



The Stockholm Network Experts' Series

The UK Pharmaceutical Industry: Current Challenges and Future Solutions



By Ross Carroll and Stuart Carroll

 STOCKHOLM NETWORK

Executive Summary

The UK pharmaceutical industry has traditionally been of major strategic importance to the UK economy, and continues to make a significant contribution. However, pharmaceutical companies are currently confronting a number of challenges as different factors and changing conditions create a rapidly evolving modern healthcare landscape.

This policy paper provides a detailed and analytical examination of the current issues and challenges confronting the UK pharmaceutical industry. Where appropriate and applicable, we seek to provide solutions and 'food for thought' on how pharmaceutical companies, and other interested parties, can best respond to these challenges during a time of increasing economic and strategic uncertainty.

The relative decline of the 'blockbuster drug' and the increase in the production of generic medicines, combined with the rising application of biotechnology to produce personalised medicines, are challenging traditional business models. Further challenges are likely to manifest themselves as governments increase their demand for preventative medicines over reactive treatments. Counterfeit medicines are also creating a major problem for pharmaceutical profits and patient health alike, as globalisation and technological advances enable easy cross-border trafficking. Diversity in the product pipeline and more investment in generics will be increasingly important components of future pharmaceutical development.

Emerging economies, such as those comprising the E7 (China, India, Brazil, Russia, Indonesia, Mexico and Turkey), are challenging established pharmaceutical markets. This is particularly pertinent to the UK in terms of strategic residence for company tax bases, manufacturing, research and development (R&D) operations, clinical trials and labour costs.

Developed economies such as Ireland, Switzerland and Singapore are also creating competitive business environments as exemplified by low corporation taxes, fiscal credits, decreased regulation, and strong investment in scientific education and skills.

The UK is falling behind its competitors on many of these issues, and therefore requires dynamic and incentivised action to address these growing concerns.

A lack of government investment is another factor adversely affecting the UK pharmaceutical industry. Spending on drugs and medicines is lower in the UK than in many other established economies. Furthermore, reimbursement schemes such as the *Pharmaceutical Price Regulation Scheme* (PPRS) are facing heightened scrutiny as the government looks to maximise value for money through the increased application of formal evaluation and cost-effectiveness criteria. As a direct consequence, health

economics and bodies such as the *National Institute of Health and Clinical Excellence (NICE)* are becoming increasingly important elements in the UK healthcare system.

Risk-sharing schemes are likely to grow in prominence and prevalence as governments seek to diversify and reduce the risk associated with healthcare investment in the future. This means industry will have to improve patient compliance in order to optimise profitable returns from such schemes and better demonstrate the intrinsic value of those products coming to market.

Long standing issues such as animal rights activism remain a concern despite a reported decrease in recent levels of activity in the UK. However, an increase in activity has been noted in Europe, accentuating the need for continued vigilance and cross-country cooperation.

1.1. Solutions and Recommendations

The paper offers the following key recommendations to address and tackle the challenges as described above.

a) *The Changing Business Model*

In response to the disintegration of the 'blockbuster' model, pharmaceutical companies should consider:

- Investing in generic products in order to stem eroding profits from patent expiries and to gain access, and a foothold, in emerging markets;
- Seeking increased and enhanced diversity in the product pipeline to encourage flexibility and to spread product risk and uncertainty; and,
- Improving understanding of the move towards personalised medicines as based on patient genomes and the increasing strategic and clinical importance of biotechnology.

b) *The Growth of Counterfeit Medicines*

Given the increase in the problem posed by counterfeiters, the following action is required:

- As a whole, the pharmaceutical industry needs to cohesively implement further measures, such as initiatives like the Anti-Counterfeiting Trade Agreement (ACTA), to improve global and systemic coordination;
- Utilise available and advancing technology, for example product "finger printing", to reduce the scope for counterfeiting activity;

- Through the UK government, ensure legislation is appropriately tightened and suitable deterrents and penalties are put into place to deal with counterfeiting; and,
- For national governments – with the help of international organisations – to work cooperatively and collaboratively to better coordinate international action against counterfeiting.

c) *The Shifting Healthcare Landscape*

As the future healthcare landscape increasingly shifts from curative/reactive to preventative medicine, pharmaceutical companies need to consider the following:

- Focusing R&D and associated activity around preventative products to respond to a likely shift in healthcare demand; and,
- Being cognisant of the fact that future reimbursement opportunities are likely to be geared around demonstrating the preventative capabilities of medicinal products.

d) *Emerging Markets*

As the forces of globalisation continue to push and pull, and emerging markets in countries such as India, China and Brazil grow in importance and significance, the UK pharmaceutical industry increasingly requires the following action:

- An improved understanding, particularly from the UK government, of the seriousness of global competition and a coherent policy strategy to accentuate Britain's competitive advantage relative to other countries;
- For the UK government to engage in cross comparison and evaluation with other countries and markets to assess dynamic competitiveness and associated opportunities; and,
- For the UK government to formulate a cohesive and creative industrial policy to reverse the current trend of decline and international displacement in pharmaceutical manufacturing and R&D.

e) *UK Competitiveness and Regulation*

In light of the increasing pressures and challenges confronting the UK pharmaceutical industry, the following action points – particularly for the UK government – confer amplified importance:

- A reduction in the rate of UK corporation tax to retain a healthy presence in British R&D, clinical trials and manufacturing plants;
- Implement tax credits for new product introduction and technological development;

- Consider strategic energy rates for manufacturing plants to overcome prohibitively high gas and utility costs as compounded by the ongoing global “credit crunch” and economic crisis; and,
- Simplify taxation rules and reduce the burden of complex legislation and regulation through the utilisation of cutting-edge approaches.

f) *Education and Tomorrow’s World*

In response to recurring and persistent concerns regarding a lack of adequately skilled scientific and technical labour in Britain, the following policy issues demand increased attention:

- For the UK government to increase investment in science at all academic levels and establish a strategy group with responsibility for monitoring progress;
- Earmark educational and university grants to protect and preserve science departments;
- Join up government policy across different departments to deal more effectively with this imperative; and,
- Promote positive campaigns to incentivise science and scientific careers.

g) *Pricing and Reimbursement*

As the UK government continues to seek value for money from healthcare spending, and more efficient and effective resource allocation, pharmaceutical companies will need to understand more fully and be aware of the following:

- The need to better and more clearly demonstrate product value, and hence the need to carefully tailor economic and clinical arguments to justify optimal reimbursement;
- The importance of improving clinical trial design and early product selection to support economic arguments when going to market;
- The increased use and application of risk-sharing schemes and thus the need for cogent and evidence-based economic strategising; and,
- The increased emphasis being placed on patient and product compliance, and the associated need to demonstrate product capabilities in this regard.

h) *Growth in Health Economics*

As decision-makers become more cost-conscious, and the shared principles of value for money and cost-effectiveness increasingly inform decisions pertaining to pricing and reimbursement, pharmaceutical companies need to understand the following:

- The intrinsic need to have economic as well as clinical evidence to justify optimal or “best case” reimbursement and hence the increased application and importance of health economics;
- The need to clearly and strategically understand the growing importance of health technology appraisal and formal economic evaluation as undertaken by institutions such as NICE;
- The opportunities for upfront application of health economics, particularly in the form of economic modelling and statistical analysis, to support decisions pertaining to R&D allocation and the efficient utilisation of scarce pharmaceutical resource; and,
- The increasing requirement to invest in and expand Global Health Outcome teams to support the use and application of health economics for pricing and reimbursement activity.

i) Animal Rights Activism

Given that the issue of animal rights activism continues to represent a problem to the UK pharmaceutical industry, the following action is recommended:

- The UK government continues to recognise the threat posed by extremist activity and utilises amending legislation as required;
- International governments, particularly at the European level, increase cooperative and collaborative efforts to deal with this persistent problem; and,
- The UK government clearly asserts and emphasises the critical importance of British based pharmaceutical and scientific research into life-saving treatments.

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Contents

1. Executive Summary	2
2. Introduction	10
3. The Changing Business Model: The Breaking of a New Dawn?	11
3.1 Putting Your Eggs in One Basket: The End of the 'Blockbuster' Era	11
3.2 The Growth of the Copycat: A Generic Market	12
3.3 "Diversity is Our Ethos"	13
3.4 Genomics	14
3.5 Solutions	15
4. Looking Over Your Shoulder: The Growth of Counterfeit Medicines	15
4.1 A Growing Problem	15
4.2 Parallel Imports	16
4.3 Solutions	16
5. One Step Ahead	17
5.1 A Pre-Emptive Strike?	17
5.2 Solutions	17
6. Emerging Markets: Finding New Frontiers	17
6.1 Discovering New Shores	17
6.2 Solutions	19
7. Is the UK Competitive?	20
7.1 The Right Economic Environment	20
7.2 Research and Innovation	20
7.3 The Bottom Line: Corporation Tax	21
7.4 Ireland	22
7.5 Switzerland	23
7.6 Singapore	23
7.7 Manufacturing	24
7.8 Clinical Trials	25
7.9 Solutions	26
7.10 You Only Get What You Give: Spending on Medicines	26
7.11 Solutions	26
8. Regulation: Striking the Balance	27
8.1 Regulation, Not Emasculation	27
8.2 Solutions	28
9. Tomorrow's World: Education, Education, Education	28
9.1 Is the Future Bright?	28
9.2 Solutions	30
10. Pricing and Reimbursement: 'We Want More Bang for Our Buck'	30
10.1 Value for Money	30

10.2 'Hedging Your Bets': The Use of Risk-Sharing	31
10.3 Comply or Die?	32
10.4 Solutions	33
11. 'Money, Money, Money': The Growth of Health Economics	33
11.1 Business is Business	33
11.2 A Marginal Business	34
11.3 Jumping the Fourth Hurdle: Got to Get it NICE	34
11.4 Health Economics and the Product Pipeline: 'Backing the Winner'	35
11.5 Don't Forget the Politics	35
11.6 Solutions	36
12. Animal Rights Activism	36
12.1 A Growing Menace?	36
12.2 Solutions	37
13. Conclusion	37
14. References	40

2. Introduction

The pharmaceutical industry is one of the UK's most important business sectors, having traditionally been a global leader for innovation and with many of the world's top companies basing their key operations here. It consistently ranks in the top three industrial sectors as measured by trade surplus, and is estimated to produce a total budget surplus of £4.3 billion annually, which is the fourth highest pharmaceutical sector trade surplus in the world, whilst the value of associated UK pharmaceutical exports amounted to £14.6 billion in 2007. This equates to over 10% of the total annual *National Health Service* (NHS) budget.¹

At present, UK-based pharmaceutical companies invest nearly £4 billion in the R&D of new medicinal products, which is akin to 30% of all sales or £10 million per day. Not only does this figure rise year on year, but this level of investment is also greater than industries such as aerospace, electrical goods and motor vehicles. The number of people employed by the UK pharmaceutical industry is 73,000, and the value added per employee to the UK economy is seen to be rising every year.²

However, despite these impressive superficial figures and statistics, the pharmaceutical industry is confronting an array of different changes and diverse challenges as the contemporary healthcare landscape continues to evolve. These challenges range from existing issues, such as exogenous threats posed by animal rights extremists, to previously unexpected issues, namely the decline of the 'blockbuster' drug business model and the drying up of pharmaceutical product pipelines.

