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The EU pharmaceuticals market: parameters and pathways

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1. Introduction

The European Union pursues two major objectives in its policy on pharmaceutical products: its policies strive to secure a high level of public health and innovation and, at the same time, provide support for a competitive industry that ensures that Europe continues to benefit from new medicines.

The first objective requires that access to medicines and treatments is affordable and that medicines are safe and effective, but also, increasingly, that patients should receive the information necessary to make informed choices about their own treatment. The second objective requires enhancing the competitiveness of Europe's pharmaceutical sector. The competence to intervene in the market, and the related tools with which the EU institutions pursue – or, rather, attempt to reconcile – these two objectives are by no means similar in legal scope or nature. Although the European Union has now created a centralized licensing agency, the European Medicines Agency (EMA), and also enjoys extensive legislative powers to determine what might be termed the 'regulatory pathway' for authorizing the marketing of new products in accordance with strict criteria on safety, quality and efficacy, it has less direct influence on what can be termed the commercial or 'market pathway' – the prices and conditions under which products are purchased by national health care providers and insurance companies, and, indeed, patients. The role of the Member States in defining the ways they provide access to medicines, the price of those medicines and how patients and consumers gain access to information on pharmaceutical products is still crucial in determining overall policy, even though a certain amount of secondary legislation adopted at the European level is of increasing importance in shaping the market pathway.

With respect to the second objective – ensuring the broader competitiveness of the industry – the picture has always been complex,

given the very processes of competition in the pharmaceutical market and the Union's overriding goal – and, indeed, constitutional duty – to create an integrated European market. On the one hand, the extensive level of harmonization and, indeed, centralization of the rules governing product licensing or marketing authorization allows the European-based industry to register and market their products across all twenty-seven Member States of the European Union. On the other hand, national rules and regulations on price and profit controls and marketing more generally can have a major impact on the competitiveness of the industry.

The persistence of national regulation that hold down prices and profits, and results in market fragmentation, is often claimed to be a major factor in explaining the alleged difference in the strengths of the European-based research industry as compared to its American counterparts. The European Federation of the Pharmaceutical Industries and Associations (EFPIA) claims that, between 1990 and 2005, research and development (R&D) investment in the United States grew 4.6 times, while in Europe it grew by only 2.8 times, and that the United States still dominates the biopharmaceutical field, accounting for three quarters of the world's biotechnology revenues and R&D spending.¹ According to Intercontinental Marketing Services (IMS) data, 66% of sales of new medicines marketed since 2001 are generated from the United States market, compared with 24% from the European market.² And according to the European Commission, if Europe was once known as the 'world's pharmacy' (where, until 1998, seven out of ten new medicines originated in Europe), today this has fallen to about three out of ten.³ Europe's industry, rightly or wrongly, is hence perceived by the sector, as well as policy-makers at the European level, to be facing serious challenges, matched only by those facing public health, challenges driven by demographic change

¹ See EFPIA, 'The Pharmaceutical Industry in Figures 2007', www.efpia.org. See also G. Verheugen, Commissioner for Enterprise and Industry, 'Delivering better information, better access and better prices', Speech to the Pharmaceutical Forum, SPEECH/06/547, Brussels, 29 September 2006, www.europa.eu.

² IMS Health data is available on www.imshealth.com.

³ See the European Commission, 'Public-Private Research Initiative to boost the competitiveness of Europe's pharmaceutical industry', Press Release No. IP/08/662, 30 April 2008.

and the high cost of innovative treatments. Europe, it is alleged, is losing competitive ground not only to the United States, but also to China, India and Singapore.

Yet the most persistent issue in European policy towards the sector is how to deal with market fragmentation.⁴ Traditionally, the Commission, parallel traders and generic competitors have relied upon the twin principles of free movement and undistorted competition to 'correct' obstacles to trade and competition that result from divergent national price and profit control legislation. This type of intervention is largely ad hoc and ex post, however, and has not succeeded in addressing the research-based industry's concerns that the returns it needs to generate new products can be guaranteed. On the contrary, the continued presence of parallel imports and the Commission's continued, if passive, support of it, is a persistent thorn in the industry's flesh. At the same time, national governments are reluctant to surrender sovereignty on pricing and profit controls and, by implication, an important part of their national health budgets to the European institutions. Hence, further attempts to harmonize price control legislation at the European level have been more or less abandoned following the adoption of the framework Price Transparency Directive in 1989.⁵ Instead, coordination and consensus-building has taken place through various stakeholders' forums, commencing with the so-called 'Bangemann' rounds in the 1990s,⁶ and the G10 Medicines Group in 2002. The latter reached agreement on fourteen recommendations, and expressed its wish to continue its work further. In response, in 2005, the Commission set up the High Level Pharmaceutical Forum, which is discussed below. This type of informal consensus-building

⁴ See also A. Gambardella, L. Orsenigo and F. Pammolli, 'Global competitiveness in pharmaceuticals – a European perspective', Report prepared for DG Industry, November 2000, http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_01_2001.pdf.

⁵ Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems, OJ 1989 No. L40/8.

⁶ For an appraisal of the Bangemann rounds and the G10 process, see L. Hancher, 'The pharmaceuticals market: competition and free movement actively seeking compromises', in M. McKee, E. Mossialos and R. Baeten (eds.), *The impact of EU law on health care systems* (Brussels: PIE-Peter Lang, 2002), pp. 235–75.

has become the preferred policy approach in an attempt to find a politically acceptable balance between the competing interests of the Member States and those of the European Union's institutions, as well as the competing objectives of public health demands and those of the research-based industry.

The simultaneous pursuit of these various objectives at the EU level has always called for a delicate balancing exercise between competing interests. If anything, this balancing exercise has become more complex in the enlarged EU of twenty-seven Member States, given the considerable differences in health care budgets across the EU, as well as the increased mobility of the sector itself, which can source not only production but also research in more conducive climates, such as China, India and Singapore. But there are other factors that complicate the picture further, and not least the changing impact of European and national competition law and policy on the sector, and the resulting possibilities and constraints that this implies for the Commission, the Member States, payers and industry alike. Important developments in the case-law of the European courts and the national competition authorities and courts may indicate that many of the traditional assumptions about the role and impact of competition policy towards the pharmaceutical sector may need to be re-assessed. But the tools to ensure affordable access to safe and effective medicines by increasingly proactive patients who are better informed on medicines and health treatment choices must also evolve to meet new demands, especially as national budget constraints dictate the need for effective pricing and reimbursement policies – policies that increasingly require a demonstration of the relative effectiveness and efficacy of new products before they can be eligible for reimbursement. The dynamics of these processes may thrust the European institutions (and, in particular, the Commission) into new roles – roles that go beyond merely creating an internal market in which products can move freely from one market to another and patients can access products from different sources, but that leave the Member States' responsibility for managing health care budgets broadly intact. As a result, the extent to which individual Member States traditionally have also been able to strike a balance between the two objectives of promoting innovation while securing affordability through price and profit regulation may have to be re-assessed.

This chapter examines these dynamics, in light of the changes to the competition policy 'tool kit', which has been an important feature

of the European pharmaceutical market for several decades, and draws some tentative conclusions on the potentially changing role of the European Union in the pharmaceutical sector. In particular, it will highlight a shift in preferences for certain of the traditional tools at the disposal of the European institutions to promote the creation of a single pharmaceuticals market. Whereas, in the past, the Commission, supported by the jurisprudence of the European courts, relied primarily on the rules on free movement of goods to condone if not actively stimulate parallel importation of pharmaceutical products into higher priced markets, recent policy and legal developments suggest that the EC competition rules may also function as effective 'tools' to pursue this goal. Against this background, this chapter will argue that the 'regulatory' and 'market' pathways are intersecting in new and challenging ways for the major stakeholders in the European Union – that is, the Member States, the different parts of the pharmaceutical industry, including the research-based industry, the generic manufacturers as well as parallel importers, wholesalers and, last but not least, health care providers and health insurance bodies, and patients. The intersection of these regulatory and market pathways may have important consequences for the way in which major policy issues confronting these various stakeholders could develop. These include the role of generics versus research-based products, pricing issues, including the emergence of value-based pricing, as well as other areas of pharmaceutical regulation, including its extension to cover clinical trials, orphan and paediatric medicines, and, further, direct marketing of prescription-based products to patients, all of which will determine the continued attractiveness of the European market for innovative medicines, as well as access and affordability for patients. As this chapter will seek to explain and illustrate, both regulation and European competition law can shape how these two pathways intersect; as such, they can impose both constraints on and, at the same time, offer opportunities for the different stakeholders involved.

The second section of this chapter will briefly outline the parameters of competition in the industry and explain the three types of competition that typify it. It will then go on to examine recent regulatory developments and their impact on these processes of competition, as well as new developments in the application of ex post competition controls in the regulatory pathway to promote generic competition.

The next sections examine potential challenges to the Commission's traditional policy on parallel imports and how this may affect the market pathway in the future. The final section reviews the current endeavours of the recently created Pharmaceutical Forum to deliver new methods to reconcile the objectives of securing affordable access to pharmaceutical products while promoting competitiveness, and considers the scope for soft-law solutions at the intersection of the regulatory and market pathways. The chapter ends with some tentative conclusions.

2. The parameters for competition in the European pharmaceutical market

The European pharmaceutical market is characterized by three types of competition.

A. Therapeutic competition

Competition between new, patented, innovative products is often referred to as therapeutic competition: research-based pharmaceutical companies compete to develop therapies that are superior to existing or future drugs developed by their competitors and then try to persuade the relevant national 'payers' to pay for or reimburse a significant part of the price for these products. Market exclusivity may be protected not only by patents and other generally applicable intellectual property rights, but also by specific regulation pertaining to marketing authorization procedures. Regulatory data protection provisions in Community legislation ensure that regulatory authorities cannot use clinical and other data submitted by the original developer of a product to subsequently assess applications from competitors for marketing authorizations for generic versions of the product for a certain period of time.

This type of competition also enjoys a relatively benign environment in the sense that European competition law generally encourages joint research and development, licensing, co-marketing and co-distribution arrangements as long as the advantages of cooperation outweigh any negative impact on competition. The fact that many government payers hold significant (or even monopsonistic) purchasing power may also shield dominant companies from allegations of abusive conduct.

B. Generic competition

The second type of competition comes from generic products. As will be discussed below, this type of competition is increasingly encouraged at the European and national levels, although the research-based industry is also protected from generic competition by a number of legal and regulatory instruments that aim to encourage R&D by granting innovative products a de facto market exclusivity in the 'regulatory pathway', at least for a specified period of time.

The advent of a generic (or non-patented) version of a leading product on the market once both patent and regulatory data protection periods have expired can have a substantial impact on prices – leading to price falls of up to 80%. A report from the British Office of Fair Trading (OFT) on the United Kingdom's price and profit regulation scheme (PPRS) published in mid-2007 found that almost 83% of prescription items in the United Kingdom are now written generically compared to just 51% in 1994.⁷ The European Generics Medicines Association (EGA) claims that demand for generic medicines has grown in the last two decades to account for nearly 50% of medicines consumed in the twenty-seven EU Member States today.⁸ As such, the research-based industry has made repeated attempts to prevent or delay registration and marketing of generic copies of their leading products. As a result of recent amendments to the European product licensing regime, however, this strategy is increasingly unattractive and companies are resorting to other tactics. As we will discuss in greater detail below, the application of Article 82 EC (which prohibits the abuse of a dominant position) is now becoming of greater importance in determining the legality of certain industry tactics to delay or deter generic competition.

