A periodical update on legal and regulatory developments in the life sciences sector

In this edition, we have reported on a range of recent developments in the life sciences sector both at EU and national level. These developments reflect fundamental reviews by Governments and legislators of innovation, regulation, economics and competition in the sector, all of which will challenge established business models at a time of worldwide financial downturn.

From an EU perspective, we summarise, amongst other topics, the European Commission’s Pharmaceutical Sector Inquiry Preliminary Report surveying the current competition landscape in the pharmaceutical industry and the Commission’s Communication setting out the key initiatives aimed at improving the availability of medicines, economic growth and employment. We also report on the EPO Enlarged Board of Appeal’s decision in WAF which it rejected a patent application that required human embryos for implementation.

At national level, we report on two recent UK cases: Generics UK Limited v Daiichi in which the court upheld the SPC in respect of the enantiomer levofloxacin and Dr Reddy’s Laboratories v Eli Lilly in which the Court upheld a patent for an individual compound, olanzapine, selected from a class that had previously been disclosed. We also report, amongst other topics, the PPRS agreement reached in the UK between the Department of Health and the ABPI, recent amendments to the reimbursement regime for generic medicines in Belgium and recent changes to the Swedish Pharmacy market.

We hope you enjoy reading this update and are happy to address any comments or questions you may have, either through your usual contact or through any of the contacts on the back page of this update.

International Life Sciences Group

Pharmaceutical Patent Update

EU: EPO Enlarged Board of Appeal rejects patent that requires human embryos for implementation

In its decision of 25 November 2008 the EPO Enlarged Board of Appeal (EBA) considered four questions referred to it by the EPO Technical Board of Appeal concerning a patent application by Wisconsin Alumni Research Foundation (WARF) with claims to “A cell culture comprising primate embryonic stem cells...”. The claims cover human embryonic stem cells (hESCs) and it was accepted that at the filing date the only starting point for the
The creation of hESCs was the destruction of a human embryo.

The Examining Division rejected the application on the grounds that the invention is excluded from patentability under Rule 28(c) of the European Patent Convention (EPC) (which excludes the patenting of “uses of human embryos for industrial or commercial purposes” and repeats Art. 6(2)(c) of Directive 98/44/EC, which in turn provides a specific example of subject matter excluded more generally under Art. 53(a) EPC on the grounds of being contrary to ordre public or morality). WARF appealed to the EPO Technical Board of Appeal (TBA), which exercised its discretion under Art. 112(a) EPC to refer four legal questions to the EBA. Representations were made to the EBA by WARF (who also requested that a reference be made by the EBA to the European Court of Justice) and the President of the EPO and amicus curiae briefs were filed by a number of third parties including the UK Intellectual Property Office (UKIPO) and The University of Nottingham (on behalf of the European Commission).

As a preliminary point the EBA refused to refer the questions before it to the ECJ, holding that it had no jurisdiction to do so as Rule 28(c) EPC merely repeats Art. 6(2)(c) of the Directive and the Directive is not a source of law to be applied directly by the EPO. Thus the referral to the EBA could not have a Community-wide effect through a decision of the ECJ, and the EBA’s decision is confined to an interpretation of the EPC (not the Directive).

The first question referred to the EBA was straightforward, namely whether Rule 28(c) EPC applies to applications filed before its entry into force (as in this case)? The EBA held that it applies to all pending applications, as was accepted by WARF.

The second, key, question was whether Rule 28(c) EPC forbids claims directed to products which at the filing date could be prepared exclusively by a method which necessarily involves the destruction of the human embryos from which the said products are derived? The EBA decided that (a) what is to be considered as an “embryo” is a matter of fact to be decided in the context of each particular patent application and (b) on the facts before it, the making of the claimed product involves the destruction of human embryos (which would be an integral part of the commercial exploitation of the invention).

The third question was not addressed as the answer to the second question resolved it. The fourth question, whether it was of relevance that after the filing date the same product could be obtained without having to recur to a method necessarily involving the destruction of human embryos, was answered in the negative (i.e. it is irrelevant).