Political changes are also apparent, with alterations to the *Pharmaceutical Price Regulation Scheme* (PPRS) and the increasing prominence of the *National Institute for Health and Clinical Excellence* (NICE). Increasingly high levels of corporation tax have hindered economic competitiveness, resulting in the retrenchment of manufacturing operations and the 'offshore relocation' of business activities to those countries offering a more favourable economic and regulatory climate.

Challenges are also being posed as healthcare itself undergoes a fundamental paradigm shift. The prevailing trend dictates a move from rewarding 'traditional' reactive/curative treatments to placing greater emphasis and importance on proactive and preventative treatments.

Despite these challenges and difficulties, there are also opportunities for industry to embrace. Traditional secondary care activities have altered in emphasis, as previously terminal and critical illnesses are now treated as chronic conditions. This in turn has seen minor surgical procedures being transferred from secondary care to the GP surgery and minor diagnostics being reassigned from the GP surgery to the pharmacy. As these changes are enacted and an increasing number of medicines become available to patients as Pharmacy Only (P) or General Sales List (GSL) patients will be presented with a

greater number of conditions allowing for self-medication*. This offers opportunities for a larger market for the pharmaceutical industry, along with greater promotional and educational openings to patients directly.

The population in the UK is ageing³, and therefore by definition a greater proportion of the population can be expected to require pharmaceutical medicines in the future. Pharmaceuticals, both curative and preventative, will clearly become increasingly important in order to alleviate strains on the NHS and the wider economy to ensure people are living healthy lives in their later years.

This paper provides a detailed overview of the current issues and challenges currently facing the UK pharmaceutical industry and, where applicable, aims to offer solutions to mitigate an uncertain time ahead.

3. The Changing Business Model: The Breaking of a New Dawn?

3.1 Putting Your Eggs in One Basket: The End of the 'Blockbuster' Era

One of the major issues confronting the pharmaceutical industry is the challenge to, and shifting focus of, the traditional business model. It is widely considered that the conventional strategy of pursuing 'blockbuster' medicines (products achieving peak sales of £1 billion or more) appears to be in sharp decline as major companies experience increasingly sparse product pipelines. This is further compounded by the stark fact that industry is investing twice as much in R&D compared with 10 years ago, but is only producing two-fifths of the resultant medicines.⁴ Even when promising new products reach the market place, very few achieve blockbuster status and generate the sufficient level of profitability relative to upfront investment.

The decline of the blockbuster drug presents a serious financial challenge to the current business model. It also calls into question the strategic focus of an industry undergoing fundamental change. In February 2007, Jean-Pierre Garnier, then of *GlaxoSmithKline* (GSK), stated of the blockbuster model: *"This is a business model where you are guaranteed to lose your entire book of business every 10 to 12 years. The first reflex of companies is to merge and that buys them a little time to deal with patent expiries, but fundamental changes will ultimately be necessary."*⁵ This has been affirmed by his successor at GSK, Andrew Witty, who recently remarked that the blockbuster model was analogous to *"finding a needle in a haystack right when you need it"*⁶, leaving a company open to "sudden torpedoes" in the form of lawsuits from generics firms or regulatory crackdowns such as that levelled against Avandia, GSK's diabetes drug.

* In the UK, "over-the-counter" medicines comprise GSL and P medicines. GSL medicines can be sold in a variety of retail outlets without prescription, where staff require no formal pharmacy training. P medicines can also be purchased without prescription, but can only be sold in a pharmacy. The pharmacist will determine whether these medicines are safe and appropriate for use based on dialogue with the patient.

Adding further credence to this shifting scene, Daniel Vasella of Novartis commented in 2005, *"In the medium-term, 50% of the market will be generics"*.⁷ In financial terms alone, it has been estimated that in 2005 total global pharmaceutical sales were \$533 billion, but of this figure \$104 billion will be lost to generics medicines between 2005 and 2010. IMS Health forecasts that \$130 billion of prescription drugs will come 'off-patent' by 2012, leaving a financial vacuum for those companies where markets will be flooded with 'me too' alternatives.⁸

3.2 The Growth of the Copycat: A Generic Market

The current growth of generics is impressively outperforming the current rate of growth in conventional drugs, with 2007 sales reaching \$72 billion. Teva, the largest generics firm, has a revenue target of \$20 billion for 2012 alone.⁹ With the blockbuster business model facing extreme difficulties, the expansion of generics has the potential to grow even further as the focus for product development essentially shifts to clinical margins rather than scientific absolutes. This in turn increases the challenges and difficulties confronting the pharmaceutical industry.

One method of combating this is for companies to acquire generics operations. Examples of this include Novartis owning an in-house generics arm in Sandoz, and Sanofi-Aventis making takeover bids for the generics company Zentiva. In July 2008, Andrew Witty also announced that GSK would enter the generics business by striking a deal with the South African company Aspen. This is seen as an attempt to smooth financial turbulence.

Indeed, some Wall Street experts have suggested that some pharmaceutical companies are not necessarily buying into generics to stem the drip of lost profits to off-patent medicines, but as a way of accessing high growth markets (see section 6). Vijay Karwal, managing director of consumer, retail and healthcare at RBS Global Banking and Markets states: *"The most effective way of accessing those markets or building brand awareness, building market share is through branded generic products because...the economic wherewithal of consumers in those markets is not yet there in terms of their ability to buy high priced, patent-protected products. Many of these markets will not have health insurance, they'll be cash-pay. And certainly large parts of the population at this stage will be buyers of generic products."*¹⁰ In other words, these new populous markets are likely to look to purchase generic products where possible due to the more attractive price.

Thus, the benefit of these acquisitions is contingent upon local market factors. In Japan, for example, which is less liberalised and competitive relative to other established markets, it is estimated that the healthcare system pays \$30 billion for off-patent medicines, which would cost just \$3 billion in the US.¹¹ As a consequence of these figures, pharmaceutical firms are not primarily interested in making generic acquisitions to access the US market, but to sell in markets such as Japan and the emerging markets of the E7 (China, India, Brazil, Russia, Indonesia, Mexico and Turkey).

However, in spite of this, some liberalised markets, such as the UK and US, are becoming increasingly competitive for generics firms as governments look to increase cost-effectiveness, thereby fostering the need for dynamic economies of scale. As such, it may be that such acquisitions are not just beneficial to the pharmaceutical industry but also to individual generics companies. This in turn may see some generics firms welcoming opportunities to merge with pharmaceutical companies. Malvinder Singh of Ranbaxy recently suggested that their alliance with Japan's Daiichi Sankyo will be beneficial not only in terms of cheap manufacturing capacity, but also for facilitating a more expansive customer base. Nonetheless, many generics firms may view mergers as being difficult and cumbersome due to differences in respective business models.

Unless pharmaceutical companies are able to resolve the prevailing issues undermining the sustainability of the blockbuster model, or decide to aggressively invest in an increasingly fluid and competitive generics market, the likely outcome is significant financial loss at a time of ongoing economic uncertainty. Sustainable and substantive resolutions for the former are unlikely, not least given the relative emptiness of product pipelines and the decreasing returns to scale associated with scientific advance. This means consolidated investment in the latter could confer potential strategic advantages moving forward.

3.3 “Diversity is Our Ethos”

Whilst each individual company has its own structure, strategy and emphasis, one method of mitigating the issues associated with the decline of the blockbuster model and the challenges posed by generics is to diversify business plans. A number of firms have developed their businesses as “healthcare companies” as opposed to pure pharmaceutical companies. Perhaps the biggest of these is Johnson & Johnson (J&J). Along with having a range of pharmaceutical products, J&J also produce a range of products including bandages, baby products, shampoos, dental products, face washes, contact lenses, and the Neutrogena skin product range.

Another company that has exemplified this approach is Abbott Laboratories. Abbott is currently one of the fastest growing companies in both the UK and Europe. In September 2008, the Abbott Board of Directors declared a quarterly common dividend of 36 cents per share, marking the 339th consecutive quarterly dividend to be paid by Abbott since 1924. The company has also had the second highest average annual return of all companies originally listed in the S&P 500¹², and in June 2008 featured in the Fortune 40 Best Stocks to Retire On list, with earnings in the previous quarter surging 35% and a growth projection of 11%.¹³

In the UK, Abbott's four main areas of business encompass pharmaceuticals, medical devices, diagnostics and nutritional products. This diversity has enabled Abbott to produce major selling pharmaceutical products, such as Humira (a fully human anti-TNF medication) and Kaletra (a protease inhibitor for HIV), whilst also being able to capitalise on the shift towards personalised medicines

through its diagnostics work. Jeff Stewart, UK General Manager, recently stated: “Having the ability to offer both molecular diagnostics and a novel therapeutic to our customers can be a real strength of our business model.”¹⁴ In addition, Abbott is also well-known for its nutritional products such as Ensure, Enlive! and Jevity, whilst Abbott’s vascular department recently attained Food and Drug Administration (FDA) approval for a drug-eluting stent[†] called Xience V. Abbott diabetes department last year received European CE mark approval for its continuous glucose monitoring system, FreeStyle Navigator.