Generic competition is also referred to as inter-brand competition, and this term covers competition from generic and, increasingly, so-called 'bio-similar' products. The High Level Group on Innovation and the Provision of Medicines (also referred to as the G10 Medicines Group), established by the European Commission in 2001 in order to provide a consultative forum on moving European pharmaceutical policy forward,⁹ had called upon EU Member States to secure the development of a competitive generic market in the European Union

⁷ www.offt.gov.uk/shared_offt/reports/comp_policy/oft885.pdf.

⁸ See www.egagenerics.com/doc/ega_factsheet-01.pdf.

⁹ See also Chapter 4 in this volume.

(Recommendation 4).¹⁰ In its Communication of 1 July 2003, the Commission had stated that ‘generic medicines can provide significant savings to health care providers, however, their use must be balanced with sufficient incentives to develop innovative products’.¹¹ The successor to the G10 Medicines Group, the Pharmaceutical Forum (discussed below), endorsed the importance of this Recommendation in its Progress Report on 29 September 2006.

C. *Intra-brand competition*

The final type of competition takes the form of intra-brand competition – usually, in the form of parallel imports of cheaper products from low-priced Member States into higher-priced markets. As a result of enlargement in 2004 and again in 2007, the extent of price differentials across the European Union has widened substantially. The European Commission, relying on the past jurisprudence of the European courts on the application of the EC Treaty rules on free movement and competition, has generally taken a positive standpoint on parallel imports as a way of cementing the internal market in pharmaceuticals. Certain of the recommendations adopted by the G10 Group in May 2002 hinted that this generally benign approach might have to be reconsidered, at least in so far as there was legal scope to do so. Nevertheless, in its subsequent Communication on parallel imports in 2003,¹² the Commission seemed to maintain its traditional pro-parallel trade line.¹³

D. *Consequences*

The impact of these different processes of competition on the two objectives of European Union policy on the pharmaceutical sector is complex and controversial. The gradual creation of a centralized

¹⁰ For an examination of the processes leading to the work of the G10 and a discussion of these recommendations, see Hancher, ‘The pharmaceuticals market’, above n.6.

¹¹ European Commission, ‘A stronger European-based pharmaceutical industry for the benefit of the patient – a call for action’, COM (2003) 383 final, 1 July 2003, p. 16.

¹² European Commission, ‘Communication on parallel import of proprietary medicinal products for which marketing authorisations have already been granted’, COM (2003) 839 final, 30 December 2003.

¹³ *Ibid.*, p. 6.

regime for granting marketing authorizations, culminating in the establishment of the EMEA in 1993, has been primarily fashioned with a view to facilitating simultaneous market access across the entire European union for new, innovative products – and, as such, to stimulate therapeutic competition. At the same time, however, this process of centralization also offers generic products the promise of wider market access, and can stimulate inter-brand competition once patents and other intellectual property rights expire. Generics can stimulate innovation through competition and also by creating significant ‘financial headroom’ for innovation, in the sense that national health care budgets can direct the savings from the use of competitive generic equivalents to finance reimbursement of new, truly innovative products. In addition, a number of generic companies have produced their own new chemical entities (NCEs) (for example, Aztromycin, Glatiramer Acetate, Deferiprone and Vinpocetine).

At the same time, it must be stressed that national marketing authorization procedures have not been entirely displaced by the ongoing process of centralization and harmonization: national regulations still play an important role in the European pharmaceutical market. Hence, a product originally licensed in Greece, for example, cannot be automatically exported to a higher-priced market such as the Netherlands and marketed there; national authorization is still required, albeit subject to the requirement that the Dutch authorities recognize the procedures followed by their Greek counterparts. In other words, significant regulatory barriers to free movement and competition across the entire European Union still remain. Regulation marks the boundary lines between the three processes of competition identified above. It follows that any attempts to modify regulation and to harmonize national rules will have a profound impact on these very processes of competition and the interests of the different stakeholders who benefit in very different ways from them. Constructing and refining the European ‘regulatory’ pathway therefore always involves a delicate balancing of competing interests. This process can be characterized as an ongoing but complex and controversial attempt at the European level to strike a balance between the competing objectives of maintaining a favourable economic environment for innovative products while securing affordable access for patients to medicines in general.

Recent developments in European and national competition law (which are now largely based on the same principles as a result of the

adoption of the so-called ‘Modernization’ Regulation 1/2003/EC)¹⁴ have only contributed to that complexity and controversy. We will consider these developments in further detail below, but the evolution of the European regulatory framework for product licensing or marketing authorization will be examined in greater detail in the next section, with a view to examining the way in which it has sought to strike a balance between competing interests and provide counter-balancing mechanisms in what may be termed the ‘regulatory pathways’.

3. Recent developments in the ‘regulatory’ pathway

It is not the intention here to examine the complex and detailed body of secondary legislation – that is, the various European directives and regulations for the approval of new products or for their generic equivalents. This body of legislation has evolved piecemeal since the adoption of the first Directive 65/65/EEC into what are known as the centralized and decentralized licensing regimes.¹⁵ It covers not only the process of product approval, but also many aspects of the subsequent marketing of pharmaceutical products, including labelling, packaging and distribution. Policy in the regulatory pathway falls primarily within the remit of the European Commission’s Directorate-General for Enterprise and Industry (DG Industry), and its central task has been to further the realization of the single market for pharmaceutical products, with the Directorate-General for Competition (DG Competition) playing an increasingly proactive role in this respect, as is discussed below. The following subsections will examine certain topical issues in the regulatory pathway with a view to highlighting their impact on the potential for stimulating therapeutic, inter-brand and intra-brand competition.

A. *The centralized and decentralized licensing regime*

In order to market a pharmaceutical product within the EU, a brand name drug manufacturer must obtain a marketing authorization covering the Member States in which the drug will be marketed. This body of law has primarily evolved with the aim of creating, through

¹⁴ Council Regulation 1/2003/EC on the implementation of the rules on competition laid down in Articles 81 and 82 of the Treaty, OJ 2003 No. L1/1.

¹⁵ For an analysis of the evolution of the European licensing regime from 1965 through to 1988, see L. Hancher, *Regulating for competition: government, law and the pharmaceutical industry in the United Kingdom and France* (Oxford: Clarendon Press, 1990).

harmonization, a single European market for newly patented and innovative products, which must be subjected to extensive testing and screening before they can be put on the market. Since the adoption of the first EEC Directive in 1965, in the wake of the thalidomide crisis, a Community-wide system of market authorization based on common principles for prior testing and screening of new medicinal products and a complex technical body of regulation has evolved, culminating in 1995 in the creation of the European Medicines Agency – the centralized European agency responsible for licensing new products, as well as issuing guidelines on various stages in the development and eventual administration of medicinal products. As this subsection will briefly explain, national governments have not been prepared to allow full centralization or total harmonization of each and every aspect of pre- and post-marketing regulation at the Community level, and have retained important powers both in the regulatory and, most particularly, in the market pathways.

Following an extensive review of the operation of the EMEA in 2000, the existing body of regulations was further streamlined. The EMEA remains primarily linked to the Commission through the Directorate-General for Enterprise and Industry (DG Industry) (responsible for the internal pharmaceutical market) and not the Directorate-General for Health and Consumer Protection (DG SANCO) (responsible for health and consumer protection policy). There are currently two methods for obtaining a marketing authorization: (a) either through a centralized application to the EMEA for a marketing authorization covering the entire territory of the EU; or (b) through a decentralized application for an authorization covering only an individual Member State, which can be recognized by other Member States under the mutual recognition procedure (MRP). This general scheme is governed now by Regulation 726/2004/EC¹⁶ (replacing Regulation 2309/93/EC, which laid down the centralized procedure and established the EMEA) and Directive 2001/83/EC on the community code relating to medicinal products for human use (as amended by, *inter alia*, Directive 27/2004/EC),¹⁷ which

¹⁶ European Parliament and Council Regulation 726/2004/EC laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, OJ 2004 No. L136/1.

¹⁷ European Parliament and Council Directive 2004/27/EC amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ 2004 No. L136/34.

sets out the general rules applicable to medicinal products, including the procedures for marketing authorization and mutual recognition. Regulation 726/2004/EC has again been recently amended in January 2007 to extend the centralized procedure to paediatric medicines.¹⁸

Under the centralized procedure, a drug manufacturer must submit to the EMEA for consideration a detailed dossier containing quality, safety and efficacy information about the drug.¹⁹ This application is considered by the Committee for Medicinal Products for Human Use, and, if granted by a Commission Decision, the marketing authorization will be valid in all Member States. Use of the centralized procedure is mandatory for biotechnology medicines, products containing NCEs, for the treatment of certain disorders and diseases, and is optional for other NCEs and sufficiently innovative products. Under the MRP, the application for a national marketing authorization is made to a single Member State (known as the reference Member State (RMS)) and, if granted by this RMS, then the MRP, which is codified in EU legislation, provides that other Member States must approve the marketing authorization. In practice, the RMS coordinates the MRP and prepares an assessment report on the medicinal product, which is sent (along with the approved information leaflets and packaging) to the other Member States selected by the applicant. Unless a Member State raises an objection on the grounds of potential serious risk to public health, the drug is given marketing approval in all the EU Member States selected by the applicant.

B. Patent protection and the supplementary patent certificate regime

In the EU, patents generally last for a maximum of twenty years starting from the date the patent application was filed. During that time, the patent holder has an exclusive right to prevent third parties from making, using, selling, importing or stocking the patented product (or method of production) that falls within the claims of the patent. Once a patent for a drug has been filed, preclinical and clinical testing will

¹⁸ European Parliament and Council Regulation 1901/2006/EC on medicinal products for paediatric use and amending Regulation 1768/92/EEC, Directive 2001/20/EC, Directive 2001/83/EC and Regulation 726/2004/EC, OJ 2006 No. L378/1.

¹⁹ See also Chapter 3 in this volume.

commence with a view to marketing authorization. However, given that, as a result of the adoption of increasingly stricter premarketing regulation, obtaining the necessary authorization is a lengthy process that can last between six to twelve years, and so the product is patent-protected for considerably less than twenty years after first marketing. In other words, ‘effective patent protection’ is much shorter than twenty years.