The decision does not sit well with current practice at the UKIPO, whose practice note of April 2003 states that patents may be granted for inventions relating to pluripotent hESCs (which do not have the potential to develop into an entire human body) but not to totipotent hESCs (which can), notwithstanding that at present
hESCs have to be sourced by the destruction of human embryos or by methods that arguably create “human embryos” (such as transfer of human nuclei into enucleated cells). It is understood that the UKIPO is reconsidering its practice in relation to pluripotent hESCs notwithstanding the absence of a judgment from the ECJ.

Gerry Kamstra
London

UK: Patents Court upholds Supplementary Protection Certificate for a novel enantiomer in Generics UK Limited v Daiichi

Generics (UK) Limited (“GUK”) was unsuccessful in its attempt before the Patents Court (Mr Justice Kitchin) to revoke Daiichi’s Supplementary Protection Certificate (“SPC”) in respect of levofloxacin. Levofloxacin is the (-) enantiomer of the racemic antimicrobial ofloxacin. GUK made a two-pronged assault on the SPC. First on the basis that there were grounds which would have justified revocation of the underlying patent EP(UK) 0206283 (“the patent”). The patent claimed the product levofloxacin (claim 2) and the method of making levofloxacin (claim 5). GUK made various challenges to these claims including on the grounds of lack of novelty and inventive step. The second separate attack was founded on the prior marketing authorisations for ofloxacin.

The patent

GUK challenged the priority date of the patent on the basis that the first priority document referred to the two fold increase in activity of levofloxacin compared to the racemate. but did not include any of the toxicity or solubility information in the third priority filing.

The judge emphasised the importance of making a distinction between the priority dates of the claimed invention and that of matter contained in an application. The invention is entitled to the priority date of an earlier application when the invention is supported by matter disclosed in such earlier application (applying Asahi Kasei Kogyo Application ([1991] RPC 485 and G02/98. Same Invention ([2001] OJ EPO 413)). On the facts the judge held that the invention of each of the claims in issue was plainly disclosed by the first priority document. The priority document enabled the skilled person to perform the inventions claimed without undue difficulty.

The judge went on to point out that Daiichi were not permitted to rely on the subsequently added toxicity and solubility information in support of its obviousness defence. As previously stated by the judge in Generics v Lundbeck ([2007] EWHC 1040) a patentee may not rely on a discovery which was neither made at the date of the priority document nor could be predicted from such document’s contents.

GUK also contended that prior publication by Daiichi of the racemate ofloxacin rendered the claimed enantiomer old. The judge
(applying Synthon v SmithKline Beecham ([2005] UKHL 59) rejected this argument. Performance of the subject matter of the prior art would result in the production of ofloxacin which does not constitute an infringement of a claim to levofloxacin. The prior art contained nothing which enabled or even pointed towards the resolution of ofloxacin into its constituent enantiomers. The judge referred to the judgment of the Court of Appeal in Lundbeck v Generics UK Ltd ([2008] EWCA Civ 311) where Lord Hoffman approved the settled EPO case law that the prior disclosure of a racemate did not in itself amount to a disclosure of its enantiomers.

With regard to the attacks on inventive step, it was argued that both claims 2 and 5 were obvious. The judge cited the approach to determining obviousness in Pazzoli v BDMO ([2007] EWCA Civ 588). He also pointed out that the Court of Appeal in Conor v Angiotech ([2008] UKHL 49) had expressly approved his approach to the question of obviousness in Generics v Lundbeck.

GUK argued that it was obvious to seek to resolve the enantiomers of ofloxacin. The judge decided on the evidence that while the resolution of ofloxacin would have been something worthwhile to explore, it was not a goal which was obvious to pursue relentlessly. It was only obvious to investigate whether the resolution could be achieved easily, but if it could not the skilled person would not have continued to pursue this line of research.