As with J&J, it is through this diversity of business operations that consistent and sustainable market advances have been achieved. As Jeff Stewart recently commented, “Diversity is our ethos. It’s what we look for when we recruit and develop our staff. Our portfolio and pipeline is diverse. It’s integral to our business model and to maintaining and expanding our competitive edge.”¹⁵

3.4 The Age of Genomics

Moving into the future, the progressive application of biotechnology, which seeks to maximise information about patient genetics and proteomics to tailor patient-specific medicines, is a growing trend. Whilst *The Association of the British Pharmaceutical Industry (ABPI)* has acknowledged through the *Ministerial Industry Strategy Group (MISG)* that the “scientific revolution” involving gene therapies and the Human Genome has been slower than expected, it has still noted that a “revolution” of this kind should be anticipated.¹⁶ New medicines, genomically-targeted to smaller patient cohorts, are likely to produce greater efficacy and fewer side effects. More pertinently, such medicines almost by definition are likely to produce better clinical outcomes against which the blockbuster model will struggle to deliver.

As advancements in biotechnology are set to enable companies to produce a greater number of products for a larger number of genetic sub-groups, and that such medicines would be genetically tailored, clinical efficacy and effectiveness is likely to be higher, which in turn should enable greater patient compliance and higher reimbursement potential from healthcare payers.

Numerous pharmaceutical companies have responded to this opening by investing in biotech opportunities. These include Novartis, Wyeth, Abbott, BMS and Roche, but also big pharmaceutical companies more generally. This trend has been triggered not simply by future potential and the logic of patient-specific medicines, but by the prevailing force of the economic bottom line. The biotech industry is expanding far more rapidly than the pharmaceutical industry, with U.S. biotech sales growing by 20% to \$40.3 billion in 2006, while pharmaceutical sales grew by a relatively modest 8%, to \$275 billion, according to IMS Health. The pharmaceutical industry is, therefore, looking to invest in a current growth trend, which is likely to increase further as the clinical imperative shifts to a more patient-specific focus.¹⁷

[†] A drug-eluting stent (DES) is a coronary stent (or scaffold) placed into narrowed, diseased coronary arteries that slowly releases a drug to block cell proliferation.

It is not just the pharmaceutical industry that is investing in genetically tailored medication R&D. The European Commission recently gave the French bank OSEO the go-ahead to make available €89.5 in grants and repayable loans to a French personalised medicine R&D initiative called Advanced Diagnostics for New therapeutic Approaches (ADNA). It is envisioned that this could have “major implications” for a range of diseases and illnesses.¹⁸

3.5. Solutions

Given that each company has its own organisational structures and business models, there are no ‘one size fits all’ solutions to these prevailing challenges. Moreover, the fundamental nature of the changes necessarily requires tailor-made responses to individual circumstances. A case-by-case approach is therefore essential.

However, there are some general considerations and rules of thumb that are likely to define a wider industry strategy. Some companies may look to invest in acquisitions of generic companies in order to partly mitigate lost profits from patent expiries and partly to gain access to lucrative emerging markets. Other companies may seek to diversify their product portfolios in order to foster a more flexible and broad-ranging business model. A blend of both options is already being sought by a number of companies.

One thing that does appear certain concerns the direction of future health care. Personalised medicines based on patient genomes, combined with the application of biotechnology is set to become prevalent and important. It is clear that companies will need to judiciously plan for this eventuality to provide opportunities for strategic advantage moving forward.

4. Looking Over Your Shoulder: The Growth of Counterfeit Medicines

4.1 A Growing Problem

Whilst the growth of generic medicines has long been an *a priori* expectation given the finite period of protection time a patent affords a pharmaceutical product, counterfeiting is perhaps a less obvious challenge confronting the pharmaceutical industry. The *Food and Drug Administration* (FDA) estimates that as many as 10% of medicines in global circulation are counterfeit,¹⁹ and that this figure is likely to be even higher in the developing world. The European Commission estimates that 2.7 million counterfeit pharmaceuticals were seized at EU borders in 2006.²⁰ With the recent development of online pharmacies and ‘medication stores’, this trend is only set to increase.

The associated cost incurred as a consequence of this is therefore likely to be high. Sanofi-Aventis have already opened a laboratory dedicated to analyzing counterfeit medicines. This is described as the first

initiative of its kind to tackle a problem that saw Sanofi experience 2.5 million counterfeit doses of their products in circulation in 2007 alone. Jean-Francois Dehecq remarked, “For too long a time we underestimated the problem of drug counterfeiting,” and that “what used to be a cottage industry is today a fully-fledged industrial process.”²¹

Currently, the *Anti-Counterfeiting Trade Agreement (ACTA)* is being negotiated by the EU, the US and Japan along with other major trade partners. According to the European Commission, the aim of ACTA is to put in place an international framework that “strengthens the global enforcement of intellectual property rights and helps in the fight to protect consumers from the health and safety risks associated with many counterfeit products” which would “enhance and render more effective the fight against counterfeiting and copying of products which are protected by patents owned by European companies.”²² However, there are fears that, whilst this would potentially make strides in the fight against counterfeit medicines, it may also interfere with the generics industry and the parallel import trade which is legally permitted within EU borders. This concern is fuelled by the fact that presently no one outside of official negotiations has seen the content of the ACTA text.

The European Commission is also expected to take action against counterfeiting by giving the *European Medicines Agency (EMA)* the power to require specific product identification. Proposals include steps to improve the collection and quality of data, the share of best practices, and increased public-private cooperation to improve enforcement. Inter-industry cooperation to crack down on the most evident forms of counterfeiting and piracy, including those on the Internet, has also been suggested as a way to diminish the scale of this problem. The *European Federation of Pharmaceutical Industries and Associations (EFPIA)* has called for an EU ban on medicine repackaging and a harmonised identification system for medicines, along with strict penalties for those caught trafficking in counterfeits.²³

4.2 Parallel Imports

Parallel imports[‡] allow for a legal flow of medicines across EU borders, although products need to be repackaged to conform to the local language. This presents an obvious opportunity for counterfeit medicines. National governments and the EU will need to work with the pharmaceutical industry to look at solutions to enable alternatives to repackaging and overcome this growing problem.

4.3 Solutions

The pharmaceutical industry as a whole will need to take further measures to tackle the problem posed by counterfeiters. Initiatives such as ACTA are necessary in order to coordinate coherent efforts against global and systemic counterfeiting. Other actions may include measures similar to those taken

[‡] A parallel import is a product imported from another country without the permission of the intellectual property owner. Parallel imports are sometimes referred to as grey products. The process of parallel trade is legal under European law.

by Sanofi-Aventis, but also supporting initiatives to aid the integrity of online outlets. A closer look at technology may therefore be needed. This could include 'finger printing' of products through laser recognition authentication to buttress verification at the point of dispensing, and the use of unique identifiers such as electronic pedigrees or DNA labelling to enable medicines purchased online to be validated.

Government must also play a role both at national and supranational level. Tightening legislation and increasing penalties against counterfeiters is essential. Furthermore, providing funding to aid inspection of pharmacy stores and wholesaler outlets would help to tackle this issue. Repackaging is a significant weakness throughout the parallel import chain and thus industry, in conjunction with governments across the EU, will need to work together to ensure that a more robust system is developed.

5. One Step Ahead: Preventative Medicines

5.1 A Pre-Emptive Strike?

A further change that is set to irrevocably transform future pharmaceutical activities and operations is the increased emphasis being placed on preventative rather than curative health care. As the population ages and demand on healthcare budgets increases, pre-empting rather than reacting to illness and disease constitutes the prevailing aspirational mission statement driving the direction of modern healthcare policy. This is an area of focus industry has thus far largely avoided.

The reason for this shift is clear. The population of the UK is ageing and as such there is a greater risk of numerous conditions and disease states increasing in prevalence. If these can be prevented, or at least mitigated by more rapid and effective diagnosis, the savings to the NHS budget could be substantial. For example, it has been reported that the cost to the NHS from diabetes stands at £1 million per day, and this figure is expected to grow.²⁴ Heart disease has been estimated by the Health Economics Research Centre at Oxford University to cost the UK economy £29 billion per year.²⁵ However, it is not just the Department of Health (DH) that would benefit from preventative medicines. The Department of Work and Pensions (DWP) would also welcome preventative medicines or novel pharmaceutical products that would reduce the number of people claiming incapacity benefits - a figure that currently stands at 2.6m people²⁶ – and that help people remain in work.

It is therefore increasingly likely that payers will confer a greater reward for diagnostic devices, vaccinations and other medicinal products that offer preventative capabilities. Future governments are likely to change pricing and reimbursement policy to reward the production of those products that preemptively offset reactive treatment costs falling on the NHS. This has been echoed in a recent report by PricewaterhouseCoopers (PWC): "*Without such a change of strategy, no country will be able to meet the healthcare needs of its inhabitants by 2020*".²⁷

5.2. Solutions

It is likely that as the health-related issues brought about by the ageing population in the UK entrench, governments will increasingly look to pharmaceutical companies to develop preventative medicines and diagnostic devices to avoid high downstream treatment costs. Reimbursement opportunities are likely to become increasingly attractive for such products, although the system of reimbursement will have to change in order to accommodate this shift in emphasis. This could take the form of improved financial incentives to reward such innovation or through extended patent protection on products that offset downstream treatment costs whilst improving public health through disease prevention. Forward-thinking companies will need to utilise their Government Affairs and Communications departments to lobby state bodies to enhance recognition of the value of this approach.