To meet the concerns of the research-based industry, which argued that, due to the adoption of stricter premarketing regulation, it was not being given sufficient opportunity to reap the benefits of its R&D and investment, the EU introduced the Supplementary Patent Certificate (SPaC) regime in 1992.²⁰ An SPaC is granted if, at the date of application, the innovative drug is protected by a basic patent in force, a valid marketing authorization is in place and the product has not already been subject to such a certificate. The application must be filed in each country where protection is sought, within six months of the grant of the first marketing authorization. An SPaC extends the period of the patent protection for up to five years, or fifteen years from the first marketing authorization in the EU, whichever is less. It extends the protection conferred by the patent and, hence, it covers the same rights (and limitations) as the patent itself. The issue of whether the SPaC only protects the product in question in the specific form stated in the marketing authorization or whether it protects the active substance in the specific, authorized form and all other forms protected by the basic patent arose in the case of *Farmitalia Carlo Erba*. The Court affirmed that protection extends to the active ingredients, so that a third party cannot obtain market authorization for the same active substance merely by using a different form of it.²¹

Clinical trials and pharmacovigilance – limited harmonization so far

Not all the stages of the development and subsequent testing of a new therapy are subject to centralization, however. Certain crucial stages of the process are only subject to partial harmonization. The regulation of clinical trials remains primarily a national matter, albeit

²⁰ Council Regulation 1768/92/EEC concerning the creation of a supplementary protection certificate for medicinal products, OJ 1992 No. L182/1.

²¹ Case C-392/97, *Farmitalia Carlo Erba* [1999] ECR I-5553.

that the procedures for conducting trials are harmonized on the basis of Council Directive 2001/20/EC, the terms of which are currently under review. This Directive has been the subject of heated debate and criticism and is generally considered to have failed to achieve its stated goals. Monitoring the potential adverse effects of products already on the market – pharmacovigilance – is also primarily a national activity and relies on spontaneous reports from patients and doctors. On the one hand, the current regulations are considered by the industry to be fragmented, contradictory and unclear and are thus in urgent need of consolidation and rationalization. On the other hand, patient organizations and some national regulators claim that the current system is not sufficiently transparent or sufficiently independent from the interests of the industry.²² The Commission launched a consultation process in April 2006 in order to obtain a variety of views on the current functioning of the EU pharmacovigilance system, followed by a consultation based on draft proposals for changes to the current legislation. The results of this second consultation exercise have been analysed in a document published on DG Industry's web site in April 2008, and are expected to lead to the adoption of more detailed proposals for further amendments to Directive 2001/83/EC, including a strengthened role for the EMEA and a better institutionalized embedding of the advisory Pharmacovigilance Committee into the current European and national systems. In particular, the EMEA could be given explicit tasks to strengthen transparency and communication and make public more information on the benefits and risks of medicines.²³

Remaining gaps

At the same time, there are still crucial issues that are not subject to harmonization at all. Although, since 1992, the relevant European legislation has banned advertisement to the public of medicines subject to prescription and has only allowed advertising for other medicines under certain conditions, information provided to patients is not harmonized at all. Although the Commission has launched various initiatives on this ongoing public debate, and it has now focused on the

²² See also G. Permanand, E. Mossialos and M. McKee, 'Regulating medicines in Europe: the EMEA, marketing authorisations, transparency and pharmacovigilance', *Clinical Medicine* 6 (2006), 87–90.

²³ Available at http://ec.europa.eu/enterprise/phabiocom/comp_new.htm.

need to address the lack of a Community framework on information to patients, the legal situation has not changed. As we will explain below, however, the attempts now being made to address this lacuna provide a poignant illustration of the policy pitfalls that can arise when the 'regulatory' pathway threatens to extend into highly sensitive – and primarily national – areas.

4. Generic competition in the regulatory pathway

This section will first focus on a number of recent developments that are illustrative of the European Union's (and particularly the Commission's) ongoing attempts to strike a balance between the competing objectives of maintaining a favourable economic environment for innovative products while securing affordable access for patients to medicines in general. Recent changes at the European level have facilitated the licensing of generic products and, to a certain extent, 'bio-similar' medicines.

At first sight, the amended EU legislation (that is, Directive 2004/27/EC²⁴ and Regulation 726/2004/EC,²⁵ which entered into force in late 2005) has exerted a major impact on the regulatory pathway for generic medicines, since it:

- permits generic R&D before patent expiry (the so-called 'Bolar' scheme);
- allows marketing of generics even where the original product has been withdrawn from the market for commercial reasons;
- provides a more efficient system for the registration of generic medicines (through the decentralized or mutual recognition procedures);
- ensures greater harmony between newly-approved generic medicines and older-approved originator products; and
- provides clear scientific and legal definitions of generic and bio-similar medicines – definitions that were not contained in earlier EU legislation.

The amended regime is again a useful illustration of the EU's continuing attempt to strike a balance between the competing interests

²⁴ Directive 2004/27/EC, above n.17.

²⁵ Regulation 726/2004/EC, above n.16.

of the R&D-based sector and those of the public and private health care institutions that benefit from greater generic competition. Nevertheless, it is claimed that, despite these improvements, there is much to be done, as the EU generic industry operates in a highly complex regulatory environment in Europe – an environment that creates barriers to market entry that do not exist in other parts of the world, such as the United States. In particular, the new legislation has increased the overall period of time that generic manufacturers must wait before registering their products. Certain Member States do not allow generic licensing applications until the original patent expires, while others create limitations on receiving applications for market authorization or for pricing status while the original patent remains in place.

A. Data exclusivity

Directive 2004/27/EC, which had to be implemented at the national level by 30 October 2005, introduced a number of important amendments to the provisions governing data exclusivity in Directive 2001/83/EC.²⁶ As this 2004 Directive did not replace the earlier 2001 Directive, the latter measure remains in force, as amended.

Data exclusivity has proved complex in the context of the so-called ‘abridged application’ procedure for marketing a generic drug. In principle, the regulatory authorities can only process a generic application after a certain number of years following the granting of the first marketing authorization of the originator or innovative medicine. The principle of data exclusivity hence precludes authorities for a reasonable period of time from using or relying on the original registration or the data submitted by the innovator for the benefit of third parties seeking to market a copy of the product without producing their own data. After the period of data exclusivity ends, the originator’s data can be relied upon by the authorities to approve the marketing of copy products, thereby obviating the need for the second applicant to repeat trials already conducted by the originator. Article 8(3) of the amended 2001 Directive states that the results of preclinical tests and clinical trials must be submitted with the application for a marketing

²⁶ Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ 2001 No. L31/67.

authorization of a particular drug. Article 10(1) allows a generic producer, once data exclusivity has expired (as well as the patent protection and, where relevant, supplementary patent protection (see above)), to submit an application for authorization without submitting the data referred to in Article 8(3)(i) – the so-called ‘abridged’ procedure. Hence, the authorities can use the original application as a reference, but this provision does not give the generic manufacturer access to the original research data.

B. From data exclusivity to marketing exclusivity

Originally, a Member State had to grant data exclusivity for either six or ten years from initial authorization. While a number of countries granted a ten-year protection period, a number opted for the shorter period. Under the 2001 Directive, generic manufacturers could only apply for an authorization once the patent, the SPaC and data exclusivity had expired. This meant that the total protection period was effectively extended for about another twelve months in practice, while the application for the authorization for the generic drug was being processed. The 2004 Directive introduces a number of changes.

8+2+1 Year data and marketing exclusivity

Generic manufacturers will be barred from referring to the results of preclinical and clinical tests of the original, innovative drug until eight years have elapsed from the date of authorization of the latter. Hence, in some Member States, the data exclusivity period has been extended by two years, but in others reduced by two. However, a new term – ‘marketing exclusivity’ – has been introduced to prevent the marketing of a generic drug during the two years following the data exclusivity period.

The period of marketing exclusivity runs in parallel with the data exclusivity but lasts for ten years. And so, at the end of the first period (data exclusivity), there is an additional two years market exclusivity, which runs from the end of the data exclusivity period. The two year additional market exclusivity period can be extended by one year if, during the eight year data exclusivity period, the innovative company obtains an authorization for one or more new therapeutic indications, which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing

therapies. Together these amendments form the so-called '8+2+1' rule. In practice, this means that a generic company must wait for eight years before submitting its marketing application and must wait a further two (or three) years, during which time that application can be processed. The 2004 Directive (Article 10(6)), however, serves to protect the interests of generic competition by allowing generic producers to commence research and development work on a product before patent (or SPaC) expiry – this is the so-called 'Bolar' scheme, which takes its name from the United States equivalent. Consequently, carrying out the necessary studies and trials will no longer constitute patent infringement.

A generic medicinal product is now defined in the 2004 Directive and this has put an end to much of the controversy – and litigation – generated by the 'essential similarity' test, which had not been defined in earlier directives. Both the European Court of Justice (ECJ) and the English High Court had been prepared to interpret this concept in favour of the generic manufacturer.²⁷ Article 10(2)(b) of the 2004 Directive defines a generic medicinal product as meaning:

[A] medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product and whose bioequivalence with the reference product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters and so on of an authorised active substance must be supplied by the applicant.

This new definition provides clarity as to when the abridged procedure (or hybrid abridged procedure) should be applied. Nevertheless, it contains vague concepts, such as when two drugs differ significantly regarding safety or efficacy, and it is likely that the different components of the definition – which has to be implemented into national

²⁷ Case C-106/01, *Novartis* [2004] ECR I-4403; Case C-36/03, *Approved Prescription Services* [2004] ECR I-11583; Case C-74/03, *SmithKline Beecham* [2005] ECR I-595; *The Case of R (on the Application of Merck Sharp and Dohme Ltd) v. The Licensing Authority* [2005] EWHC 710 (Admin).

law – will require further clarification from the courts. In particular, the registration and use of generic medicines is allegedly hampered due to a lack of EU-wide harmonization of indications of reference products (also known as ‘originators’) on which the generic applicant must base its common European-wide approval. This, in part, is attributed to patents being granted on particular uses of products and to allowing data exclusivity for ‘new’ indications, which in fact do not represent any real innovatory value,²⁸ as well as the extension of the types of properties eligible for intellectual property rights (IPR) protection in general, through the combination of patent, trade-mark and patent. The scope of IPR includes not only methods of treatment but also methods of treatment and action mechanisms, while IPR may also be invoked for packaging, delivery profiles and dosing, screening methods, etc.²⁹ Further delays in bringing generics to the market are attributed to market approval/authorization or licensing processes, as well as the granting of substitution/reimbursement status (see below).

C. *Bio-similar medicines or products*

The concept of a bio-similar product was introduced into EU legislation in 2003 and further defined in Directive 2004/27/EC. In essence, the registration process for this type of product allows a manufacturer to submit an application for an authorization for a product claimed to be similar to another biological medicine. The rationale for creating this new licensing route is that biological medicines or biologics do not usually meet all the conditions to be considered as a generic (see Recital 15 of the Directive). Given the complexity of biological molecules, and the fact that they are produced in living organisms, it is virtually impossible for applicants to produce an identical copy of a reference biological product. Hence, the licensing route is based on the principle that biologics are not chemical drugs and that the generic approach is very unlikely to be applicable to biologics: dissimilar

²⁸ See, in particular, M. N. Graham Dukes, ‘Priority medicines and the world’, *Bulletin of the WHO* 83 (2005), 321–400.