GUK also alleged that the method for carrying out the separation was obvious. GUK sought to establish obviousness by performing experiments purporting to show obvious ways in which the skilled person could have resolved ofloxacin at the priority date. However, a reproducible, scaleable resolution was not achieved with the conditions attempted. Daiichi levelled a number of criticisms at GUK’s experiments. Those criticisms which the judge found particularly persuasive were firstly in relation to the diastereomeric salts approach: GUK’s expert did not ‘select’ the successful resolving agent himself, but rather the answer was ‘put under his nose’ by GUK’s solicitors. In addition the preparative HPLC experimental team optimised their approach on modern equipment and then attempted to replicate the optimised method on modern versions of apparatus available at the priority date. The dangers of allowing hindsight to affect the design of experiments intended to prove obviousness are apparent from this case.

The judge accepted that there were a number of possible methods available to persons seeking to resolve a racemate at the priority date. The evidence was that such methods break down into an almost infinite number of permutations, such that no resolution was simple and there was no guarantee of success. Applying the law to the facts, the judge held that there was no evidence based on any of the publications in evidence and the common general knowledge that either the claimed product or the process claim were obvious. The judgment keenly illustrates the uphill struggle faced to present a successful obviousness case in the
light of experiments which fail to achieve the purportedly obvious.

The SPC

The SPC Regulation (No 1768/92) was enacted in recognition of the fact that the time period between applying for a patent and obtaining authorisation to put a new medicinal product on the market rendered the monopoly granted under the patent too short to encourage the development of medicinal products.

The SPC Regulation confers, by means of a Supplementary Protection Certificate (SPC), post patent expiry "patent like" protection on products protected by a basic patent, for which there is a marketing authorisation. Such product must not have already been the subject of an earlier authorisation or SPC in the country in which it is sought. The duration of protection is a maximum of 15 years from the date of first authorisation in the Community, including the life of the basic patent (or 5 years from patent expiry, whichever is the shorter). For the purpose of the Regulation a ‘product’ is defined as the active ingredient or combination of active ingredients of a medicinal product.

GUK brought two challenges against the SPC. The first was that the 6 June 1997 UK marketing authorisation for levofloxacin was not its first UK marketing authorisation. GUK contended that the 1990 marketing authorisation for ofloxacin was in fact the first UK marketing authorisation for levofloxacin because levofloxacin was present in the racemate in a 50:50 mixture with the (+) enantiomer. The second was that the reference point for the 15 year maximum period of protection conferred by the SPC was the first authorisation in the Community and was the marketing authorisation for ofloxacin that had been granted in Germany in 1985.

GUK argued therefore that the term of the SPC granted to Daichi in 1997 should have been zero.

GUK’s challenge to the SPC is of particular interest because despite the many cases concerning the resolution of enantiomers, this is the first time this particular argument has been brought before the courts. There are many enantiomer products on the market in the same position as levofloxacin, where the duration of the SPC protection was determined from the date of the marketing authorisation for the enantiomer and not the prior marketing authorisation for the racemate.

The judge set out the policy considerations behind the institution of the SPC Regulation. He then reviewed the UK and European Court of Justice jurisprudence on the point. BASF AG v Bureau Voor De Industrielle Eigendom ([2002] RPC 9) is a case concerning products within the meaning of the Plant Protection Products Regulation No. 1610/96 and that in many respects parallels that for medicinal products here in issue. In BASF it was held that two products which differ only in the proportion of the active chemical compound to the impurity they contain must be regarded as the same product. The fact that a new marketing authorisation must be obtained for plant protection products with different quantities
of impurities is irrelevant. Another case, Massachusetts Institute of Technology ([2006] FSR 34) determined that an ingredient of a medicinal product cannot constitute a “product” for the purposes of the Regulation unless it has an effect on the human or animal body on its own.

The judge viewed the fundamental question to be “whether or not the product the subject of the 1985 and 1990 authorisations was ofloxacin or levofloxacin”. He concluded that the marketing authorisation for ofloxacin did not amount to the first authorisation to place levofloxacin on the market.