6. Emerging Markets: Finding New Frontiers

6.1 Discovering New Shores

Traditionally, the pharmaceutical industry has produced and marketed its products in developed markets such as the UK, Central Europe and the US, largely as a result of prevailing business opportunities as well as better infrastructure and regulatory frameworks.

However, this is likely to change as growth continues to slow in traditional markets and the populous nations of China, India and Brazil experience dramatic economic growth rates. The consultancy firm McKinsey has estimated that the value of the Indian drugs market will grow from an already significant \$6.3 billion in 2005 to \$20 billion in 2015. It is further forecasted that such growth is likely to be replicated, or even exceeded, by the Chinese healthcare market, which grew by a massive 25.2% between 2006 and 2007, and which was estimated to be worth \$86.8 billion at the end of 2007.²⁸

While China and India are the two nations that tend to make the headlines, other countries are developing with similarly impressive growth rates. The E7 nations – China, India, Brazil, Russia, Turkey, Mexico and Indonesia – are expected to share the potential to account for 20% of global sales by 2020, according to PWC.²⁹ More specifically, PWC predicts that the real GDP of the E7 nations will triple from a respectable \$5.1 trillion to a hefty \$15.7 trillion in 2020. This is in contrast to a 40% rate of growth for the G7 nations (USA, Japan, Germany, UK, France, Italy and Canada) of \$25.8 trillion to \$36.1 trillion. The E7 currently account for 8% of the \$518 billion global pharmaceuticals market. However, should the G7 and E7 continue to spend in 2020 the amount of GDP exhausted in 2004 on prescriptions (1.31% and 0.91% respectively), and the economies of these countries grow as projected, the global pharmaceuticals market could increase to \$800 billion, with the E7 accounting for a significant 14%.³⁰

Given the current rates of growth of India and, in particular, China, it is entirely possible that these forecasts are conservative estimates. Large numbers of people in these countries are ageing. This will increase the market share for many pharmaceutical products and as economic growth delivers national prosperity the spending on healthcare is likely to increase as a proportion of GDP. It is therefore conceivable that by 2020 the global pharmaceutical market will be worth in excess of \$1 trillion, with the E7 accounting for a whopping 20%.

This unquestionably represents a big opportunity for pharmaceutical companies to tap into emerging and sizeable markets, not least when considering the issues surrounding generic medicines (see section 3.2) and ongoing reforms to reimbursement systems (see section 10). Whilst there is the potential threat of E7 governments riding roughshod over product patents, as has occurred on occasions, the growth opportunities in such high-volume markets represent attractive investment openings. As Mark Feinburg of Merck recently stated, *“You’ve got to be in these markets — it’s a great opportunity”*, whilst Andrew Witty of GSK has announced his intention to increase the company’s investment portfolio in emerging world markets.³¹

However, from a UK standpoint these developments constitute a potential threat as companies may look to capitalise on these market openings in new and attractive investment climates. There is the real danger of companies downsizing pharmaceutical operations currently based in the UK. This has already been occurring in areas such as manufacturing (see section 7.6), and is primarily driven by the economic imperative to cut overall costs.

It is also the case that, should companies want to adequately serve the populations of these new markets, there will be an increasing need to set up a range of operations in these countries in order to maximise profits. Many companies have already embarked upon this, seeking to utilise local market potential to optimise regional return. With companies confronting increasingly tight budgets, difficult choices concerning national investment will ineluctably play a central part in strategic decision-making. It is from this premise that it is vital for the economic climate in the UK to be competitive and dynamic in order to ensure investment is consolidated rather than transferred offshore.

6.2. Solutions

The competitive threat posed by emerging markets and developing economies is an essentially exogenous reality for the UK economy and, in large part, a direct consequence of globalisation. To this extent, there are no direct or easy solutions to this growing problem, but rather a need to cultivate a favourable economic environment to retain and attract pharmaceutical investment. This is particularly relevant when considering manufacturing, production and operational activities. It is of strategic importance that the UK government continually cross-compares, evaluates and assesses its own competitiveness against other economies. This is not only central to ensuring a clear and focused understanding of prevailing market factors and consideration, but also for fostering policies to better

accentuate the UK's 'unique selling point'. Without such candid self-analysis, the UK will struggle to dynamically incentivise inward investment opportunities.

It is evident, as exemplified by the absence of a "future plan" and relative to the strategic approaches be adopted by other countries, that the UK is badly lacking a focused and coherent industrial policy for the British pharmaceutical industry, which is surprising if not worrying given its significant economic contribution. Apart from the clear economic and strategic argument in favour of a strong UK pharmaceutical base, there are clear political advantages from retaining in-house scientific and clinical expertise. At present, industrial policy is signalling a lack of concern and interest in British pharmaceutical industry, and in turn a lack of priority and understanding for the challenges currently being experienced and those that lie ahead.

It is an incumbent responsibility of *The Department for Business, Enterprise and Regulatory Reform* and its leadership to 'beat the UK drum' overseas in order to cogently make the case for domestic and foreign investment in British pharmaceuticals. This has added pertinence during the current period of economic recession and uncertainty.

It is often said that there are three types of nation: 1) those that make things happen, 2) those that think about making things happen, and 3) those that wonder what the hell did happen! Although some of the challenges confronting us are sufficiently global in nature, it is worth wondering which type of nation the UK government will choose to be in relation to its pharmaceutical industry. Formulating a strategy that would seek to focus minds on maintaining and consolidating the UK's unique selling points in global pharmaceuticals relative to other nations is essential and fundamental to cogently answering questions about Britain's competitive advantage.

7. Is the UK Competitive?

7.1 The Right Economic Environment

With the above challenges and changes currently confronting the UK pharmaceutical industry, it is vital that a competitive business climate is fostered. Traditionally, a number of factors have determined whether a country provides a competitive climate to enable world-class pharmaceutical performance. These include a history of stability and reliability, low taxation and manageable bureaucracy, a balanced regulatory environment, a flexible labour force, a commitment to developing scientific skills, and a business environment that supports and promotes innovation and research.

7.2 Research and Innovation

The UK has traditionally contributed strongly to pharmaceutical innovation and R&D. The most recent House of Commons Health Select Committee report on the influence of the pharmaceutical industry

(2004/2005) noted the significant benefits of innovation, research and medicines to the NHS, and the “substantial” role industry plays in this process. It also reaffirmed the UK’s traditional place as a world leader in pharmaceutical innovation, noting that in 2003 the pharmaceutical industry invested £3.5bn in R&D with 25 of the world’s top 100 best-selling drugs discovered and developed in the UK, which is more than any other nation outside of the US.³²

The amount invested in R&D has further increased since 2003 to nearly £4 billion per annum, whilst the amount invested as a percentage of sales compares favourably with other manufacturing sectors.³³ However, for this investment to remain sustainable, which in turn delivers important economic and employment benefits to the wider UK economy, a competitive politico-economic climate is essential. This requires a competitive corporation tax, a flourishing and focused education system to provide the necessary skills base, and a suitably flexible regulatory environment.

This is all the more important given that the *Ministerial Industry Strategy Group* (MISG) reported in 2007 that the US attracts 20% more R&D investment compared with Europe, and the emerging nations of India, China and Singapore are providing an alternative source of pressure to Europe (and the UK) as well. The MISG noted that China has trebled its R&D spending within 5 years alone, India is now producing more science graduates than Europe³⁴ and Singapore is creating an attractive economic climate for pharmaceutical investment. A competitive environment for R&D is also vitally important in the present, given that industry in general is now investing twice as much into R&D as it was 10 years ago to produce just two-fifths of the medicines it did then. Given these difficulties, a competitive climate to enable a flourishing R&D environment is essential.³⁵

The UK therefore needs to respond to these challenges. Ensuring government policy is clearly focused is seminal to facilitating a strong and continued industry presence, whilst being cognisant of the rapidly evolving pharmaceutical landscape, and in turn the need to provide dynamic incentives, is the *sine qua non* for retaining existing economic benefits and attracting new investment.

7.3 The Bottom Line: Corporation Tax

The Ernst & Young report of 2007, ‘*Helping Britain Thrive*’, stated that amongst OECD countries in 2001, the UK had the 10th lowest tax rate. However, by 2006 the UK’s position had slipped to the 18th lowest.³⁶ The report accentuated the failure of government to monitor and act upon this relative position, not least given its primary importance as a key factor for deciding investment location. The net result has been a reduction in the UK’s economic and investment attractiveness. This was also highlighted in a 2007 survey by KPMG, which ranked Britain’s tax regime 12th out of 22 countries. It particularly noted concerns over the overall rate of tax, the volume of tax legislation and the clarity of its interpretation.³⁷ Overall, respondents to this survey ranked the UK tax regime as the 14th most attractive, with a relative net attractiveness of just 50% (versus 100% for nations such as Ireland and Switzerland).

Currently, the UK corporate tax rate stands at 28%, which is high compared to many other competitor nations. As Richard Lambert, Director General of the CBI, said in relation to Shire's recent decision to move its tax base to Ireland: "We are particularly worried that an uncompetitive corporate tax system is spoiling the UK's attractiveness as a place to do business, and that other internationally mobile firms will follow Shire's path."³⁸ Shire is by no means the first company to move key operations away from the UK, and earlier this year AstraZeneca refused to rule out relocating its tax headquarters to Ireland as a result of the UK's high levels of tax, whilst former GSK CEO Jean-Pierre Garnier hinted that there could be an exodus from the UK unless the tax regime is reviewed.³⁹ In addition to this worrying trend of relocating tax bases, many companies have already moved their manufacturing operations abroad in order to take advantage of more competitive tax rates, lower levels of regulation and red tape, and a cheaper and more flexible labour force.

Three examples of nations that have fostered competitive tax and investment regimes are Ireland, Switzerland and Singapore.