²⁹ See the presentation of E. Larson, ‘Evolution of IPR and pharmaceutical discovery and development’, Paper presented at the Conference on ‘Intellectual Property Rights: How Far Should They Be Extended?’, Washington, DC, 22 October 2001.

products are not biogenics. The three main eligibility criteria are, first, that the product must be a biological medicine. In legal terms, this means any type of biologic, including not only blood-derived products but all vaccines or products derived from gene/cell therapy, etc. Secondly, the reference product must have been authorized within the European Community, although it is not required that the reference product still be authorized at the time that the bio-similar application is filed. Thirdly, the application has to be submitted after the expiry of the data exclusivity period (the 8+2+1 rule discussed above).

Commission officials have acknowledged this to be one of the most complex issues that the European Community has faced in the area of pharmaceuticals in the last five years. In particular, as regards the kind of data required to file a bio-similar application, the EU legislation is based on the principle that a uniform approach is unworkable in this area. The type and amount of preclinical and clinical data are not predefined in legislation but are determined on a case-by-case basis. Thus, the requirements to demonstrate safety, efficacy and quality of a bio-similar product are class-specific and the amount of information required can range from that required for an 'abridged' generic application to being nearly as complete as a full, stand-alone application. The legislation makes specific reference to the obligation of compliance with detailed scientific guidelines to be produced by the EMEA, and the first of these guidelines was released in November 2004. These guidelines make it clear that the quality attributes in the bio-similar and reference products should not be identical, as minor molecular structural differences are inherent to biologics. However, these differences must be justified on scientific grounds and must be considered on a case-by-case basis in relation to their potential impact on safety and efficacy.

The EMEA approved the first two bio-similar products in the EU in 2006. By mid-2008, five authorizations had been granted, and two more were expected to be granted by the end of 2008. One application for an interferon was given a negative scientific opinion in June 2006 because of major concerns regarding comparability with the originator product, including impurities. A debate has also arisen as to whether the European regulatory framework can also be used to evaluate interchangeability – i.e., is a bio-similar product actually interchangeable in medical practice with the reference product? The EMEA does not consider that it has the legal competence – either

through the legislation provisions or on the basis of its guidelines – to conduct this type of assessment.³⁰

The generic manufacturers' association, the EGA, predicts that by 2010 highly expensive biopharmaceutical products will make up 25% of pharmaceutical sales in the EU and 50% of new applications. As a result, bio-similar medicinal products will become, in its view, a necessary component of future health care management policies. It claims that even a 20% price reduction on six off-patent biopharmaceutical products would save the EU Member States some €1.6 billion per year. The Association claims that, while the regulatory pathway for bio-similars has now been established, much remains to be done to establish a market pathway at the national levels.³¹

D. Competition law and the regulatory pathway: the AstraZeneca Case

As discussed above, the European institutions have sought to strike a balance between the objectives of stimulating innovation while securing affordable access through regulation *ex ante* – regulation securing rights to data exclusivity and, more recently, marketing exclusivity in the interests of the research based industry – while at the same time harmonizing the marketing authorization procedures for generic products. The Commission has, however, considered it necessary to expand this 'tool kit' in the form of stricter *ex post* control on certain practices on the part of the research based industry – practices that have consisted in using the regulatory pathway to frustrate the market pathway for generic competitors.

In June 2005, the Commission imposed a fine of €60 million on AstraZeneca (AZ) for abusing its dominant position in the market for proton pump inhibitors by delaying generic market entry of generic copies of its best-selling product, Losec, through its use of procedures before national patent offices and regulatory authorities.³² This

³⁰ See testimony of N. Rossignol, Administrator, Pharmaceuticals Unit, European Commission Directorate-General for Enterprise & Industry, before the HELP Committee on 8 March 2007, http://help.senate.gov/Hearings/2007_03_08/Rossignol.pdf.

³¹ See EGA, 'Building a 'market pathway' for bio-similar medicines', Press Release, 3 May 2007, www.bogin.nl/ega-press.

³² Commission Decision 2006/857/EC of 15 June 2005 relating to a proceeding under Article 82 of the EC Treaty and Article 54 of the EEA Agreement (Case COMP/A.37.507/F3, *AstraZeneca*), OJ 2006 No. L332/24.

case is particularly significant because it confirms that the behaviour of pharmaceutical companies before regulatory and other authorities can be considered abusive, whereas it was previously considered that this was unlikely, if only because these procedures were open to all competitors regardless of the market share of the leading manufacturer. AZ developed a central strategy to protect Losec's market position in Europe after expiry of the basic patent on the active ingredient – omeprazole. AZ sought to obtain additional patent protection through the SPaC regime of up to five years in a number of countries by providing national patent offices not with the required date of the first marketing authorization of Losec in the EU but with the date the product was first reimbursed (a later date).

The Commission found that AZ's 'misleading representations' to the patent authorities were abusive, since they were part of a centralized strategy to prevent generic market entry. The Commission was not persuaded by the argument that the terms of the EC Regulation relevant to the information to be submitted to the patent offices (Regulation 1768/92/EEC) was not clear, nor was its view changed by the fact that questions on the interpretation of the Regulation had been referred to the ECJ, which had only clarified the scope of Articles 3, 13 and 19 of the Regulation in a ruling in 2003.³³ According to the evidence in the Commission's possession, AstraZeneca concealed from the national patent offices the date upon which it had received its first marketing authorization for Losec as the marketing authorization was given prior to the cut-off dates provided for in the Regulation.

The Commission also found a second type of abuse in AZ's strategy of selectively withdrawing the market authorization of Losec in favour of an improved version – Losec MUPS – in the four countries where, due to the specific market situation, generic competitors, as well as parallel importers, would have been able to launch generic copies unless the 'reference product' was made unavailable. AZ attempted to ensure this by withdrawing its own market authorizations for Losec in capsule form (the original formulation) and applying for a new authorization based on a tablet formulation. At the time these practices were implemented, they could (and did) give rise to foreclosure effects on the market, since generic producers could only obtain a marketing authorization and parallel importers could

³³ Case C-127/00, *Hässle AB v. Ratiopharm* [2003] ECR I-14781.

only obtain import licences if there was an existing reference market authorization for the original corresponding medicinal product.

Subsequent changes to Directive 2001/83/EC as introduced by Directive 2004/27/EC, as discussed above, should make it impossible to repeat this specific conduct. The amended legislation provides that: (a) all marketing authorizations granted for the same medicinal product (including not only the initial marketing authorization but also subsequent marketing authorizations relating to change in strength, pharmaceutical form, administration route or presentation of the product) shall be considered to belong to the same 'global' marketing authorization (Article 6(1)); and (b) a generic marketing authorization shall be granted even if the reference product is not authorized in the Member State in which the application is submitted, as long as it is authorized in any other EU or EEA Member State (Article 10(1)).

The *AstraZeneca* decision represents an important plank in the Commission's strategy of dealing strictly with any restrictions on parallel imports and on market access for generic products. Indeed, it is the first time that the Commission has relied on Article 82 to penalize conduct before national patent offices and regulatory authorities responsible for marketing authorizations. In particular, it marks an interesting extension of the case-law on Article 82 with regard to the exercise of intellectual property rights by dominant companies, and the decision has raised question marks as to how this fits in with the Commission's wider review of Article 82, in which it has considered the need to adopt a more economics-based approach (as opposed to a form-based approach) to allegedly abusive practices.³⁴

The recent case-law on the application of the competition rules to intellectual property rights has focused on the question of whether the grant of compulsory licences for intellectual property rights could be imposed on dominant companies by competition authorities. The ECJ has ruled in a series of cases that the exercise of an exclusive right and, more specifically, the refusal of only a company holding a dominant position to grant a licence for an intellectual property right may, in

³⁴ European Commission, 'Discussion Paper on Article 82', DG Competition Discussion Paper (2006), p. 7, <http://ec.europa.eu/comm/competition/antitrust/art82/discpaper2005.pdf>.

certain exceptional circumstances, constitute an abuse of a dominant position.³⁵ In the *IMS* case, the Court held that in order for such a refusal to be regarded as abusive it must prevent the emergence of a new product for which there is potential demand, be without objective justification and capable of eliminating all competition on the relevant market.³⁶ In the *AstraZeneca* case, the Commission not only examined the exercise of intellectual property rights but also possible abuses in obtaining, protecting and extending these very rights. The Commission has essentially argued that the dichotomy between the existence of an IPR and its exercise has gradually been abandoned in the case-law and has been replaced by the concept of the subject matter of the right in question.³⁷ Furthermore, the Commission held that the use of public procedures and regulations may, in specific circumstances, constitute abuse, as this concept is not limited to behaviour in the market only.

As regards the second issue, the economics-based approach to Article 82, a report published in July 2005 pointed out that, with regard to a 'refusal to deal' case, the competition authorities should be particularly reluctant to intervene when the source of the bottleneck is an intellectual property right, since any intervention may reduce the incentive to innovate.³⁸ In other words, the Commission should conduct a full balancing exercise and take into account not only the exclusionary effects of the conduct vis-à-vis generic drug companies, but also the potential pro-competitive effects and efficiencies of the conduct, as well as the effects that its own enforcement actions might have on the innovative sector. In the *AstraZeneca* case, the Commission distinguished marketing authorizations, which, unlike patents, SPaC and data exclusivity, are not intended to reward innovation but instead merely bestow the right to sell products on the market.³⁹

³⁵ Joined Cases C-241/91 P and C-242/91 P, *Magill* [1995] ECR I-743.

³⁶ Case C-418/01, *IMS* [2004] ECR I-5039.

³⁷ Commission Decision 2006/857/EC, above n.32, para. 741; Case C-223/01, *AstraZeneca* [2003] ECR I-11809; Case C-238/87, *Volvo Veng* [1988] ECR 6211.

³⁸ J. Gual *et al.*, 'An economic approach to Article 82', Report by the EAGCP, July 2005, http://ec.europa.eu/comm/competition/publications/studies/eagcp_july_21_05.pdf.

³⁹ See also N. De Souza, 'Competition in pharmaceuticals: the challenges ahead post *AstraZeneca*', European Commission, Competition Policy Newsletter No. 1 (2007), pp. 39–43.

The Commission's decision has now been appealed to the Court of Justice⁴⁰ but, in the meantime, the Commission has launched similar investigations into alleged abusive conduct by Boehringer – which is believed to have been involved in similar practices⁴¹ – and, in January 2008, the Commission launched a sector-wide inquiry – the most wide-ranging and flexible tool in its competition tool-kit, allowing it to consider the industry as a whole, rather than focusing on specific companies or practices.⁴²

E. The Commission Inquiry

The Commissioner for Competition has now publicly acknowledged that 'generic competition is an area which has suffered from under-enforcement in the past', and has taken action accordingly. The launch of the Commission's anti-trust, sector-wide inquiry on 16 January 2008, unusually, was heralded by dawn raids at the offices of at least eight major pharmaceutical companies. In May 2008, the inquiry was extended to a further eighty companies. The Commission's major concerns are its perception that fewer new pharmaceuticals are being brought to market and that the entry of generic pharmaceuticals may be being 'delayed'. The objective of the inquiry is to obtain a better understanding of competition in the sector and to determine whether these two concerns result from anti-competitive practices. The inquiry will focus on two particular issues: agreements between pharmaceutical companies, such as settlements in patent disputes, and establishing whether companies have created artificial barriers to product entry, through misuse of patent rights, vexatious litigation or other means. This latter concern obviously arises from the Commission's investigation into AstraZeneca, and it is clear that the Commission will review registration and litigation

⁴⁰ Case T-321/05, *AstraZeneca v. Commission* (judgment pending); registered in OJ 2005 No. C271/24.