He reasoned that ofloxacin was in itself a recognised as a good antimicrobial. Its properties had been determined and until the invention of the patent the characteristics of the enantiomers were unknown. Therefore the marketing authorisation for ofloxacin was just that, permission to place the named active ingredient ofloxacin on the market and not levofloxacin.

He went on to say that it is now known that each of the racemate and the two enantiomers have different properties. The (+) enantiomer is not inactive: it has antimicrobial properties in its own right. Therefore ofloxacin is either an active ingredient in its own right or a combination of active ingredients. The (+) enantiomer is not an inactive impurity as in BASF or an excipient as in MIT. To this extent his reasoning does not necessarily close the door on similar challenges to single enantiomer products where it has been determined that the biological activity of the racemate resides only in one enantiomer. It is unclear from the judge’s reasoning what the outcome would have been had the (+) enantiomer not exhibited biological activity.

In further support of his findings, GUK had accepted that ofloxacin does not fall within the scope of the patent. The judge’s decision would not for that reason cause undue extension of the protection for ofloxacin.

As Mr Justice Kitchin himself concluded, this decision is consistent with the policy reasons for the SPC Regulation in the first place. It required invention to make levofloxacin. The application for the Patent was filed in 1986 but authorisation to place levofloxacin the market as a medicinal product was not granted until some 11 years later, in 1997. Mr Justice Kitchin pointed out that if GUK’s SPC challenge had been successful Daiichi would have had only nine years of protection from the date of the authorisation to the date of expiry of the Patent. and this is precisely the vice at which the SPC Regulation is aimed.

Victoria Evans
London

UK Patents Court judgment in Dr Reddy’s Laboratories v Eli Lilly

In a judgment handed down in October of this year, the Patents Court (Mr Justice Floyd) upheld EP (UK) 0.454.436 (the “Patent”) which is owned by Eli Lilly and which protects the schizophrenia drug olanzapine. Olanzapine is one of Lilly’s blockbuster drugs.

Dr Reddy’s Laboratories (“Dr Reddy’s”) challenged all of the
claims of the Patent on the grounds of anticipation and obviousness and some of the claims of the Patent on the ground of insufficiency.

The main anticipation attack on the patent was based on the disclosure in an earlier patent application filed by Lilly back in 1974 of a class of thieno-benzodiazepines (the “235 Application”). The general formula extended to more than 1019 compounds one of which was olanzapine. Although the 235 Application specifically disclosed some closely related compounds to olanzapine, it did not specifically disclose olanzapine itself.

The judge first had to decide whether the disclosure in the 235 Application was an anticipation of the later claim for olanzapine and then secondly if so, whether the later claim to olanzapine was nevertheless valid by virtue of being a selection invention.

The judge first addressed the general law of novelty. He reviewed the decision of the House of Lords in Synthon’s Patent ([2006] RPC 10). In that decision, the House of Lords cited with approval the well-known passages from the speech of Lord Westbury LC in Hills v Evans and the Court of Appeal judgment in General Tire and Rubber Co v Firestone Tyre and Rubber Co Ltd. In the light of those the judge held that "... a generic disclosure will not normally take away the novelty of a subsequent claim to a member of the class."

The judge then focused on the particular issue in the case namely the effect of the prior disclosure of a chemical class formula or "Markush" formula. He then went on to consider the law developed by the EPO on this issue.

He noted that the case law envisaged two ways in which a novel selection could be made. First, when the selected compound falls within territory marked out in the state of the art but is "unmentioned". Second, when the selected compound is arrived at by choosing a combination of starting materials from "two lists of some length".

The judge concluded that as a general matter, a prior disclosure would not take away the novelty of a claim to a specific compound unless the compound was disclosed in “individualised form” and that a general formula with multiple substituents chosen from lists of some length would not normally take away the novelty of a subsequent claim to an individual compound.

He then went on to consider the law of selection patents as it had been developed in the UK under the 1949 Act and in particular the IG Farbenindustrie’s Patent case.

