, with regulatory interventions spanning product safety, quality, efficacy, manufacturing processes, product cost effectiveness, pricing, health system reimbursement, promotion and use. In addition, the sheer diversity of pricing regimes across European countries adds significantly to the complexity for companies. UK and European policies can both encourage and discourage investment in pharmaceutical R&D and manufacturing.

UK Policy

British governments have a long record of recognition of the importance of a strong biotech and pharmaceutical sector, both to the UK and European economies as well as to patients. Very recently Lord Sainsbury, a minister at the Department for Trade and Industry, restated this understanding saying:

“We are well aware that in order to maintain and improve the environment here for research, development and manufacturing we must build on the UK's strengths and work to reduce and remove the barriers to growth. ...The UK needs to continuously improve its appeal in the face of growing competition from other countries”²³.

Parallel Trade: Parallel trade between EU Member States is a significant challenge to the industry in Europe, and most particularly to the UK-based industry, and is due to the variety of price-setting systems deployed by governments. It directly undermines national policies to support innovation and primarily benefits the entrepreneurs who deal in parallel traded products^{24,25}. In doing so it also undermines progress against the Lisbon Strategy. Anecdotal evidence supports the contention that parallel trade has contributed to the relative decline of pharmaceutical manufacturing in the UK²⁶.

The UK suffers particularly badly from parallel imports. Around 70 percent of parallel trade in the EU (2004) is into the UK market²⁷, undermining the declared aim of the PPRS to reward innovation and research. Estimates put the cost of parallel trade to the UK-based pharmaceutical industry at £1.4bn a year, with more than one in eight prescriptions filled with a parallel-imported product²⁸. Germany and the Netherlands also experience significant parallel importation²⁹. Systems of reimbursing pharmacists often provide significant incentives for parallel trade, as is the case in the UK.

Launch Delays: Whereas in the past the UK had no delay between a medicine being licensed and its UK launch, the creation of NICE in England has had a serious effect, with many prescribers awaiting official guidance before putting their patients onto newly available medicines. The situation is not confined to the English NHS, as organisations similar to NICE have developed in Scotland and Wales, namely the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSC). It currently takes an average of 18 months for a NICE appraisal to be completed, and cancer drugs have suffered particularly from delays. NICE has recently announced a new ‘fast track’ Single Technology Appraisal (STA) procedure,

which has been broadly welcomed as a step to reducing these new delays for some “life saving” medicines.³⁰

As mentioned earlier, the UK also suffers from very slow adoption of new medicines, the causes of which are not solely financial, but also deep-rooted in the culture and operation of the NHS³¹. Data for 2002 show that none of the top-20 medicines purchased by the NHS had been licensed in the previous three years, and only one had been licensed in the preceding five years³². Current proposals to decentralise decision-making and to introduce a diversity of supply of NHS services could have a positive impact in tackling some of the cultural barriers to the adoption of innovative technologies in patient care. Despite the intention that NICE guidance would address the UK’s poor record in the adoption of effective new medicines, the implementation of guidelines has itself been poor. Research commissioned by NICE found that almost half of all guidance had not been implemented as expected³³, and a study by the Audit Commission found that few providers were able to verify that they had complied with NICE guidance³⁴.

Rewarding R&D: The UK was on a par with comparable industrialised countries in terms of investment in R&D until the intensity of R&D in other countries accelerated in the 1980s. Eurostat data for 2003 suggest that *gross* domestic R&D spending stood at 1.88 percent of GDP in the UK, compared to 2.2 percent in France³⁵, 2.52 percent in Germany, 3.15 percent in Japan, and 2.59 percent in the USA³⁶. The British Government aims to achieve an eventual level of 2.5 percent of GDP.

Tax credits for R&D have a long history. Estimates put the fiscal value of US R&D tax credits at \$2.24bn between 1997 and 2002, and incentives in EU Member States at over \$1bn per annum during the early 1990s³⁷. The UK was late in introducing tax credits, creating a scheme for SMEs in 2000, which was extended to large firms two years later³⁸.

The UK Government claims that its R&D tax credit scheme is both simple and generous by international standards, not least because it rewards total R&D rather than additional R&D (as in the US scheme). In the pharmaceutical sector the effect of this structure is to concentrate most of the benefit in the largest firms, rather than focus on winning new R&D investments. In the UK pharmaceutical sector just two firms account for 72 percent of eligible R&D³⁹. The DTI’s recently published R&D scoreboard demonstrates, however, that despite the new fiscal incentives UK R&D has not kept pace with principal competitors, in particular the US, and industrial R&D declined slightly in 2004, driven by a reduction in UK investments by firms based elsewhere⁴⁰.