7.4 Ireland

Since 2003, Ireland's has had a 12.5% rate of corporation tax on trading profits. Previously, it had a 'manufacturing' corporation tax of 10% which in some cases is still applicable until 2010, provided that eligible trades qualified for it prior to July 1998. In the 2009 budget, Minister for Finance Brian Lenihan, T.D stated:

"The 12.5% rate of Corporation Tax is an important element in our taxation system. It has been a cornerstone of our industrial development in the last decade. I want to emphasise that this rate of tax is not for changing upwards and it will continue to be a central part of Ireland's economic brand. Ireland's economic prospects are dependent on a vibrant and modern business base and I know that virtually all sides of this house will agree with me that our rate of Corporation Tax is essential to this."⁴⁰

Mr Lenihan also announced that the R&D tax credit available to companies will increase from 20% to 25%, which will increase Ireland's attractiveness as a location for R&D activity. Other measures proposed to improve competitiveness included a remission in Corporation Tax and Capital Gains Tax for companies in their first three years of operation with certain limits.⁴¹ There are also favourable tax agreements to mitigate 'double taxation' with other countries, which consequently helps to encourage inward investment and business presence.

Ireland now boasts substantial investment from 13 of the world's top 15 companies, many in manufacturing, and this shows no sign of abating. For example, Shire recently announced that it is seeking to relocate its tax base to Ireland "to help protect the group's taxation position". The aforementioned KPMG survey indicated that volume of legislation and regulation, along with the interpretation of this as favourable, with Ireland's overall tax regime ranked number one with a relative net attractiveness figure of 100%.⁴² Ireland also benefits from membership of the EU, its proximity to

the UK market, and the fact that its workforce is fluent in English enabling easy opportunities for global trade and economic development.

7.5 Switzerland

Switzerland also boasts a competitive and attractive taxation regime. Corporation tax ranges from 16% to 28%, depending on individual cantons. In addition, Switzerland is known for its incentivising approach to innovation as exemplified by the presence of organisations such as the CTI (the Swiss Confederation's innovation promotion agency) and the Swiss Biotech Association.

Given its stable environment as a leading financial centre combined with a strong skills base and a consistent level of pharmaceutical investment and employment (some 13,000 people are estimated to be employed in pharmaceuticals and biotechnology), Switzerland continues to provide a strong economic climate for pharmaceutical companies. Along with Ireland, Switzerland was placed at the top of the recent KPMG survey of the most attractive places to do business in Europe. Unlike Britain, it fared well in relation to complex rules and mass legislation, scoring highly (like Ireland) for its combination of easy-to-understand rules, low tax rates and stable fiscal laws.⁴³

7.6 Singapore

In 2008, Singapore lowered its rate of corporation tax to 18%, and like Ireland has numerous agreements in place with other countries to avoid 'double taxation'. It has also spent significantly on R&D, with a tenfold increase in public and private investment between 1990 and 2006 to \$5 billion. A further \$13.6 billion of public money has been allocated for investment in R&D between 2006 and 2010.⁴⁴ This will see total national R&D spending increase to 3% of GDP by 2010.

In the 2008 budget speech, the Minister for Finance, Tharman Shanmugaratnam, announced that Singapore would increase the tax deductions allowed for R&D conducted in Singapore from 100% to 150%, meaning that for every \$100,000 of local R&D spending, a company will be able to deduct \$150,000 from its taxable income.⁴⁵ He also announced the introduction of new broad-based tax allowance, where companies will be granted R&D tax allowances each year, up to an amount of 50% of the first \$300,000 of their chargeable income. This allowance can then be used to defray incremental expenditure on R&D conducted in Singapore in subsequent years, and will provide additional resources – particularly for small to medium enterprises (SMEs) – to invest in innovation, whatever their field of business. Schemes to help start-up companies, and to aid the transition of R&D into marketable products, were also included in this budget.

A pro-business environment is also dynamically incentivised through the Economic Development Board (EDB). For a set time period, full corporation tax exemption on qualifying profits is available, followed by lower corporate tax rates for a set period on all qualifying profits to encourage expansion and development. An 'Investment Allowance' – an allowance on qualifying equipment costs incurred within

a set period – and an R&D and ‘Intellectual Property Management Hub Scheme’ to encourage companies to channel more funds into R&D activities, are also attractive fiscal features. Tax deductions on expenses allied to R&D outsourced to any R&D organisation and Single Tax Deduction for patenting costs are also part of the competitiveness strategy to promote Singapore as an attractive base for IP management.⁴⁶

7.7 Manufacturing

UK manufacturing is highly reliant upon the competitive levers described above (see sections 7.1-7.3). Currently, UK manufacturing capacity is in decline as emerging markets are able to offer lower tax incentives, reduced regulation and cheaper labour costs, whilst continually increasing their graduate and skills base. Indeed, it has been reported that 25% of companies are looking to increase their manufacturing capacities in Asia alone. This compares with the UK where 15 manufacturing plants have been closed between 1996 and 2008, with GSK and AstraZeneca the latest companies to announce plant closures and job losses, respectively. In the case of GSK, its Dartford site is due to be closed in 2013 affecting 620 people.⁴⁷ This trend is likely to accelerate in the future if action is not taken to improve UK competitiveness.

This is of major concern - not just for the UK pharmaceutical industry - but for the wider economy. As a manufacturing sector, pharmaceuticals is estimated to produce a total trade surplus of £4.3 billion annually, which is the fourth highest worldwide, whilst the value of associated UK pharmaceutical exports accounted for £14.6 billion in 2007.⁴⁸ It is estimated that manufacturing in the UK employs over 22,000 people.⁴⁹

There is the added concern attached to the current trend in manufacturing operations, i.e. closures and relocation overseas, insofar as there is often a symbiosis between manufacturing and R&D. R&D operations are typically based close to manufacturing plants in order to maximise efficiency throughout the development, production and launch process of a pharmaceutical product. Thus, if manufacturing plants are closing or relocating overseas, R&D operations could also be under threat.

Labour costs are estimated to be responsible for 50% of primary costs and 60% of secondary manufacturing costs⁵⁰, and in this area of pharmaceuticals it is difficult for the UK to compete directly with emerging nations. However, a primary driver for manufacturing investment is corporation tax and associated tax incentives. Although the UK does offer R&D tax credits, capital allowances on manufacturing assets and certain Department for Business, Enterprise and Regulatory Reform (BERR) grants, the effects of these incentives tend to be minimal in comparison to the type of benefits offered by other countries (see sections 7.4 -7.6).

Manufacturing is currently facing additional pressures due to high energy prices. Manufacturing machinery consumes disproportionately high levels of energy, including petrol for haulage and

transportation of raw materials. Thus, the recent rises in electricity, gas and oil prices are having a punitive effect on this important area of the UK pharmaceutical industry.

7.8 Clinical Trials

Another major pharmaceutical activity, which has seen increased investment overseas, is clinical trials. This is particularly the case in East Asia where pharmaceutical companies are seeking to pursue innovation at lower costs. Major companies such as AstraZeneca, Pfizer and Novartis have already invested significantly in research operations within this region,⁵¹ and the growth consultancy firm Frost & Sullivan has estimated that by 2010 contract overall research revenues could increase from \$1.2bn in 2006 to \$2bn.⁵²

China has some particularly attractive qualities – it is predisposed to scientific expertise, has huge patient populations, a broad spread of illness and disease states, flexible regulation and low trial related costs. There is also a great degree of ethnic diversity, which is of central importance as personalised medicines are likely to develop further in the future.

Nonetheless, China is not the only nation offering an attractive investment and regulatory climate at relatively low cost. South Korea, Taiwan, Hong Kong and Singapore are all favourable destinations for clinical research having recently experienced strong investment growth. Where regulation is investment friendly, cost savings can be huge. Keiko Oishi, the Senior Managing Director of the Japanese contract research organisation CMIC, has stated that costs are on average 50% lower per patient than in the US or Europe.⁵³ Trial-related costs (involving patient care, medicines and hospitalisation) is estimated to be between 25 and 45% lower than in the US, whilst the cost of vendors and contractors is approximately 50% lower.

By comparison with the aforementioned countries, the UK is becoming increasingly uncompetitive as a location for conducting clinical trials. In a recent British Medical Journal (BMJ) article, a number of academics stated that: *“The UK has slipped from one of the most attractive to one of the least attractive places to undertake clinical trials”*. They attribute this in large part to an increasing regulatory burden, including the EU clinical trials directive 2001/20/EC, which they claim is now *“the biggest single threat to the UK clinical research base and warrants immediate action”*. The Medicines and Healthcare products Regulatory Agency (MHRA), which necessitates separate approval of all clinical trials in the UK, was also criticised for stifling clinical research: *“The application is difficult to complete, cannot be submitted online, and is sometimes lost by the MHRA...no improvement in patient safety has been demonstrated as a consequence of the extra tier of bureaucracy for such studies; on the contrary, the MHRA notably failed to prevent the TeGenero disaster at Northwick Park – or even acknowledge its failure.”* The authors commented that the MHRA process adds long delays with no perceived benefits, particularly when the drug concerned is already licensed.⁵⁴

7.9 Solutions

A reduction in corporation tax is vital to retain a healthy presence in R&D, clinical trials and manufacturing plants in the UK, and to enable increased investment in the future. The UK cannot compete with the low labour costs offered by some emerging economies; tax-related incentives are therefore vital. Aside from a cut in corporation tax, tax credits for new product introduction (NPI) and new technology development should be offered to advance technological capability. A high value manufacturing credit or grant system along with central planning support to reduced time delays and costs in developing a new plant would also make the UK more flexible. Strategic energy rates for manufacturing plants should also be considered. This could be achieved innovatively; for example, by 'pegging' the rate of industry payments to the price of energy.

It is also important that the UK simplifies its taxation rules and reduces the burden of complex legislation and regulation which are stifling economic attractiveness. In the absence of an incentivised business environment, R&D and clinical trials will continue to move to more desirable overseas locations, and the UK will continue to experience further withdrawals at a time when economic injections are badly needed to buttress a decidedly uncertain macro-economy.