The judge concluded:

(i) In relation to lack of novelty, it is doubtful in the light of the EPO jurisprudence whether a newly discovered effect complying with Maugham J’s principles could overcome a finding that a compound was specifically disclosed in a prior document.

(ii) Whether or not that is so, provided there is novelty on conventional grounds.
obviousness is to be decided according to ordinary principles.

(iii) The existence of an advantage possessed by the selected compound will be relevant to the overall assessment of obviousness, but is not an essential pre-requisite.

(iv) Compliance with Maugham J’s principles in I. G. Farbenindustrie’s Patent is equally not an essential requirement for inventive step to be found.”

His conclusions on the applicability of that law in the light of the EPO jurisprudence on the issue were obiter as he held that the disclosure of the chemical class formula in the 235 Application did not take away the novelty of the subsequent claim to olanzapine.

He also held that the claim to olanzapine did not lack novelty over the other two cited documents.

As regards inventive step, Dr Reddy’s relied on four pieces of prior art including the 235 Application as well two papers authored by Dr Chakrabarti, the leader of the anti-psychotic drug team at Lilly. The judge applied the test for obviousness set out in Pozzoli v BMDO ([2007] FSR 37) and Lundbeck v Generics ([2008] EWCA Civ 311). He found that on the evidence, the invention namely olanzapine was not obvious over any of the cited prior art as it would not have been obvious to have synthesised and tested olanzapine on the basis of the information disclosed in each of those pieces of prior art.

He went on to say that in the circumstances of the case, the evidence of commercial success was unhelpful in deciding the question of obviousness. Although he accepted that in some circumstances evidence of commercial success could be a relevant secondary indication of non-obviousness, where the product is the subject of anterior patent protection then commercial success arguments “are more or less doomed to failure”.

Finally, dealing with the allegation of insufficiency, the judge reviewed the Court of Appeal’s recent decision in Lundbeck. Dr Reddy’s arguments on sufficiency were to a large extent tied into their arguments on selection inventions. As noted above, the judge determined the claim to be novel in any event.

The case is of considerable interest for several reasons not least the Judge’s approval of the approach taken by the EPO to the issue of generic disclosures as well as his comments on the law on selection inventions. It is understood that Dr Reddy’s has been granted leave to appeal. It is perhaps also of interest to note that in Germany the decision of the German Patents Court revoking the patent inter alia on the ground of lack of novelty has recently been overturned by the German Supreme Court who found that the patent was valid i.e., novel, inventive and sufficient.

Victoria Evans
London
Regulatory Update

EU: Specification of references and titles of standards regarding medical devices

On 27 November 2008, the following three Commission communications about standards in the medical devices area were published in the Official Journal of the European Union:

• Commission communication in the framework of the implementation of Council Directive 90/385/EEC on the approximation of the laws of Member States relating to active implantable medical devices (2008/ C 204/04) whereby the titles and references of harmonised standards under the directive concerning essential requirements about the rules governing active implantable medical devices for all the Member States were published.

• Commission communication in the framework of the implementation of Council Directive 93/42/EEC concerning medical devices (2008/ C 304/06) whereby the titles and references of harmonised standards under the directive concerning essential requirements about the rules governing medical devices for all the Member States were published.

In these communications, the references and titles of the standards (and reference documents), the references of the superseded standards and the dates of cessation of presumption of conformity of the superseded standard appear.

Teresa Mercadal
Madrid

Sweden: Changes in the Pharmacy Market

The Swedish Government sent a proposed Bill regarding changes in the pharmacy market to the Council of Legislation for comments last week. The proposed Bill includes the following suggestions: The monopoly of the State owned company Apoteket AB to carry on retail business with certain drugs and goods shall be replaced by a system in which those who have permission from the Swedish Medical Products Agency shall be allowed to carry on retail business with the drugs and goods that are currently covered by the monopoly. In applying for permission, the applicant must meet certain suitability requirements and illustrate that it will be able to meet certain business requirements, for example, that pharmacists are present during opening hours. that
all prescribed drugs and goods can be supplied. that counselling can be provided and that the business is conducted within appropriate premises. Drug manufacturers, holders of marketing authorisations and persons eligible to prescribe drugs shall, as a matter of principle, not be permitted to carry on retail business with certain drugs and goods. The regulation of retail and wholesale businesses is to be included in a new Act on Trade with Drugs, which is to replace the old act of the same name. The Medical Products Agency is to be the supervisory authority responsible for ensuring that the new law is observed.