DTI analysis suggests that the UK needs to encourage more pharmaceutical firms to invest in R&D in the UK, rather than simply encourage existing firms to increase their R&D spending⁴¹. In July 2005 the Government began consultation on “enhancing” the R&D tax credit scheme, which may provide an opportunity to enhance the attractiveness of the UK as a base for new global investments by large pharmaceutical firms, including research into malaria and other diseases of importance in the least developed countries.

Aside from fiscal policy there are many other factors affecting R&D location decisions by global firms, particularly the availability of skilled scientists, and level of

public investment in R&D. Research has suggested that publicly-funded basic research can have a significant effect on industrial innovation⁴². In the US the National Institutes of Health (NIH), a government agency, has benefited from large increases in its budget, which currently stands at a level in excess of \$27bn. In Ireland, the Industrial Development Agency cites the quality of the local workforce as an important factor in the country's achievement of new and repeat pharmaceutical investments⁴³.

Science and society: The activities of animal rights extremists remain a serious threat to the UK's research based industries, including medical, pharmaceutical and biotech research. Fortunately, the levels of extremism seen in the UK have not been replicated elsewhere. Substantial steps have been taken to deal with this UK problem, including the creation of a National Extremism Tactical Co-ordinating Unit (NETCU) in 2004 to assist police forces; the use of Anti-Social Behaviour Orders (ASBOs) to restrain individuals; and new legal powers in the Serious Organised Crime and Police Act.

The Government's policy document on animal welfare and extremism outlined further possible actions, and included a Foreword from the Prime Minister, in which he commented:

*"Only the United States has a more successful bioscience sector than Britain. But these scientific advances and this economic success story is under threat from a tiny minority of animal rights extremists who are behind an illegal campaign of intimidation and violence against individuals and firms involved in this vital work"*⁴⁴.

European Policy

Price regulation and market access: The impact of price regulation of pharmaceuticals, and its negative effects on European pharmaceutical R&D and manufacturing has now been widely recognised, and the need for action has been heightened by the ongoing process of EU enlargement and court decisions relating to parallel trade and pharmaceutical supply and pricing. European Commission Vice-President Verheugen has said:

"The G10 process highlighted the constant friction between rewarding innovation and protecting severely overstretched health care budgets. However, if we are to make Europe a place attractive to investors we must find a resolution. In our response to the G10 report we undertook to review alternative approaches to pricing. This was agreed by Member States. We will take this forward in close cooperation with the upcoming Presidencies in the Council.

*"Our objective is to examine the benefits of giving industry more flexibility in establishing prices without sacrificing any capacity of Member States to protect their health care budgets. In addition, this reflection should look at the speed of access to the market, lifting of pricing controls for medicines that fall outside the state sector, parallel trade and the impact of the Transparency Directive"*⁴⁵.

Market regulation of the pharmaceutical industry in Europe creates levels of commercial uncertainty and complexity that work against the retention and development of a globally-competitive European pharmaceutical sector.

As noted earlier, the UK Government imposed a 7 percent price cut on pharmaceuticals from January 2005. Other European countries too have continued to take *ad hoc* actions on prices, not least in Germany, where a mandatory discount on patented products was recently introduced. Since 1 January 2003, the “Beitragssatzsicherungsgesetz” (law to secure contribution rates) obliges manufacturers to grant a discount on the retail prices of their products when these are sold to members of the statutory sick funds. Initially the discount was set at 6% but was increased to 16 percent for 2004.

In January 2005 the French government signed a medical agreement with three major physicians’ associations that sets targets for cutting spending in 2005 on several widely prescribed drug classes including a 12.5 percent reduction in spending for statins, saving €161 million; a 10 percent reduction for antibiotics, saving €91 million; and a 10 percent reduction for anxiolytics and hypnotics, saving €33 million. The agreement also called for physicians to save €55 million in 2005 by increasing their prescribing of generic drugs.

In Spain, where pharmaceutical prices are set by the Ministry of Public Health and Consumer Affairs through negotiations with the pharmaceutical industry, negotiations have at times resulted in profit-payback agreements and/or price reductions. For instance, a 6 percent price reduction was applied to all pharmaceutical products over a certain price in 1999⁴⁶. In Denmark, there has been a succession of price freezes since the beginning of 1994. The latest meant that prices of prescription and reimbursable OTC drugs were frozen between 1998 and 2000, and patients are faced with high co-payments for innovative drugs⁴⁷.