7.10 You Only Get What You Give: Spending on Medicines

In addition to the prohibitively high rate of corporation tax, concerns have also been voiced around the lack of investment by the UK government into new products and manufacturing technology. The ABPI reports that in 2007 the UK spent £195 per person on medicines compared with £467 in the US and £322 in France. This level of spending is also behind nations such as Austria, Belgium, Ireland and Spain. Furthermore, as a percentage of GDP the UK spends only 0.85% on medicines compared with 2.08% in the US, 1.54% in Japan and 1.52% in France. In other words, of the entire NHS budget (which is roughly £111 billion), medicines account for just 10.3% of overall expenditure – a figure lower than most people would expect.⁵⁵ Indeed, this should also be placed within the context of medicines now being 21% less expensive in real terms than they were 10 years ago.⁵⁶

It has been argued that this limited spending places the NHS and, in particular organisations such as NICE, in a very difficult and often invidious position. NICE frequently bears the brunt of patient, industry and clinician anger when a new technology is not approved for use. However, with a relatively tight healthcare budget and comparatively lower spending on medicines compared with many developed countries, decisions pertaining to cost-effectiveness and value for money are determined within a narrowed framework of economic feasibility.

7.11 Solutions

The government should look to increase spending on medicines to bring the UK more closely in line with Europe and the US. This would be beneficial not just for patient health but also from the standpoint of incentivising innovation and UK-orientated R&D.

One thing is for certain – spending on drugs and medicines should not be seen as a soft target, but viewed in the same light as other healthcare imperatives. Although governments rightly need to scrutinise the value of every penny spent, it should be remembered that pharmaceutical medicines often bestow life-saving qualities and offer preventative capabilities, which in turn can generate significant healthcare savings through the avoidance of future disease and illness. For example, the use of statins has shown to have widespread benefits. One trial of nearly 25,000 patients showed that patients taking a statin had a reduced risk of mortality of approximately 25% and a 22% lower risk of hospitalisation resulting from heart failure.⁵⁷

8. Regulation: Striking the Balance

8.1 Regulation, Not Emasculation

Regulation of pharmaceutical products is vital within any healthcare system in order to ensure patient safety. However, this needs to be balanced against the risk of stifling innovation and unnecessarily delaying the release of medicines into the market.

In the UK, the two agencies responsible for the regulatory process are the MHRA and the European Medicines Agency (EMA), which was created in 1995 by the EU to harmonise, but not replace, the work of national regulatory authorities. It is clear that, in the future, such agencies will be increasingly stringent on efficacy and safety issues as governments look to safeguard public health. However, concerns have already been voiced about there being too much regulation in the existing UK system.

One area where improvement across the European system should be sought is earlier scientific dialogue between stakeholder parties. This would help industry to better understand regulatory requirements and thereby dispense with unnecessary, and often expensive, clinical trials. There is also an issue around different member states taking the lead in these processes, resulting in different and inconsistent criteria being applied. Greater European harmonisation of clinical trial criteria would help to eliminate national differences. This would add a greater degree of stability and predictability to the European market, fostering greater clinical research in Europe and in turn the UK.

Through the MHRA, it is possible that certain changes are likely to occur which could make the regulatory process more flexible both for the pharmaceutical industry and patients. First, technology may evolve to see the use of biomarkers in clinical trials, which could classify patients with related conditions.⁵⁸ This would enable the industry to produce treatments aimed at specific population sub-groups, thereby increasing the precision and focus of trials and decreasing the usual size and time required for trials to effectively demonstrate clinical efficacy and patient safety. The cost savings accrued to the pharmaceutical industry would be significant, with allied benefits to patients through speedy access to new treatments.

Any such shift in regulatory focus is likely increase uptake as the move towards patient-tailored genomic treatments develops further (see section 3.4) and biomarkers are used *ex post* to track treatment response. However, this form of regulation would be reliant upon regulators permitting ‘live licences’ – allowing a company to market a product on a restricted basis – in response to the pharmaceutical industry submitting data from such small but highly specific clinical trials. Once granted, the company could expand ‘in life’ testing across greater population sub-groups and in turn enhance a treatment’s evidence base to support the development of a broader product licence.

It is clear that this type of regulatory system would be controversial, requiring open and transparent communication between key stakeholders. However, there are potential benefits for all parties. The pharmaceutical industry would be able to recoup costs more quickly and reduce overall trial expense, leading to opportunities for earlier uptake and lower market prices. Patients would gain expanded and more rapid access to cutting edge medicines. And for the government, regulation would be less onerous but more responsive as regular evidence reports assessing product efficacy and safety would become more readily available within a shortened timeframe.

8.2 Solutions

While public safety must always be the over-riding concern when dealing with medicinal products, the pharmaceutical regulators at UK and EU levels should increasingly look to grant smaller scale yet highly focused ‘live licences’, which could then be expanded as further clinical data becomes available. This would enable cutting-edge medicines to reach patient cohorts more rapidly, improving treatment overall options for those that need it.

9. Tomorrow’s World: Education, Education, Education

9.1 Is the Future Bright?

Success today is necessarily determined by the plans we make for tomorrow. A world-class education system that equips the future workforce with the skills and scientific disciplines required for excellence within the pharmaceutical industry is evidently important for sustained success of the pharmaceutical industry in the UK. However, there are concerns in the UK over the closure of science departments within the higher education system and the dwindling number of students opting to take science-based subjects at Advanced (‘A’) Level and beyond.⁵⁹ This trend contrasts with the number of science graduates being produced by nations such as China and India. In 2006, the CBI reported that China was producing 300,000 graduates every year in science, technology, engineering and mathematics – a figure three times higher than the UK output.⁶⁰

The number of Chemistry ‘A’ Level entrants has dropped by a staggering 37% since 1982.⁶¹ In recent years, the field has seen a number of university departments close down. In 2004, the Royal Society of

Chemistry (RSC) predicted that by 2014 only 20 or so departments may still be in operation compared with the current 35-40, and as few as 6 departments could still be functioning as a worst case scenario.⁶²

This downward trend has been triggered by an acute drop in undergraduate applications for chemistry. It has been argued that this sharp reduction is in part a by-product of university top-up fees since chemistry courses are more expensive to run. In addition, funding itself is thought to be a key issue. The Director of Communications at the RSC recently stated: *"At the moment we are seeing departments closing, not because of a decline in student numbers, but because funding is dropping. Vice chancellors want to focus on subjects, which are less expensive to teach. Clearly, we do not know what the effect of top-up fees will be, but it does not help. The funding situation is very serious."*⁶³

Physics departments are also suffering a similar fate. It is estimated that since 1982 the number of 'A' Level entrants has halved, whilst the Institute of Physics has reported that, since 2001, 30% of university departments have either merged or closed.⁶⁴ Just as worrying are reports that leading scientific experts are leaving the UK due to the increasing levels of bureaucracy and a lack of appropriate funding. For example, Professor Neil Turok recently left the UK for Canada saying: *"Many colleagues were so ground down by bureaucracy, teaching and hunting for grants that it is increasingly hard to do good research... Over the years it has become increasingly clear that British politicians understand very little of how science works and of its value for the country and its economy."*⁶⁵

Recently, the ABPI had suggested that the UK is in danger of losing its prominent position in R&D to emerging economies due to skills shortages in core laboratory and mathematical skills. This in turn has led to a skills deficit in areas vital to R&D, such as clinical pharmacology, drug metabolism, pharmacokinetics and statistics. If this current trend continues, Dr Philip Wright, Director of Science and Technology at the ABPI, warns that *"the UK stands to lose an industry that contributes billions of pounds to its economy every year and the UK academic base will not be sustainable in the long term"*.⁶⁶

Investment in science is therefore necessary – it would benefit the wider economy and not just the pharmaceutical industry. According to the PWC report, a graduate in chemistry or physics is likely to earn £187,000 more during their career than someone with 'A' Levels but no degree, whereas a History or English graduate may increase their earnings by only about half as much. This report also demonstrates that Chemistry and Physics graduates pay approximately £135,000 more in tax than those with 'A' Levels and £40,000 more than the average graduate during their working lives.⁶⁷ It is therefore clear that a greater investment in science would not only be beneficial to the pharmaceutical industry, but would aid employment opportunities for individuals and present the government with a greater return in tax revenues.

The issue of adequate education in the UK, and creating an appropriately skilled workforce for tomorrow, undeniably represents a major concern. If eminent scientists from other disciplines are taking such drastic actions, scientists within the pharmaceutical industry must also be feeling the strains

of these difficult conditions and the shared frustrations concerning the lack of incentivisation to properly advance scientific excellence in the UK.

9.2 Solutions

It is clear that without adequate numbers of high calibre scientists in the workforce, the UK pharmaceutical industry is likely to suffer in the future. With emerging economies such as India and China producing large numbers of science graduates, the UK is in danger of losing the skills required to make it a sustainable and attractive long-term location for pharmaceutical operations. There is the obvious danger of companies relocating to skills-rich states.

The government must therefore invest in science at all academic levels. In line with recent ABPI recommendations⁶⁸, the Department for Innovation, Universities and Skills (DIUS) should look to establish a High-Level Science, Technology, Engineering and Maths (STEM) Strategy Group. It could bring together key funders, industry, scientific institutes and academia to harness a co-ordinated approach to developing the necessary skills pool required to sustain the UK as an attractive location for pharmaceutical operations. Giving consideration to strategic cash grants or tax breaks for university science departments is a practical way of recognising the value added contribution science graduates bring to the wider economy. Positive campaigns to incentivise science and scientific careers from the classroom to university level need to be developed. This investment will not just be of inherent benefit to the pharmaceutical industry, but to the wider UK economy.

10. Pricing and Reimbursement: 'We Want More Bang for Our Buck'

10.1 Value for Money

Spiralling healthcare costs and tighter budget constraints have impelled modern governments to place additional emphasis on allocating scarce resources efficiently and effectively. The pricing and reimbursement of pharmaceuticals is a policy tool which governments use for these purposes. In the UK, approximately 10% of the entire NHS budget – roughly £11 billion per year – is spent on drugs and medicines. Of this expenditure, around £8 billion is exhausted on branded products alone.⁶⁹ It is from this premise that national decision-makers are paying increasing attention to the way in which drugs are reimbursed.⁷⁰

The *Pharmaceutical Price Regulation Scheme* (PPRS) is the voluntary agreement between the UK Department of Health (DH) and the Association of the British Pharmaceutical Industry (ABPI) whereby companies negotiate profit rates from sales of branded drugs to the NHS every five years. The scheme has been running since 1956 (formerly the *Voluntary Price Regulation Scheme*), but has recently been the subject of growing scrutiny and debate.