⁴¹ Case COMP/39.246, *Boehringer* (judgment pending), details of initiation available at <http://ec.europa.eu/comm/competition/antitrust/cases/decisions/39246/initiations.pdf>.

⁴² Case COM/D2/39.514 initiating an inquiry into the pharmaceutical sector pursuant to Article 17 of Council Regulation 1/2003/EC, above n.14. See also European Commission, 'Antitrust: Commission launches sector inquiry into pharmaceuticals with unannounced inspections', Press Release No. IP/08/49, 16 January 2008.

strategies that are designed to extend the effective patent life of a 'blockbuster' product.

Anti-competitive agreements

The Commission has not previously considered patent settlement agreements in any detail, nor has there been any finding of infringement in relation to such agreements in the past. In contrast, this area has been a hot topic in United States anti-trust practice for some time. The latter is heavily influenced by the relevant legislation, including the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act amendments), which does not have a direct European equivalent. These arrangements typically arise in the context of settlement of patent infringement claims between a manufacturer of branded pharmaceuticals and a manufacturer of a new generic product. Settlements of such claims have raised complex anti-trust concerns, particularly where the settlements provide for delayed entry of the generic into the market, with a 'reverse' payment from the patent holder to the alleged infringer. The United States courts of appeals have taken different approaches to these arrangements, with some holding that such settlements are per se an illegal allocation of markets. In addition, the principal United States anti-trust regulators appear to hold different views on the issue. The Federal Trade Commission views reverse settlements as anti-competitive while the Department of Justice appears to take a less formalistic standpoint.⁴³

The Commission has stated that its inquiry will not challenge intellectual property law protection, but the launching of the inquiry seems to indicate the Commission's willingness to get to grips with the impact of competition on the patent strategies of manufacturers, particularly towards the end of a product's patent life. The launching of the inquiry raises complex legal and policy questions as to where the boundary lies between legitimate protection of patent rights and anti-competitive conduct. Much will depend on the follow-up steps taken on completion of the Commission's final report, scheduled for spring 2009. Enforcement action against particular firms is not necessarily

⁴³ G. Robert and F. Falconi, 'Patent litigation settlement agreements in the pharmaceutical industry: marrying the innovation bride and competition groom product', *European Competition Law Review* 27 (2006), 524–33.

an inevitable outcome of a sector-wide inquiry. Indeed, previous Commission inquiries have resulted in a wide range of outcomes. The adoption of legislation dealing with particular areas of concern is one possibility (for example, measures in relation to payment systems and consumer credit as a result of the retail banking sector inquiry), but there are also examples of the Commission encouraging industry participants to address issues themselves (as, for example, in the business insurance inquiry).

5. Developments in the marketing pathway

In this section, we will focus on issues relating to the post-authorization of prescription-only products and, in particular, examine the issue of the provision of information to patients on medicines and direct-to-consumer advertising of these products, the present regulation of which is currently under review.

A. Pricing and marketing

Although the introduction of new medicinal products into European and national markets is subject to extensive, but closely harmonized, regulatory procedures, two key features of the marketing pathway – pricing and the provision of information to patients – remain primarily the preserve of Member States.

Indeed, only a minimal level of harmonization has been achieved with respect to pricing and profit controls, whereas the increasingly sensitive issue of access to information for patients is entirely a matter for the Member States, subject only to the common basic principle, as enshrined in Directive 2001/83/EC, that advertising of prescription products to the public is prohibited.⁴⁴ Attempts to reform the essentially procedural requirements introduced by the Price Transparency Directive of 1989 have met strong resistance and, instead, the European Union has sought to evolve a wider policy consensus on the substance of national price and profit control through a series of political initiatives based on consultation and coordination and the development of general guiding principles. In the meantime, however, the Commission has continued to support intra-brand competition

⁴⁴ Directive 2001/83/EC, above n.26.

by relying on the fundamental principles of free movement and competition. Recent case-law at both the European and national levels suggests that the scope for the application of competition-based principles, as a result of the introduction of a more economics-based approach, may be more restricted in the future. These developments are examined in the next subsection below.

B. Intra-brand competition: the setting sun?

Parallel trade in the pharmaceutical sector has been the subject of decades of heated dispute and litigation between industry players and wholesalers, as well as the European Commission and Member States. Economic studies are advanced on both sides of the debate. There are studies to support the contention that parallel trade is a key factor undermining European pharmaceutical competitiveness by diminishing revenue flows and reducing innovation potential, and yet it brings no clear benefit to consumers, since gains accrue mainly to the traders rather than the health care buyers (or payers) or patients.⁴⁵ But, equally, there are studies that identify a positive impact for this latter group as the research-based industry attempts to keep market share by lowering prices.⁴⁶

Nevertheless, the Commission's prevailing view, as last expressed in its Communication of 2003,⁴⁷ is that parallel trade should be supported as a lawful form of trade within the European Union. In addition, parallel trade affects market practices. Pharmaceutical companies claim that the often volatile activities of wholesalers result in an unpredictability of demand and intricate supply chain problems. This complicates the allocation of resources for these companies and may have a detrimental effect on their ability to ensure the appropriate level of stock to meet patient needs in each EU Member State. In response, the research-based companies have resorted to dual-pricing strategies

⁴⁵ P. Kanavos *et al.*, 'The economic impact of pharmaceutical parallel trade in European Union Member States: a stakeholder analysis', London School of Economics and Political Science (2004), <http://mednet3.who.int/prioritymeds/report/append/829Paper.pdf>.

⁴⁶ M. Ganslandt and K. E. Maskus, 'Parallel imports and the pricing of pharmaceutical products: evidence from the European Union', Swedish Research Institute of Industrial Economics Working Paper No. 622 (2004).

⁴⁷ European Commission, 'Communication on parallel import', above n.12.

and supply quota systems. Supply quota systems come in a variety of forms, but usually they involve a restriction of supplies to wholesalers commensurate with the latter's requirements in the domestic market, plus a limited margin. Dual pricing strategies seek to reduce the price differential between geographical markets and, as a result, the incentive for arbitrage in the form of parallel trade. Manufacturers set a standard price for unregulated markets as well as export products, but may agree a discounted price in regulated markets.

From an EU competition law perspective, the first strategy may give rise to a breach of Article 81(1) EC if the supply quotas result from an agreement with the wholesalers concerned; if there is no consensus – that is, if the wholesalers oppose the quota – then the quota system can only be caught if the company imposing it unilaterally is dominant in the relevant product and geographical markets.⁴⁸ Dual pricing strategies, however, may be subject to Articles 81 and 82 EC if there is agreement between the supplier and the wholesaler and, in the case of Article 82, the supplier is dominant. Recent case-law at the European and national levels indicates, albeit cautiously, that both strategies may be pursued under certain conditions. In a number of respects, the Commission's standpoint in its 2003 Communication on parallel imports now appears to be undermined.

C. The GlaxoSmithKline Case: dual pricing upheld

On 27 September 2006, the Court of First Instance (CFI) handed down its long-awaited judgment on the Commission's decision to refuse to grant an exemption under Article 81(3) of the EC Treaty to a dual pricing system operated by GlaxoSmithKline (GSK) in Spain.⁴⁹ GSK was compelled under Spanish law to charge reduced wholesale prices for sales on the Spanish domestic market, but imposed higher prices for parallel export by its wholesale customers, prices that were equivalent to the prices it originally applied to register in Spain. The Commission, taking its traditional formal approach to clauses in agreements leading to export bans as a 'per se' restriction of competition, had concluded that any attempt to limit parallel exports was

⁴⁸ Case T-41/96, *Bayer AG v. Commission* [2000] ECR II-3383; Joined Cases C-2/01 P and C-3/01 P, *BAI and Commission v. Bayer* [2004] ECR I-23.

⁴⁹ Case T-168/01, *GlaxoSmithKline Services v. Commission* [2006] ECR II-2969.

contrary to Article 81(1) and as a so-called ‘hard-core’ restriction, was not eligible for exemption. The CFI rejected the Commission’s approach that GSK’s policy had the object of restricting competition but upheld the Commission’s reasoning as regards to the effects of the arrangements on competition. Nevertheless, it concluded that the Commission should have fully examined the legal and economic context of the pharmaceuticals sector, and should have carried out a full balancing exercise of all the relevant evidence before reaching a conclusion on Article 81(3). Hence, the CFI referred the decision back to the Commission. In the meantime, appeals to the ECJ were lodged by the Commission and by GSK, as well as by two European wholesalers’ associations (the European Association of Euro-Pharmaceutical Companies (EAEPC) and Aseprofar) against the CFI ruling.⁵⁰

This judgment will have significant repercussions for future Commission policy. In the past, the Commission has always contended that, while it was broadly sympathetic to the claims of the research-based industry that divergent national price and profit regulations that give rise to parallel trade could threaten their capacity for innovation and their global competitiveness, its hands were tied by the jurisprudence of the Courts, which supported parallel trade as an important stimulus to completing the internal pharmaceuticals market. That the Commission had already entertained doubts as to the wisdom of this approach was evident in its 1998 Communication on the single market in pharmaceuticals, where it recognized that unless parallel trade could operate dynamically on prices, it creates inefficiencies because the financial benefit accrues to the parallel trader and not to the national health care system or to patients.⁵¹

Although it is not possible to examine the judgment in full detail here, it may be noted that the CFI rejected the Commission’s main argument that the arrangements must be considered to be per se contrary to Article 81(1) because they have the object of restricting parallel trade.

⁵⁰ See Case C-501/06, *GlaxoSmithKline Services Unlimited v. Commission* (not yet reported); Case C-513/06, *Commission v. GlaxoSmithKline Services Unlimited* (not yet reported); Case C-515/06, *European Association of Euro-Pharmaceutical Companies v. GlaxoSmithKline Services Unlimited* (not yet reported); and Case C-519/06, *Asociación de exportadores españoles de productos farmacéuticos v. GlaxoSmithKline Services Unlimited* (not yet reported).

⁵¹ European Commission, ‘Communication on the single market in pharmaceuticals’, COM (98) 588 final, 25 November 1998.

The CFI concluded that, as the prices of the relevant medicine were to a large extent shielded from the free play of supply and demand due to national regulatory controls, it cannot be taken for granted that parallel trade tends to produce prices that increase the welfare of final consumers. In other words, there is no automatic protection for parallel trade under Article 81, but rather this activity must be shown to have given final consumers the advantage of effective competition in terms of supply or in respect of price, rather than simply benefiting the parallel traders as such. Therefore, GSK was correct to maintain that, in the specific legal and economic context, the Commission could not merely presume, in the absence of a more detailed examination of the essential characteristics of the sector, that the parallel trade restricted by GSK's sales conditions would have a beneficial impact on the prices charged to final consumers and, as a result, that this policy would have the object of restricting competition. Importantly, however, the CFI stated that, even though the clause was attributable to, and allowed by, the regulatory context, this did not mean that it could not be said to infringe competition rules.