Pricing systems in Europe create damaging uncertainty in an industry where decision making must take a long-term perspective. As systems are modified and decisions taken for short-term expediency, companies cannot predict what price a new medicine is likely to achieve when it reaches market, or if it will be reimbursed at all⁴⁸.

Moreover pricing and reimbursement difficulties are behind many of the delays before patients can benefit from important new medicines. This is worse in the new member states than the EU15. The delays caused by pricing and reimbursement procedures vary widely, between countries and between products. Average times for such procedures have been documented as 394 days in France, 284 in Italy, 161 in Spain and 100 in Sweden⁴⁹. In Poland, no new innovative products have been reimbursed for almost seven years. Prior to the creation of NICE a significant and welcome strength of the UK system had been that the PPRS enabled a direct route to market without the hindrance of formal pricing procedures, as has also been the case in Germany.

Aside from general uncertainty and fragmentation, Europe’s pricing and reimbursement regimes in large part encourage firms with relatively low levels of R&D intensity in comparison with the US market. There is neither a strong ‘carrot’ nor ‘stick’ in relatively restrictive environments to engage in a greater intensity of research.⁵⁰ According to the Pammolli study on competitiveness in pharmaceuticals:

“Systems that rely on competition promote a clear distinction between firms that act as innovators and firms that act as imitators after patent expiry. ... systems that rely on administered prices nurture strategies of pre-emptive brand proliferation and horizontal differentiation by imitative brand name products well before patent expiry”⁵¹.

The result is that while in Europe many new drugs are cheaper, market structures mean that the scope for market-based competition can be limited, particularly in the off-patent sector so that prices for old and widely-used medicines can be high.

European Research and the “7th Framework Programme”: Research has been put at the core of the Lisbon Strategy. The proposed European Technology Platform for Innovative Medicines, announced by the European Commission (DG Research) in April 2005, alongside the 7th Framework Programme, could become an important institution for the strengthening of biomedical research in Europe. The Commission’s latest Framework Programme⁵² covering the period from 2007 to 2013 identifies three areas of research in the health field: Biotech, generic tools and technologies; Translating research for human health; and optimising the delivery of healthcare. Across all these areas, it identified the two strategic issues of child health and health of the ageing population as the core of its activities.

The Commission’s strategy for improving competitiveness in the pharmaceutical industry includes a €2.6 billion entrepreneurship and innovation programme which will give help to SMEs at the forefront of the biotechnology sector.

Patient Information: European Commissioners Verheugen and Kyprianou have stated a shared aim to follow up on the G10 recommendation that public-private partnerships should be formed to improve public access to quality information on medicines. The improved flow of information from a wide range of sources, including manufacturers, can improve patient compliance with drug regimens, cutting waste and improving health outcomes. It can also improve diagnosis and therefore preventative treatment of serious illnesses, such as diabetes, with severe long term consequences; and assist in de-stigmatising many medical conditions⁵³. European citizens are losing out from current restrictions on the dissemination of medicines information, and face considerable risks from the volume of “information” now available to them on the Internet from completely unregulated sources.

Clinical Trials Directive: Some have argued that new Clinical Trials Directive, introduced in May 2004, may prove to be an obstacle to efficient medical research, penalising small teams of researchers without the resources to submit paperwork and afford the fees required to gain authorisation for studies using healthy volunteers. Last December, The Guardian noted that “*Small-scale clinical trials at British universities have become too expensive and the problems could eventually move research to Eastern Europe and Asia*”⁵⁴.

Sir Liam Donaldson, the Chief Medical Officer for England, recently commented that: “*It is important that we are willing to reflect on the Directive if it is having an adverse effect ... It would benefit to do an early, informal review of the Directive. When you have so many authoritative voices expressing concerns then you probably do have a problem*”⁵⁵.

Whilst the Directive has been widely welcomed, it is important that it does not become a barrier to research, thus compounding Europe’s relative decline in R&D.

Paediatric Medicines Regulation⁵⁶: The European Commission’s recently revised proposals on Paediatric Medicines recognise the need to stimulate paediatric research

in Europe, given that many medicines used for children are not licensed for paediatric use. The Directive creates obligations for pharmaceutical companies to conduct often complex, costly and lengthy paediatric research, whilst also giving incentives to do so through a six month extension of market exclusivity. The Directive currently awaits approval from the Council of Ministers. The UK government has also highlighted the importance of paediatric research, and around 10 percent of the public budget for clinical research is earmarked for paediatrics⁵⁷.