The workings of the PPRS are complex. However, in essence the scheme encompasses two key elements: 1) profit controls, which set a maximum level on company profit earnings; and 2) price controls, which provide industry with some freedom to set initial prices for new medicines but with subsequent restrictions.⁷¹

Advocates argue that the PPRS has facilitated the sustained retention of UK-based pharmaceutical companies, fostering the appropriate mix of incentives between investment in R&D and profit-making.⁷² Opponents contend that the scheme is arcane, serving more the purposes of industry rather than delivering value for money to the patients and the NHS.⁷³

A recent Office of Fair Trading (OFT) report into UK drug pricing has recommended replacing the PPRS with *ex ante* value-based pricing (VBP).⁷⁴ The report argues that the PPRS does not optimise taxpayer value for money, nor does it dynamically incentivise R&D and innovation or assist the efficient uptake of new medicines.

Despite the OFT's recommendation, the PPRS was renegotiated in early 2008.⁷⁵ The headline changes include a price freeze between 1 September 2008 and 31 December 2008, the introduction of a price cut of 3.9% starting in 2009, and starting in 2009, measures to link the prices of out-of-patent branded medicines to the prices of any equivalent generics.⁷⁶

The DH has also outlined statutory proposals to control the price of branded medicines. Essentially, these involve the elimination of 'price modulation' as enshrined in previous schemes. These measures apply to any company not participating in the new PPRS. The DH expects these changes will deliver savings of an equivalent price cut of 5%, with the new arrangements being reviewed within a year.⁷⁷

The PPRS offers the pharmaceutical industry a degree of certainty over drug pricing even when price cuts occur in renegotiations. It enables companies to predict revenues over a 5-year period and therefore provide stable medium to long-term investments.

However, as healthcare budgets face greater scrutiny and governments wise up to the real importance of inculcating the shared principles of cost-effectiveness and value for money in pricing and reimbursement decisions, it is very likely that the PPRS will evolve over time. Instead a system of drug pricing as envisaged by the OFT is likely to gain momentum. Indeed, risk-sharing type schemes are set to increase in prevalence, with clear steps already being taken in this direction.

10.2 'Hedging Your Bets': The Use of Risk-Sharing

Risk-sharing schemes are likely to increase as governments look to maximise value for money. Indeed, the UK Shadow Health Secretary, Andrew Lansley MP, recently wrote in a national newspaper: "We should encourage the NHS to use new medicines which are clinically effective, and agree subsequently to pay the drugs companies according to the therapeutic benefit. In other words, drugs companies should only be paid

according to the benefits that a drug brings to patients.”⁷⁸ In this article, Mr Lansley heralded the benefits of existing risk-sharing schemes such as that for Lucentis, a product for wet age-related macular degeneration. Under the risk-sharing agreement, the NHS reimburses the drug cost of Lucentis for the first 14 injections in each eye being treated, but where further treatment is needed, the pharmaceutical company pays for the drug rather than the NHS.⁷⁹ The Conservative Party has since pledged as way of policy commitment to expand the use of risk-sharing and VBP.⁸⁰

Another example of risk-sharing is Velcade, which costs approximately £18,000 per patient.⁸¹ The drug has been approved by NICE on the basis that if patients show a “full or partial response” to the treatment the NHS will fully reimburse the drug. However, if patients show “no response or minimal response”, the company would have to “pick up the bill”.

For certain disease areas, this system of risk-sharing is likely to expand given the clear advantages to healthcare payers. Governments will only be fully paying out for medicines in cases where demonstrable clinical efficacy and cost-effectiveness have been reasonably evidenced. As Dr Allen Roses, GSK’s worldwide vice president of genetics, commented in 2003: “The vast majority of drugs – more than 90% - only work in 30 to 50% of people.”⁸² Increasingly, governments are going to want to make sure wherever possible that they are only paying for the 30 to 50% of cases.

10.3 Comply or Die?

As the terms of reference defining modern health care change, patient compliance will become ever more important as a way of optimising clinical efficacy. Company medical information departments will be ideally placed to support this strategic imperative.

As healthcare professionals continue to experience intensifying time pressures and the advent of skill mix cuts across different medical professions[§], industry could be well placed to provide more thorough non-promotional information about why medicines should be taken, their designed and intended health impact, and the implications of non-compliance on health. From a business perspective, this is an important development for industry. If patients are prescribed medicines through risk-sharing schemes, but are non-compliant and are subsequently deemed to be non-responsive by their doctor (leading to treatment cessation), the cost to industry through lost revenue and reimbursement would be profound.

This may also be an important development for the patient. Patients face an increasingly large choice in medicines, with numerous medicines having switched from prescription only medicines (POM) to pharmacy medicines (P) and P to general sales list (GSL). Indeed, since loperamide (the first medication to switch from POM to P at the request of the manufacturer back in 1983) over 80 medicines have switched in this way⁸³, with many more having switched from P to GSL. This trend is likely to increase

[§] Skill mix – sometimes referred to as ‘skill substitution’ – is the idea of different healthcare professionals complementing one another through greater use of multi-disciplinary crossover. For example, a pharmacist taking on greater responsibility for prescribing as well as dispensing medicines to reduce GP workloads and improve patient outcomes.

further, with the MHRA predicting further switches, and with Orlistat set to be the first European wide POM to P switch this year.⁸⁴

It has also recently been reported that advice received by patients at pharmacies is routinely poor, with a recent survey of patients suggesting that “unsatisfactory” advice was given on a third of occasions.⁸⁵ As medicines become more personalised and the choice of over-the-counter medicines increases, patients may wish to consult industry for information on products manufactured by a given company.

The cost of non-compliance for any healthcare system is hugely significant, and should not be underestimated. Speaking at the Eye for Pharma Patient Compliance Conference in February 2005, Cedric Tuck Sherman stated that the reported rate of overall non-compliance is 43%. One report has placed this figure for the US at a staggering cost of \$77-330bn. From a purely pharmaceutical perspective, Datamonitor estimates that better compliance could generate more than \$30bn a year in additional sales. In the context of tighter profit margins and reduced revenue generation, this is a substantive statistic for any pharmaceutical company.⁸⁶

10.4 Solutions

It is clear that the UK government will continue to seek value for money from healthcare spending, and thus is likely to pursue the ‘more bang for our buck’ approach, as part of formal pricing and reimbursement decisions in the future. Companies will therefore need to better demonstrate product value and carefully tailor economic and clinical arguments to justify optimal reimbursement. This is particularly the case in the context of risk-sharing agreements and possible volume controls. Improved clinical trial design and the upfront use of health economics are seminal in this regard.

Linked to this is the issue of compliance, which has always been of great importance to the pharmaceutical industry. This is set to increase in significance as payers seek to invest in those medicines and treatments that can optimise patient compliance and thereby offset costs from poor clinical and medicinal adherence. Whilst it is inappropriate to market POMs directly to patients, medical information departments offer an enriched source of disease-related and product-related information, having taken medicines from the test-tube to the bedside, and should therefore evolve and expand to aid in patient compliance. By doing so, there are opportunities to provide patients with an additional source of information on medical conditions and the associated properties of available products. Technology could be embraced so that ‘virtual conversations’ are enabled. Compliance aids could also be used to track and alert patients when a pill or dosing schedule has been missed.

11. 'Money, Money, Money': The Growth of Health Economics

11.1 Business is Business

Whilst the pharmaceutical industry exists to develop medicinal products to improve patient health, it is also by definition a profit-maximising sector that seeks to optimise revenue streams and enhance the economic bottom line. This is fundamental to meeting shareholder requirements and retaining overall competitiveness. One of the greatest challenges confronting companies is to augment product output in the face of increasingly limited and exhaustive investment resources. It is from this perspective that the need to effectively target investable propositions, and thereby minimise associated opportunity costs, has amplified the real importance of health economics for fostering sound product development and strategic decision-making.

11.2 A Marginal Business

The disintegration of the blockbuster model and the growth in generic products has essentially scuttled the economics of pharmaceutical development to a business of margins. To a large extent, this is being driven by a narrowing of product pipelines and the shifting of clinical advances away from scientific absolutes in previously untouched disease areas to a more nuanced battleground of medicinal relativity. The role and importance of health economics to guide investment decisions is therefore growing.

Furthermore, decision-makers are becoming more cost-conscious as healthcare budgets are subjected to increased scrutiny and resource pressures. Demonstrating clinical safety, quality and efficacy is no longer enough. There is also a 'fourth hurdle' to jump, namely cost-effectiveness, that constitutes an intrinsic component for reimbursement requirements. It is this final hurdle that forms the essence of health economics.

11.3 Jumping the Fourth Hurdle: Got to Get it NICE

The UK is often cited as being the pre-eminent example of using health technology assessment (HTA) for healthcare evaluation.⁸⁷ Founded in 1999 to counter geographical variations in healthcare and control costs, NICE is the independent watchdog responsible for recommending which drugs and treatments should be provided by the NHS.⁸⁸

In recent times, the role and profile of NICE have dramatically increased. Well-publicised controversies and damning media headlines over Alzheimer's drugs (e.g. Aricept) and oncology drugs (e.g. Herceptin) have catapulted the Institute firmly into the public spotlight, whilst a recent parliamentary inquiry into NICE has accentuated the importance of decisions pertaining to NHS drug availability.⁸⁹

From an industry perspective, the entrenchment of formal economic evaluation and the increasing emphasis being placed on cost-effectiveness makes NICE a key element in the equation, not least given

the international reach of the Institute. Keeping abreast of the changing requirements for 'getting through NICE' is vital to ensuring a lucid understanding of the shifting requirements for jumping an elevated fourth hurdle.⁹⁰ This is essential for developing appropriate strategies for maximising reimbursement opportunities.