Therefore, the CFI concluded that, even if GSK's pricing was merely consistent with the regulatory context, this did not justify the pricing policy as such for the purposes of Article 81. It then went on to consider the application of the exemption criteria as provided for in Article 81(3). GSK had argued that the higher revenues resulting from the dual pricing scheme contributed to efficiency by means of increased capacity for R&D expenditure. This, in turn, facilitated innovation, which, it argued, is the determining parameter on inter-brand competition. As GSK financed its investment in R&D from its own funds, and not from borrowing, any reduction in its returns undermined its capacity to innovate. At the same time, the parallel exports did not compete on price and therefore had no pro-competitive effect on the market.

GSK also argued that these issues had to be assessed in the context of the Commission's Communication of 1998,⁵² where precisely these characteristics of the pharmaceutical market were acknowledged. The CFI concluded that the Commission had failed to undertake a rigorous examination of these arguments and, in particular, that it should have examined whether a parallel trade led to a loss

⁵² *Ibid.*

of efficiency for the industry in general and for GSK in particular. The evidence on which the Commission had relied was ambiguous, as it had failed to compare the gain in efficiency for intra-brand competition with a loss of efficiency in inter-brand competition. The CFI set the required standard of proof that it expected in such a case at a high level: the Commission was not entitled to reject GSK's efficiency and innovation arguments on the grounds that the advantages claimed by GSK would not necessarily be achieved. The Commission was required to consider whether it was more likely than not that the claimed advantages would be achieved. Therefore, the Commission had not properly substantiated its conclusions on the ineligibility of the arrangements for exemption under Article 81(3) nor had it properly balanced the available evidence in reaching its final conclusion.⁵³

D. Abuse of a dominant position

A related question dealt with by the Court was whether or not it was abusive conduct, contrary to Article 82(c), for a dominant company to refuse to supply to a parallel exporter. It reasoned that GSK was responding to, rather than creating, different pricing areas and Article 82 only prohibits a dominant company from applying artificial price differences between Member States. As each Member State constituted a distinct national market due to different national pricing and profit controls, it was possible for GSK to apply different prices because different markets exist. This line of reasoning reflects case-law at the national levels, in particular in the lower-price Member States, including France, Greece and Spain, to the effect that a refusal by a dominant company to supply an exporter so as to prevent the exploitation of price differences in the destination market will not constitute abuse of a dominant position.

E. Supply quotas and refusals to supply

The Greek Syfait Case

The Greek Competition Commission (HCC) issued a decision on 5 September 2006, shortly before the CFI ruling in the *GlaxoSmithKline*

⁵³ The EAEPCC lodged a complaint against Pfizer for the introduction of a similar system on 17 October 2005, but at the time of writing no formal action had been taken on this.

v. *Commission* case discussed above, also concerning a complaint against GSK for its refusal to supply certain quantities of three products – Imigran, Lamctal and Serevent – to Greek wholesalers trading outside Greece. GSK initially discontinued supplies in 2000, but subsequently resumed supplies in 2001 on the basis of restrictive quotas. On reference to the ECJ, the Advocate General concluded that, in the circumstances of the case, it was not abusive for GSK to refuse to supply the orders, taking into account the pervasive regulation of price and distribution in the Member States that were imposed upon rather than made or chosen by the pharmaceutical companies. The ECJ declined to rule on the reference, finding that the Greek Competition Commission was not a court that was entitled to make such a reference, but the Greek Commission went on to rule that GSK did not abuse its dominant position when it applied the quota system, although cutting off supplies for the initial period did amount to an abuse. It may be noted that the HCC did not assess GSK's supply quota system on the grounds that this was under review by the Commission.

Nevertheless, the ECJ is now confronted with several references from the Greek courts to which the ruling of the Competition Commission has now been appealed. In particular, the Greek Appeal Court asked the Court for further guidance on the nature and scope of the duties of the national competition authority to apply Community competition rules in the same way to markets that function competitively as to those in which competition is distorted by state intervention. The Court was asked to give further guidance on the criteria for establishing abuse in the event that the 'standard' approach does not apply and to consider whether an approach entailing the balancing of interests is appropriate. If this indeed is correct, what interests are to be compared? Is the answer affected by the fact that the ultimate consumer/patient derives limited financial advantage from the parallel trade, and should account be taken of the interests of social insurance bodies in cheaper medicinal products? The Court took a rather traditional, formal approach, however, and held that any refusal by a pharmaceuticals company in a dominant position to meet orders sent to it by wholesalers involved in parallel exports constitutes an abuse, although such a company must "be in a position to take steps that are reasonable and in proportion to the need to protect its own commercial interests".⁵⁴

⁵⁴ Joined Cases C-468/06 to C-478/06, *Sot. Lélos Kai Sia EE (and Others) v. GlaxoSmithKline AEVE* [2008] ECR I-7139, paras. 69–70.

In the meantime, EAEPCC has sought the annulment of a Commission decision rejecting three complaints against GSK. The Commission, in fact, rejected the complaint on the basis that the Greek authorities were dealing with the case and EAEPCC, in turn, appealed this decision to the CFI.⁵⁵

The French Competition Council and the Paris Court of Appeal

The previous year (20 December 2005), the French Competition Council (FCC) held that GSK, Pfizer, Merck Sharp & Dohme (MSD), Lilly, Sanofi and others had not abused any dominant position in refusing to supply certain exporters. When the price of a product is regulated, it should not be regarded as abusive to refuse to supply such products to another operator that is not itself active on the market affected by the price regulation and that only seeks to purchase the products in order to export at a profit. Furthermore, the competition tribunal dismissed allegations of discrimination in favour of wholesalers with mixed operations involving domestic and exporting activities and to the detriment of purely exporting wholesalers. It also concluded that a difference in treatment could be justified in light of the public service obligations resting on the wholesalers with domestic activities.⁵⁶ However, the FCC appears to have concluded that a quota system for pure exporters would not be justified and would be anti-competitive, and that it would keep this subject under review. Furthermore, the French tribunal rejected the argument that Article 81 should be applied even if there was no evidence of an agreement between the companies to target wholesalers who exported.

In a separate ruling, the Paris Court of Appeal, again relying on the Commission's 1998 Communication, doubted that, even assuming that the suppliers in question were in a dominant position, their

⁵⁵ Case T-153/06, *European Association of Euro-Pharmaceutical Companies v. Commission*. The Commission relied on Article 13 of Regulation 1/2003/EC, above n.14. Removed from register on 28 February 2008.

⁵⁶ Article 81(2) of Directive 2001/83 provides that the holder of a marketing authorization for a medicinal product and the distributors of that product must ensure appropriate and continued supplies of the product to pharmacies and persons authorized to supply medicinal products so that the needs of patients in the member state in question are covered.

decision to limit the supplies of certain products to wholesalers on the basis of allocations of a quantity of products by reference to the market shares that they had in the French market would, in itself, constitute abuse.

The Spanish Tribunal for Fair Trading

In dealing with the same question, the Spanish Tribunal for Fair Trading doubted if the companies involved could be held to be dominant, given the degree of market regulation and the purchasing power of the national health system, so that suppliers did not have the independence of action normally associated with a dominant position. Furthermore, it stated that there could be no abuse of any dominant position, as a company in such a position could not be required to initiate commercial relations with all customers or potential customers who request it. The complainant, who had never had regular, stable or continuous dealings with the manufacturer, GSK, had access to alternative sources of supply, such as other distributors.

F. Implications

This recent spate of cases at the European and national levels indicates that conventional competition law methodology is not always being adhered to and that courts and competition authorities at both levels are willing to recognize the specific characteristics of parallel trade and arbitrage between high and low-priced markets. The different national regulatory conditions must be taken into account, not only to assess the agreements at issue but also to understand the position of the different parties in the relevant market. Competition analysis depends on the delimitation of a relevant product⁵⁷ and a relevant geographic market. In these recent cases, there is a discernable trend, culminating in the recent case of *GlaxoSmithKline v. Commission*, towards

⁵⁷ In most cases, a preliminary idea of the appropriate market definition is obtained by looking at the products grouped together in Level 3 of WHO's Anatomical Therapeutic Classification (ATC) scheme. The Commission generally uses these ATC Level 3 categories as the starting point of its analysis of the relevant market. In many cases, this category will be the relevant product market, although the Commission (and national authorities) may conclude that the market should be narrower. IMS sales data is also grouped according to the ATC categories so market share data is relatively easy to obtain.

recognition of the fact that wholesalers who purchase products for the purposes of parallel export are operating in a different geographical market that is outside the market of the Member State of export, and as suppliers into the higher-priced Member States of import. This is of importance because it makes it harder to sustain the argument that companies who are at first sight dominant because they have high market shares cannot necessarily restrict competition in the sense that their action would eliminate competition in a substantial part of the relevant market. Furthermore, and as indicated above, the CFI also suggested that it was necessary to assess what form of competition should be given priority with a view to ensuring the maintenance of effective competition, inter-brand or intra-brand? This prioritization would have to be based on careful economic analysis. As many commentators have observed, the burden on the Commission and also, of course, on national courts and authorities, is daunting. Full assessment of the efficiency argument involves addressing in detail whether a company such as GSK, as a rational operator facing competitive pressures at the innovation level, would invest a significant part of the increased funding that would result from dual pricing in R&D. The economics of innovation is a global matter that must be weighed in a balancing exercise against the restrictive effects of parallel trade between individual EC Member States. And this assessment must be prospective.⁵⁸ This is a long way from the simple 'per se' approach that had formed the cornerstone of Commission practice (and rhetoric) until now.

Decentralization of competition law enforcement

A further trend that is already evident from the number of cases on the application of Articles 81 and 82 now being decided by the national competition authorities and courts, discussed above, is the impact of the so-called 'modernization' of European competition law on the Community tool kit. Regulation 1/2003/EC, which came into force on 1 May 2004, removed the Commission's exclusive right to apply Article 81(3) to exempt anti-competitive agreements, as well as the

⁵⁸ See, for an outline of the economic approach to assessing the impact of parallel trade on competition, CRA International, European Competition Practice, 'Parallel trade in pharmaceuticals: more harm than good?', Competition Memo, March 2008, www.crai.com/ecp/assets/Parallel_Trade_in_Pharmaceuticals.pdf.

prior notification procedure. The Regulation also provides for various mechanisms to coordinate the application of Article 81 EC by the national competition authorities, including a network, the European Competition Network (ECN), to provide a framework for applying and developing the EC competition rules at the national level. To enhance the effectiveness of the ECN, a number of subgroups have been established, some with a sectoral focus. In 2005, the ECN Pharmaceuticals subgroup was established. It is intended that this group will function as a valuable vehicle to support its members' enforcement and advocacy efforts in the pharmaceutical sector, as well as a better and more consistent approach to the application of the European competition rules.