Draft Financial Penalties Regulation⁵⁸: The Draft Penalties Regulation provides for EU-enforcement of firms' obligations linked to the licensing of medicines. It covers medicines approved through the EMEA, but not authorisations that take place through national bodies. It gives the EMEA powers to carry out regulatory investigations, including into provision of information in marketing applications and post-marketing requirements.

As it stands, the Draft Regulation leaves many issues in need of clarification, including questions of subsidiarity and the risks of parallel enforcement by national authorities and by the European Commission, as well as the potentially punitive levels of the penalties that could be imposed on large firms.

Conclusions and Recommendations

Five years on from Lisbon very little at all has changed. The US continues to dominate pharmaceutical R&D and manufacturing, and European firms are increasingly moving towards the US as a base rather than vice versa. R&D growth rates in the US continue as a multiple of European levels, and the US public sector commitment to basic research and collaboration with innovative firms continues to draw research intensive firms to them and reinforce the American lead. The US was first to reward orphan medicines research and paediatric trials, and has operated a system of R&D tax credits since the 1980s. The National Institutes for Health dates back more than a century. The support for innovation has been deep-rooted. It is this cultural shift, as much as anything, that needs to be made if Europe is to succeed against the Lisbon Strategy. In the UK, the slow adoption of new medicines is due not only to NICE and its counterparts in Scotland and Wales, or rationing by cash-constrained prescribers, but also a widespread culture of caution within the NHS, that can easily be reinforced by government policies.

Next steps in Europe and the UK must address this cultural challenge, if achieving the Lisbon goals is to become possible.

At the European level the 1st December roundtable meeting could be used as the platform for Vice-President Verheugen to offer real progress in the realisation of the Lisbon goals, rather than wait for the first meeting of the new Pharmaceutical Forum. The G10 made 14 recommendations, and the follow-up on these needs to be charted. Already some six months will have passed since the announcement of the Pharmaceutical Forum. Further detail on how the Commission proposes to take forward the review of alternative approaches to pricing would be valuable, given the extensive evidence that expected local returns on investments are a major factor in firms' decision-making.

As proposed by the Chief Medical Officer for England, an early review of the Clinical Trials Directive could be a worthwhile exercise, not only to investigate the concerns of the academic community, but also to probe the wider issues relating to the conduct of clinical trials in Europe.

Further analysis of the effectiveness of R&D tax credits across Europe would be welcome, not least to investigate their impact on levels and location of R&D investments, to assist Member States in ensuring that these funds are used to maximum effect.

European and Member State policies on taxation, labour markets, and industrial regulation need to be better co-ordinated to ensure that the burdens on the pharmaceutical industry are reduced rather than increased. Current policies to encourage pharmaceutical innovation, particularly in the review of pharmaceutical legislation, are largely negated by countervailing policies imposing price cuts, restrictions on patients' access to new medicines, and increased labour costs. The G10 recommendation to investigate new pricing systems needs to be actively pursued.

In the UK the creation of NICE led to the first ever delays in the UK between marketing authorisation and patients' access to new medicines. Whilst the

development of fast track appraisals for some “life saving” medicines will be a positive development, NICE has also recently had to reduce the number of appraisal committees. It should be provided with additional resources in order to accelerate the speed of all appraisals. The impact on patients of the slow adoption of new medicines warrants further investigation, following the recent analysis of the use of new cancer treatments, and the introduction of the new commissioning framework for the NHS should be used as an opportunity to encourage more rapid adoption of innovation and to improve upon the culture of caution that holds back the prescribing of effective new medicines.

In view of the Office of Fair Trading (OFT) selection of the UK pharmaceutical price regulation scheme for investigation, the Government should itself investigate how financial restrictions placed on the industry might be eased to further promote supply-side competition and innovation.

After three years in operation the impact of the UK R&D tax credit scheme in the pharmaceutical sector should be re-evaluated, as an extension of the current consultation on enhancing the scheme. The UK continues to fail to gain major new investments, particularly by foreign-owned companies. By rewarding total R&D investment rather than additional investments the bulk of the support is concentrated on a very small number of pharmaceutical companies. The UK scheme needs to be compared with its counterparts, for its effectiveness in attracting new investment. In view of the Office of Fair Trading (OFT) selection of the UK pharmaceutical price regulation scheme (PPRS) for investigation, the Government should itself investigate how financial restrictions on the industry might be eased to promote competition and innovation.

Finally, the UK Government should review the pharmaceutical manufacturing base. Currently a major positive contributor to the UK balance of trade, the emerging trend of decline needs to be addressed if the UK is not to lose a major part of the science base given the strong association between these two activities.

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