11.4 Health Economics and the Product Pipeline: 'Backing the Winner'

Although health economics has traditionally played an 'end stage' role in the wider milieu of pricing and reimbursement decisions, upfront application of basic principles is becoming increasingly important for optimal preference selection during product development.⁹¹ This is particularly the case when accounting for the disintegration of the blockbuster model and the marginalisation of product differentiators as scientific advances confer diminishing returns to scale. Backing the winner and investing wisely are now absolute imperatives in this new pharmaceutical world. Speculative punts and 'clinical flutters' can no longer be justified when apportioning out tightly constrained budgets and assuaging shareholder demands.⁹²

It is from this premise that the *ex ante* use of health economics offers strategic advantages for maximising the allocation of scarce R&D resource and ensuring a steady flow of 'winners' through the product pipeline. With the advent of the fourth hurdle and increasing attention being paid to drug pricing and NICE decisions, getting the economics right is just as important as demonstrating clinical efficacy. This can focus attention around blockbuster or profit-maximising potential, whilst tapering the pursuit of unprofitable and cost-ineffective products.⁹³

Better use of health economics on initiation can lead to better outcomes at fruition, not least when seeking to efficiently utilise limited resource exhausted during development cycles. It will be those companies that understand this reality best that will benefit most in a more vigorously competitive but narrow international market.

11.5 Don't Forget the Politics

The pharmaceutical industry is completely unique among all other economic sectors for one striking reason – it deals with health care and therefore with people's lives. For publicly funded healthcare systems such as the NHS, the reality and importance of politics is central to a clear understanding of the prevailing policy environment.

Although elected representatives acknowledge the centrality of NICE as a decision-making lodestar, gone are the days of 'leaving it to the experts'. Indeed, the recent parliamentary inquiry into NICE by the Health Select Committee exemplifies this point.⁹⁴ This shift in focus is as much the result of the political imperative, namely the need to respond to voter/patient concerns, as it could ever be about rational health economics. As health assumes the mantle of the number one priority, patient demands

for improved healthcare are at all times high. Pricing arrangements and reimbursement deals are an easy target for the modern and power-seeking politician.

Increased scrutiny combined with a political desire to rein in drug expenditures points to one thing – sharper and tighter economic evaluation on the grounds of cost-effectiveness and hence the need for pharmaceutical companies to better demonstrate product value.⁹⁵ This has clear implications for the design of clinical trials and the possible employment of subgroup analyses. Companies will need to better handle the reality of incomplete or ‘missing data’, utilising evidence-based techniques such as meta-analysis where appropriate.

11.6 Solutions

The extra emphasis being placed on cost-effectiveness through NICE has ineluctably increased the importance of demonstrating economic value in addition to product efficacy. Economic evidence to justify optimal prices is critical. To this extent, companies will need to continue investing in the expansion of global health outcomes teams to ensure health economic and strategic argumentation for products are soundly developed. Moreover, improving general understanding of the requirements to jump the fourth hurdle and get through NICE is essential for product planning.

For manufacturers to maximise their lot, integrated clinical trial design with economic input is central to achieving positive outcomes. The demands of economic evaluation are set to magnify, thereby intensifying the need for watertight submissions. Thinking and planning ahead are therefore critical.

It is clear that the upfront application of health economics, particularly in the form of economic modelling and statistical analysis, will become increasingly important. This is particularly the case when confronted with early strategic decision regarding product selection and thereafter product positioning. Those companies that invest in the appropriate skill set and human resources will be best placed to optimise this process and in turn achieve optimal reimbursement when taking a product to market.

12. Animal Rights Activism

12.1 A Growing Menace?

Animal rights activism continues to represent a recurring problem to the UK pharmaceutical industry. Its presence and notoriety are seen to be a source of significant disruption to the operational activities of many pharmaceutical companies.

Although the right to peaceful protest is an incontrovertible British value, a small number of animal rights activists – or at least those professing to be so – have spilled over into extremism. Despite obvious difficulties in accurately estimating the cost consequence to industry, a BBC report in 2000

suggested that damage to property reached a staggering £2.6m with approximately 1,200 separate actions or attacks.⁹⁶

The intensity of this extremism has led some to cite animal rights activism as the primary cause of violence in the UK since the troubles in Northern Ireland.⁹⁷ It has been estimated that animal rights activism has added £30-70m to annual company bills due to the need to increase security measures⁹⁸ This figure stands at an average of £175,000 per scientific and research university.⁹⁹ In the most recent Health Select Committee Report on the pharmaceutical industry (2004/2005), Novartis alone stated that it has spent an extra £1m in less than 2 years on increased security costs.¹⁰⁰ The number of attacks and threats to individuals is likely to add a greater indirect cost through extra police time and increased security costs amongst pharmaceutical suppliers. Thus, the net result of animal rights activism is often a costly disruption to vital medical research and innovation.

The majority of the public are supportive of vivisection to aid medical advancements. Recent MORI polls indicate 86% of people are either supportive or neutral.¹⁰¹ The European Federation of Pharmaceutical Industries and Associations (EFPIA) state that the European Union provides “the best standards of protection for laboratory animals in the world” through Directive 86/609.¹⁰²

Industry is attempting to reduce the number of tests that it conducts using animals. Figures show that over the last 10 years the number of animal tests has been reduced by approximately a third.¹⁰³ In 2007, the ABPI reported that there was “a sustained downward trend in violent and intimidating animal extremism.”¹⁰⁴ However, in spite of this downward trend in the UK, the EFPIA recently warned “more co-ordination, collaboration and well-designed communication about animal rights extremism across the EU” is required as indications appear that the incidence of activism overseas is possibly on the increase.

It is therefore important that future governments continue to recognise the threat posed by amending legislation as necessary, as occurred in the 2004/2005 Queen’s Speech through the Serious Organised Crime and Police Act.¹⁰⁵ It is also necessary that cooperation and collaboration is furthered at the EU level to sustain the improvements seen in recent years in the UK, and to prevent any of the bad experiences witnessed here from being exported to other parts of the globe.

12.2 Solutions

Whilst the ABPI has recently reported a lower level of animal rights related disruption and activity, both industry and the UK government must remain vigilant. Collaboration at a European level must increase in order to facilitate intelligence sharing and to promote cohesive cross-border policies to stem future problems. In the UK, the government must continue to regularly review the prevalence of animal rights activism in conjunction with the ABPI. Where applicable, Parliament should look to tighten existing legislation to minimise operational disturbances and protect the rights of pharmaceutical companies to continue researching and developing life-saving products.

13. Conclusions: The Road Ahead

Despite the fact that the UK pharmaceutical industry continues to make a significant contribution to Britain's economy, it is currently facing a number of important challenges. Successfully addressing these challenges, and alleviating the associated pressures confronting individual companies, is seminal to a sustainable future.

Although each company has its own business model and strategic objectives, there are common actions that can be taken to help mitigate systemic issues. In response to the apparent decline in the blockbuster drug, some companies have looked to invest in generic medication operations to stem the flow of lost revenue from off-patent products. Other companies have looked to diversify their product portfolio in order to buttress financial turbulence across targeted disease areas.

All companies must prepare for an increase in demand for personalised medicines. These will be based on patient genomics, which offer scope for greater efficacy and improved tolerability profiles. Governments are also likely to put a premium on preventative products, meaning companies should look to proactively establish a presence in this flourishing area. Governments in turn should coherently commit to providing favourable reimbursement for those products that can prevent illness, and thereby offset downstream treatment costs falling on national healthcare systems.

Counterfeit medicines are becoming a more prevalent and cross-border problem for industry. Global trade agreements, such as ACTA, and concerted action through the EU is essential, whilst cross-company collaboration is also necessary. This can help tackle recurring problems surrounding the repackaging of parallel imports, the existence of online 'medicine stores' and the difficulties associated with more porous and globalised borders.

Emerging markets, such as those in the E7 group, are presenting a direct challenge to the UK pharmaceutical industry. This is due to their increasing expertise and numbers of qualified graduates, smaller labour costs and reduced regulation, and dynamic incentives for attracting industry investment. Indeed, the economic desirability of some of these markets, particularly India and China, is clear. Established economies, such as Ireland, Switzerland and Singapore, are conferring 'unique selling points' and are providing location hubs for operational activities. It is critical for the UK to learn from these countries and seek to reduce its increasingly uncompetitive levels of corporation tax and cumbersome regulation. Strategic R&D and manufacturing credits should be considered along with support for science in the education system, especially at the university level.

The UK government should also aim to bring the level of investment in pharmaceutical medicines in line with that of other established economies. By doing so, patients would benefit from the uptake of new technologies, and may give NICE greater scope for approving new treatments. It would also reflect the

huge advantages the pharmaceutical industry provides to the wider economy; something that should be further encouraged through a more incentivised tax and regulatory environment.

The UK pharmaceutical industry must also be aware of the increased importance of health economics for future decision-making, and expect an increase in the use of risk-sharing schemes. Responding to these structural challenges necessarily requires better investment in internal resources to maximise patient compliance, enhance clinical trial design and preference selection between competing alternatives in the product pipeline. This is the elixir for optimising financial revenue returns from such schemes.

Animal rights activism has been reported to have decreased in recent times by the ABPI, but industry and government must remain cognisant of this threat. Where necessary, legislation should be tightened to protect workers within the pharmaceutical industry and to enable important scientific innovation to continue. The UK pharmaceutical industry should look to impart its knowledge and experience in this area to prevent a spread of this problem across European borders. Coordination and collaboration with the EU is essential in this regard.

It is clear that the UK pharmaceutical industry is undergoing a period of dynamic and sweeping change. Pharmaceutical companies must seek new and creative solutions today in order to best meet and overcome the challenges of tomorrow. Indeed, preparing for and understanding this necessity is the *sine qua non* for future success.

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