As part of the modernization strategy, the Commission is also promoting private damages actions for infringements of competition law. It is acknowledged that private enforcement of European competition law before national courts is widely underdeveloped. Since the case of *Courage v. Crehan*,⁵⁹ it has become apparent that some form of remedy should be available to those who have suffered financial harm as a result of infringements of Article 81 and 82 EC. Damages actions must be brought at the national level and must comply with the relevant legal and procedural requirements of the relevant Member State. As was recently noted in a report on private enforcement produced for the Commission, an 'astonishing level of diversity' characterizes national rules and procedures.⁶⁰ Efforts by the Commission aimed at dealing with the various barriers to action faced by private plaintiffs, albeit cautious in nature, are likely to mean that private enforcement could become an important complement to public enforcement in the future.⁶¹ The spectre of United States experience looms large, including massive settlement agreements on brand name manufacturers

⁵⁹ Case C-453/99, *Courage and Crehan* [2001] ECR I-6297.

⁶⁰ E. Clark, M. Hughes and D. Wirth, 'Study on the conditions of claims for damages in case of infringement of EC competition rules – analysis of economic models for the calculation of damages', Ashurst Report for the European Commission (2004), <http://ec.europa.eu/comm/competition/antitrust/actionsdamages/study.html>; D. Waelbroeck, D. Slater and G. Even-Shosan, 'Study on the conditions of claims for damages in case of infringement of EC competition rules – comparative report', Ashurst Report for the European Commission (2004), <http://ec.europa.eu/comm/competition/antitrust/actionsdamages/study.html>.

⁶¹ European Commission, 'Damages actions for breach of the EC antitrust rules', Green Paper, SEC (2005) 1732, 19 December 2005. The follow-up White

for engaging in the types of practices that the Commission recently condemned in the *AstraZeneca* case. The Commission imposed a fine of €60 million in that case. On the other side of the Atlantic, the manufacturers of BuSpar, Taxol and Platinol agreed to damages award settlements amounting to US\$535 million, US\$135 million and US\$50 million, respectively. But public enforcement, too, is taking on a new dimension in Europe, as some Member States have opted to criminalize certain anti-trust offences. The industry remains a major target for investigation and litigation, but the potential penalties are becoming more severe and far-reaching. Against this background, the industry may welcome rather than resist legislative reforms that bring greater clarity with respect to their rights and, as such, may be more favourably disposed to centralized, legislative solutions.

6. Further efforts at policy compromise: the role of the pharmaceutical forum

Set up to track the further implementation of the non-binding G10 recommendations, published in 2002, this high level political platform for discussion⁶² – which was chaired by the Commissioners of Health and of Enterprise, and in which the major stakeholders⁶³ at the EU and national levels took part – set up three expert working groups to come up with guidelines for further action on a number of key issues, which are discussed below. The Pharmaceutical Forum, which met annually between 2005 and 2008, concluded its work with a final report in October 2008. It sought to provide the political mandate for further reform, as well as a broader platform for discussion on competitiveness and public health issues. It was supported by a Steering Committee, chaired by DG

Paper on private enforcement is European Commission, ‘Damages actions for breach of the EC antitrust rules’, White Paper, COM (2008) 165 final, 2 April 2008.

⁶² See G. Verheugen, ‘Future post-G10 pharmaceutical strategy’, Speech to the EFPIA, SPEECH/05/311, Brussels, June 2005.

⁶³ These include the EFPIA, the EGA, the European Self-Medication Industry, EuropaBio, the European Association of Full-Line Wholesalers, the European Patients Forum, the Standing Committee of European Doctors, the Pharmaceutical Group of the European Union, Association Internationale de la Mutualité and the European Social Insurance Platform. In addition, ministries from each Member State are invited and three representatives from the European Parliament are members.

SANCO and DG Industry.⁶⁴ The constitution of the Forum marked a continuation of the policy of the open method of coordination as the better way to proceed towards balancing the interests of the industry and those of national health care systems in the 'market pathway'. As the Commissioner for Enterprise stressed in his speech to the first Forum meeting, it is not the intention to produce new European legislation but to find better ways of learning from each other.

Even if it was not the mandate of these working groups (WGs) to draft new legislation, their final recommendations could well form the basis for a further restructuring of the regulatory framework or pathway. Their reports may also result in additional functions being transferred from the national to the European level, or even the creation of new functions. A Second Progress Report was published by the Forum in July 2007, outlining concrete results and implementation proposals, albeit that further implementation, as such, will be developed through concrete work packages following the political direction given by the Forum in the course of 2008.⁶⁵ The Commission adopted a new Communication with three legislative tools on the future of the single market in pharmaceuticals in December 2008, drawing on the work of the Forum.⁶⁶ The EFPIA has called upon the Commission to use this as an opportunity to

⁶⁴ Membership of this Committee was restricted to seven Member States and representatives of the European Parliament and the ten stakeholders mentioned above.

⁶⁵ The First and Second Progress Reports are available via the Commission's web site, http://ec.europa.eu/enterprise/phabiocom/comp_pf_en.htm. The Final Report of the Forum was published in October 2008 and is available at http://ec.europa.eu/pharmaforum/docs/final_conclusions_en.pdf.

⁶⁶ Whilst finalizing this book, the European Commission launched the so-called 'pharmaceutical package', which includes a communication to launch reflections on ways to improve market access and the price-setting mechanism and a proposal to enable citizens to have access to information on prescription-only medicines. European Commission, 'Communication on safe, innovative and accessible medicines: a renewed vision for the pharmaceutical sector', COM (2008) 666 final, 10 December 2008; European Commission, 'Proposal for a directive amending, as regards information to the general public on medicinal products subject to medical prescription, Directive 2001/83/EC on the Community Code relating to medicinal products for human use', COM (2008) 663 final, 10 December 2008; and European Commission, 'Proposal for a regulation amending, as regards information to the general public on medicinal products for human use subject to medical prescription, Regulation (EC) No. 726/2004 laying down Community procedures for the authorisation and supervision

develop a strategic vision for the sector, which should recognize the need for the future EU regulatory framework to deliver high quality, science and risk-based decision-making that will accommodate the global nature of drug development and retain the confidence of all stakeholders through excellence in execution of its responsibilities. It remains to be seen if the two Commissioners responsible, as well as the other stakeholders represented at the Forum, will subscribe to this approach. Again, a careful balancing of competing interests through a difficult consensus-building process is the order of the day.

The most sensitive topic, following established tradition, was undoubtedly pricing policy, but the WG on relative effectiveness and the WG on information to patients also faced their own challenges.

A. Pricing

The key task of the WG on pricing was to examine alternative pricing and reimbursement mechanisms to support Member States in fulfilling their commitment to the G10 recommendations, as well as towards the public health objectives of offering equal access to medicines at affordable overall cost. Although the WG aimed to help Member States meet the rising challenges of high expenditure, inequality of access and calls for earlier access to innovative products by exchanging information on different pricing mechanisms, it is for Member States themselves to decide how to implement the mechanism that suits them best.

Yet the future direction of pricing and profit regulation can also have an impact on the interaction between the processes of therapeutic and generic competition. Generic manufacturers now also claim that it is important to ensure that national pricing and profit control systems can ensure that the long-term sustainability of the EU-based generic medicines industry is maintained so that it can compete effectively on EU and global markets. This means not only that pricing and reimbursement approvals and substitution status should be automatic once they have obtained a market authorization or licence, but also that the pricing of generic medicines should not be linked to a constant,

of medicinal products for human and veterinary use and establishing a European Medicines Agency', COM (2008) 662 final, 10 December 2008. See http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/pharmpack_en.htm.

set percentage of the originator product (for example, always 25% to 50% lower than the originator).⁶⁷ This form of linkage allegedly enables originators to force generic competitors out of the market by constantly lowering prices to the point where generic manufacturers cannot remain on the market or afford to enter a market. Hence, calls from this quarter are now heard for further amendments to the Price Transparency Directive (Directive 89/105/EEC)⁶⁸ in order to ensure automatic pricing and reimbursement approvals in cases where the price request is lower than the comparable originator product.⁶⁹

External expert reports commissioned by the WG on pricing have developed a detailed overview of the application of different pricing and reimbursement practices in the Member States and have compared six specific techniques in greater detail. The WG was also asked to examine ways to increase transparency, consistency and interchangeability of information regarding prices, price components and related issues – including through collaboration with the Transparency Directive Committee (made up of Member States only). In this respect, the work of this WG, which draws upon the input of a much wider range of stakeholders, could increase pressure for reform of this measure, which has been criticized for being too narrow in scope (see below in relation to the discussion on relative effectiveness assessments) and inadequately enforced at the national level.

The aim is to improve consensus at the national level on general principles and good practices when performing relevant assessments and to encourage national authorities to set up a data sharing network both prior to and after a market authorization has been awarded. The requisite ‘tool box’ to encourage effective data sharing was developed over the course of 2007–8, but Annex A to the report recommends the promotion of generic products through demand-side as well as supply mechanisms. The reports from this WG also stress that affordability has a European dimension. A similar price level leads to a different level of affordability depending on the economic situation of

⁶⁷ See EGA, ‘EGA urges price de-linkage for off-patent medicines at EU High Level Forum on Pharmaceuticals’, Press Release, 26 June 2007, www.bogin.nl/ega-press.

⁶⁸ Council Directive 89/105/EEC, above n.5.

⁶⁹ See Contribution by the EGA to the Pharmaceutical Forum Pricing Working Group, 7 November 2006, www.egagenerics.com/doc/ega_pwgcontributionIIAT_2006-11-06.pdf.

each Member State, as the WG states. The WG goes on to suggest that attention should be given to measures that allow companies to offer medicines at affordable prices in each European market. Limiting price control only to nationally-used volumes would allow differential prices. Furthermore, the WG recommends that manufacturers should commit to register and supply all EU markets at reasonable prices. These types of recommendations may also support manufacturer policies on dual pricing, or non-extraterritoriality as it is also known, as discussed above. The EFPIA has called for clear guidelines in this area, as opposed to harmonizing legislation, and has condemned the ‘commoditization of clinically-different medicines in reference price systems’ as rewarding imitation (i.e., generic competition) and stifling incremental innovation.⁷⁰ As we noted in section two above, the EGA (the generic association) has also called for guidelines to reward generic products and stimulate their uptake in health budgets.

Regarding the WG’s overall recommendations, as presented in the Forum’s final report,⁷¹ therefore, these relate to three main issues: (i) increasing access to medicines with a specific focus on access issues around orphan products and smaller markets; (ii) better incentivising and rewarding innovation which serves public health needs; and (iii) optimal use of resources via the ‘toolbox’ approach and use of so-called ‘guiding principles’ for policy-makers and national authorities.

B. Relative effectiveness

The WG on relative effectiveness assessments (REAs)⁷² aimed to support Member States in applying relative effectiveness assessment

⁷⁰ EFPIA, ‘Response to the Commission’s Consultation on the future of the single market in pharmaceuticals for human use in Europe, the future of pharmaceuticals for human use in Europe – making Europe a hub for safe and innovative medicines’, EFPIA Views (2007), www.efpia.org.

⁷¹ The Final Report of the Forum was published in October 2008 and is available at http://ec.europa.eu/pharmaforum/docs/final_conclusions_en.pdf.

⁷² ‘Relative effectiveness’ is defined as the extent to which an intervention does more good than harm compared to one or more intervention alternatives for achieving the desired results when provided under the usual circumstances of practice. Relative effectiveness assessments (REAs) are carried out to investigate to what extent a medicinal product does more good than harm compared to one or more other medicinal products or alternative health interventions for achieving the desired result when provided under the usual circumstances of practice. The working group has agreed that the quality of life dimension should be part of the assessment of relative effectiveness.

systems in order to allow containment of pharmaceutical costs, as well as a fair reward for innovation. The REAs should help identify the most valuable medicines, both in terms of clinical efficiency and cost-effectiveness, and thus help governments set a fair price for these medicines. So far, the draft proposals stress the potential for improving both the principles and practicality of sharing and using data for relative effectiveness assessments. Issues related to cost-effectiveness have not been discussed at this stage, however. In some quarters, there was some optimism that the Forum would recommend extending the procedural requirements of the Transparency Directive of 1989 to REA procedures as a means of speeding up the time taken for new products to go through each and every regulatory hoop. Although the case-law of the ECJ has required strict application of the Directive to all measures affecting price and reimbursement, including insurance coverage, REA procedures are not (yet) covered by the various timetables imposed under the Directive.⁷³ The research industry and a number of Member States remain resolutely opposed to a pan-European assessment of relative effectiveness.

Amongst the WG's final recommendations, therefore, were that: (i) there was a need for working definitions and good practice guidelines and principles for relative effectiveness assessment - this with a view to ensuring a balance between growing medicine costs (and those of healthcare more generally) and measures to promote innovation, towards ensuring the most effective medicines make it to market; and (ii) there was need for a clear understanding of the current state-of-play regarding national approaches and barriers/challenges to overcome.

C. Patient information

Finally, the WG on information to patients advised the Forum on ways to improve the quality of, and access to, information on authorized medicines and related health areas. So far, this is the only WG in which certain stakeholders have distanced themselves from the results.⁷⁴ A key aim for the research-based industry is to reform the

⁷³ Case C-229/00, *Commission v. Finland* [2003] ECR I-5727.

⁷⁴ See the Joint ESIP and AIM Position Statement on Information to Patients on Diseases and Treatment Options, attached to Annex B of the Second Progress

existing legal framework, which is claimed to be anachronistic and no longer a reflection of the demands of the ‘empowered patient’. Again, self-regulation is the preferred way forward.

The majority of the members of the WG, however, agreed upon core quality principles, as well as a toolbox of good practice to help patients evaluate information. Data sharing and a European database for patient information is also under discussion, as is a form of model information package produced by a ‘public–private partnership’ – that is, industry, patients, carers, health professionals and the relevant national authorities. Different regulation techniques to validate, *ex ante*, an agreed common core set of information are also being explored, including an *ex ante* validation system, which could provide a system for national authorities to assess and validate information provided to patients on diseases and treatment options prior to its provision to the general public, and co-regulation mechanisms, which would include a review process that would be built on *ex post* controls, including sanctions and self-regulation, according to agreed codes of practice.

The WG’s final recommendations thus focused on: (i) ensuring better availability of and access to information for patients and citizens more generally; (ii) better quality of information including that all stakeholders achieve consensus over core principles of good information (it also recommended that the ban on the direct to consumer advertising of medicines remain in place); and (iii) participation and involvement of all relevant stakeholders towards generating the best and most up-to-date information possible.

Much of the work streams of the working groups seems to point in the direction of the promotion of shared general or core principles and shared information, but there is also more than a hint of a suggestion that the Commission itself could play a key role in building up and managing European-wide databases⁷⁵ on pricing, relative effectiveness

Report of 26 June 2007, http://ec.europa.eu/enterprise/phabiocom/docs/pf_20070626_esip_aim_joint_statement.pdf.

⁷⁵ A first step in this direction was in fact made in late 2006 with the launch of the European database – www.eudrapharm.eu – which currently contains information, in English, on centrally authorized medicines. Later phases will add the information in all the other official languages, together with improved search functions. The aim is to include information on all authorized medicines in the EU.

and perhaps on patient information, eventually taking on a policing role to ensure the quality and reliability of the data it will be called on to acquire and manage. This last topic has also resurfaced in the context of the report on current practice with regard to provision of information to patients on medicinal products, which the Commission is required to produce on the basis of Article 88(a) of Directive 2001/83/EC.⁷⁶ On the basis of its recent consultation exercise, the Commission has announced that it intends to propose to the European Parliament and the Council a series of amendments to Directive 2001/83/EC. The Commission indicated the policy objectives that will be pursued by its intended proposals – namely, that, while the ban on direct-to-consumer advertising of prescription products will be maintained, a framework will be introduced to ensure access by patients to objective non-promotional information about the benefits and risks of medicines. This, in turn, requires the introduction of measures to ensure a clear distinction between promotional and non-promotional information and on the roles of different players in providing that information.⁷⁷ In a follow-up public consultation document on its legal proposal on information to patients, the Commission proposes to place continued emphasis on co-regulation – that is, the involvement of public authorities and a mix of stakeholders including health care professionals, patient organizations and the pharmaceutical industry. These co-regulatory bodies would be responsible for adopting a code of conduct on information to patients and monitoring and following up all information activities by the industry.⁷⁸

Irrespective of the eventual legal form that these and the other measures discussed here are likely to take, it may be observed that progress on building up the requisite ‘toolbox’ for assessing relative effectiveness, and informing patients on this type of issue, will surely take European policy (and perhaps regulation) in the direction of encouraging (or compelling) national authorities to examine and compare therapeutic effectiveness, at least in the context of their pricing and

⁷⁶ Directive 2001/83/EC, above n.26.

⁷⁷ See, further, European Commission, ‘Report on current practice with regard to provision of information to patients on medicinal products’, COM (2007) 862 final, 20 December 2007.

⁷⁸ The consultation document is available at http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_02/info_to_patients_consult_200802.pdf.

reimbursement management schemes.⁷⁹ Attempts to include a ‘needs’ criterion or a comparative efficacy criterion for marketing authorization in the early days of European harmonization met with considerable resistance, not least from the industry, and were abandoned.⁸⁰

7. Conclusion

The organization of the demand side of the market for medicinal products – the ‘market pathway’ – has always been the preserve of Member States. Subject to the very limited procedural constraints imposed by the Price Transparency Directive of 1989, they may opt for the system of price or profit control that suits their own policy needs best. Diversity of approach is a fact of life in the twenty-seven EU Member States, and it is unlikely that we will see any attempts to introduce Union-wide harmonizing legislation on price control in the near future. However, increasingly, national price and profit control regimes aim not only to deliver lower prices for patients, but also value for money. Value-based pricing, as the recent Office of Fair Trading report in the United Kingdom has stressed, could lead to a more effective use of health budgets, not only keeping prices down but also releasing funds that could be used to give patients better access to medicines and other treatment, which they may currently be denied. Over time, value-based pricing would also give companies stronger incentives to invest in drugs for those medicinal conditions where there is greatest patient need. Options to introduce ex post value-based pricing or ex ante value-based pricing (probably in addition to ex post controls) are under consideration in the United Kingdom and are being debated at the EU Pharmaceutical Forum.

It is unlikely that these types of principles will be incorporated in binding legislation: guidelines and self-regulatory instruments offer more scope for flexibility and for balancing European and national interests. A pan-European approach to relative effectiveness is likely to be resisted on the grounds that any assessment remains intrinsically linked to national specificities and priorities. Inevitably, however, the options considered within the Forum and its WGs will put greater

⁷⁹ See n. 66.

⁸⁰ See Hancher, *Regulating for competition*, above n.15, Chapter 4.

emphasis not just on comparing therapeutic efficacy and value of different types of products, but on setting up new pathways, mechanisms and even institutions for coordinating and comparing experiences between, and facilitating inter-exchangeability across, the national levels.

Such developments could result in a new role for the European institutions – and, in particular, the Commission – which may not only be facilitative, in the sense of providing the necessary data to enable such comparisons, but also even prescriptive if it becomes involved in policing the accuracy and reliability of this type of data. Follow up pressure from various stakeholders in the Pharmaceutical Forum’s WGs could also lead to extension of the procedural requirements of the Price Transparency Directive – the only legal regulatory instrument that regulates the market pathway – to new areas such as REAs. The scope of the Directive could be extended to impose more exacting standards on the compilation of value assessments, as well as for the regulatory timetables involved.

More importantly, spillover effects into the supply side, the regulatory pathway and into the myriad of regulations that govern marketing authorizations, data exclusivity and SPaCs cannot be ruled out if comparative therapeutic data also could be used in decisions by European as well as national authorities in making these regulatory decisions. As we have seen, data generated in this ‘regulatory pathway’ are subject to a considerable amount of protection, and to the benefit of the research-based industry. This chapter has also indicated that, here too, balances have been struck between the competing objectives of rewarding innovation and promoting generic competition and parallel trade. In the future, new balances may have to be struck – for example, patent and other IPR protection could be prolonged in exchange for better, safer and more affordable innovation.⁸¹

However, the further streamlining of legislation governing the regulatory pathway no longer appears to be the main method of balancing the competing interests and objectives that have traditionally characterized policy in the sector. The *AstraZeneca* case, and the launching of the sector-wide inquiry, which was discussed in detail in this chapter, makes it clear that not only legislation but also the application of

⁸¹ See S. Garattini and V. Bertele, ‘How can we regulate medicines better?’, *British Medical Journal* 335 (2007), 803–5.

competition law can be used to strike a balance between competing interests in the regulatory pathway. It will be interesting to see if, and to what extent, similar demands for European-wide protection will be called for by the innovative industry if it is under pressure to produce comparative efficacy data for national price control and reimbursement agencies. The pressure is surely likely to rise as coordination of data sharing and evaluation techniques across the Member States becomes more streamlined. Here, again, the regulatory and market pathways may well begin to intersect, offering, perhaps indirectly, greater potential, after all, for a European-wide, substantive approach to price and profit control.

As has also been argued in this chapter, decentralization of competition law enforcement is also an important new development affecting the industry, but decentralization does not necessarily imply isolated national action: on the contrary, here, too, the Commission – and Commission policy – is very much a driving factor. Nevertheless, as national courts and authorities are required to engage in complex economic and market analysis when applying competition law principles in this market, the Commission's preferred formalistic approach to protecting parallel imports and intra-brand competition is certainly under challenge at the national as well as European levels. The recent application of competition law principles to prevent abuse of regulatory practices may prove to be an interesting *ex post* complement to *ex ante* balancing exercises in the regulatory pathway. Irrespective of which pathway will prove the most effective route to dealing with market fragmentation, it is unlikely that the delicate balancing act that lies at the basis of European pharmaceutical policy and all of its legal manifestations is likely to become more complex.