Furthermore, the proposed Bill includes suggestions regarding new laws to deal with the IT-systems of Apoteket AB to which all new participants within the pharmaceutical market will need to have access and the personal data and registers that they will be obliged to handle.

Moreover, it is suggested that the Dental and Pharmaceutical Benefits Agency shall decide the new pharmacies’ purchase price and selling price for drugs that are included in the pharmaceutical benefits and it is recommended that the Agency becomes the supervisory authority responsible for ensuring that the Act on Pharmaceutical Benefits etc is observed.

Ida Smed Sörensen
Stockholm

Industry Update

EU: Summary of the European Commission’s Pharmaceutical Sector Inquiry Preliminary Report

This article summarises the key findings laid out in the European Commission’s Pharmaceutical Sector Inquiry Preliminary Report, which was published on Friday 28 November 2008. At the same time a full day a presentation of the Report was held in Brussels.

The purpose of the Report is to survey the competition landscape in the pharmaceuticals industry.

The Report confirms the Commission’s concerns in relation to delays in generic market entry and apparently low levels of innovation. The Commission attributes these largely to the behaviour by companies on the market, and in particular competitive strategies adopted by originator pharmaceutical companies.

As a result, these originators are the prime targets of the sector enquiry, and are most likely to be affected by the Commission’s final report, which is expected in spring 2009. The prime focus for the report is on medicinal products whose data exclusivity expired during the seven-year period 2000-2007 and involves a detailed examination of 219 medicines. These individual medicinal products represent 53% of the total pharmaceutical market, and included a high number of products where marketing exclusivity was lost during the period examined.

The Report estimates that generic entry accounts for approximately €14 billion savings in health service expenditure during the above period, but that these savings could have been approximately €3 billion
more in the absence of the delay factors identified in the Report. There is now a period of consultation until the end of January 2009, before the final report is published in the spring of 2009. The purpose of the final report will be to provide the Commission with a factual basis to determine whether further action is needed, in the form of proposals for legislative or regulatory change, and/or anti-trust action in individual cases. In the short term, it is more likely that individual anti-trust investigations will be launched as a result of the types of practices and agreements that have been uncovered by the Commission’s investigation, though the Report may also cause further debate on possible longer term modifications to marketing authorisation systems in Member States to remove bottlenecks.

In terms of immediate action on the Commission’s Preliminary Report, stakeholders should consider the comments they wish to submit to the Commission on the Report by the deadline of 31 January 2009. In this way, stakeholders at all industry levels can seek to influence the outcome of the Commission’s final report. Bird & Bird are happy to discuss these issues with also where appropriate to include responses on behalf of companies in a separate submission to the Commission.

**Summary of key findings of the Report**

The key delay factors which the Commission found to be affecting generic entry are the following:

- Legal uncertainty caused by originators’ “patent clusters” or “patent thickets” and the filing of divisional patent applications;
- Patent enforcement litigation by originator companies not based on the merits of the case but as a strategy to deter generic entry; the Report stated that the number of patent litigation cases between originator and generic companies increased by a factor of four between 2000 and 2007, most of the cases being initiated by originator companies, but the majority of the cases in which final judgment was given, 62% were won by generic companies;
- Delays to generic entry caused by the need to oppose and overcome secondary patents obtained by originator companies in the European Patent Office: generic companies were found to have prevailed in approximately 75% of final decisions rendered by the European Board of Appeal, during 2000 to 2007. yet 80% of these decisions took more than two years;
- Delays caused by intervention and litigation by originator companies interfering in marketing authorisation and pricing/reimbursement proceedings for generic medicines: it was found that originator companies had a low success record on patent and data exclusivity matters, but that such interventions delayed generic entry by an average of four months;
- Originator companies’ strategies of launching second generation
products of questionable innovative value, in order to switch a substantial number of patients to the new product prior to market entry of a generic version of the first generation product:

- Patent dispute settlement agreements deterring or restricting generic entry: a significant proportion of such agreements involved value transfers from the originator company, and in many cases, licence or distribution agreements for the sale of generic medicines concerned originator medicines which still benefitted from exclusivity; and

- In many cases, the parallel use of two or more of the above strategies.

In addition, the Report considers various factors affecting competition between innovators themselves (for example “defensive patent strategies”). It also sets out various comments, but not conclusions, concerning the patent system and pharmaceutical regulatory framework, in particular with regard to delays and discrepancies in assessment criteria on the part of national marketing authorisation agencies and delays and uncertainties created by national pricing and reimbursement procedures. These aspects of the Report are summarised further below.

**Possible Commission competition law action against individual companies**

As mentioned, the Commission may pursue individual companies in relation to possible Article 81 and Article 82 infringements.

With regard to infringements of Article 81 (the prohibition of restrictive agreements), the Commission has stated that it will focus primarily on settlement agreements where there has been a value transfer from the originator company to the generic company.

Regarding unilateral anti-competitive conduct, the Commission would need to show an abuse of dominant position contrary to Article 82, for which purpose the Commission will first have to show that the company in question is dominant in a relevant market, which will in turn depend on the market definition. Such actions will follow the cases of AstraZeneca (appeal pending before the European Court of First Instance. Case T321/05) in which the Commission found abuses in the form of misuse of the patent system (concerning supplementary protection certificates) and misuse of the marketing authorisation system, and also the Commission’s current investigation of Boehringer Ingelheim for alleged misuse of the patent system.

It will be challenging for the Commission to prove abuse of dominant position through multiple patent applications (“patent clusters”), or litigation actions as a deterrent strategy against generic entry, as there would be a heavy evidential burden on proving an anti-competitive strategy as the motivation and reason for the action as distinct from the substantive merits of the applications or actions. Such types of practices that concern the
Commission can be characterised as legal or illegal depending on the intent of the company, including the creation and also the enforcement of intellectual property rights. There is limited precedent regarding this type of abuse, and there is no actual finding as yet on an abuse of this nature, though the possibility of abuse of dominant position through vexatious litigation has been confirmed in principle by the European Court of First Instance in a case outside the pharmaceutical sector but concerning intellectual property enforcement. *ITT Promedia v Commission (Case T-111/96)*. However, recent developments suggest that the Commission may be more inclined to initiate actions of this nature in the future.

Moreover, it should be noted that the Commission has announced that it has conducted additional dawn raids on 24 and 25 November of a “number of pharmaceutical companies” in several European Union Member States, suspecting them of having operated a cartel or of abuses of their dominant market position. Therefore, it seems likely that there will be a focus on the activities of the pharmaceutical industry for some time to come.

**Competition issues as between different originator companies**

The report suggests that originator companies develop defensive patenting strategies primarily to block the development of new competing products. Typically this is to protect compounds closely related to their candidates, which would be of interest to competitors. This can lead to higher costs to the second originator company e.g. having to pay royalties or in delays. There were 1,100 examples of an overlap between the R&D of one originator company and the patents of another originator company. In contrast, the European Consumers Association’s representative, in her presentation to the hearing on 28 November criticised “me too” medicines, which she considered stifled innovation.

The Commission stated that a large number of agreements (over 1,450) between different originator companies will be analysed more fully during the second phase of the enquiry.

**Potential future regulatory developments**

The Commission has acknowledged that company behaviour does not account for all of the problems it has identified. Based on the Preliminary Report, we can expect recommendations on changes to the regulatory framework to make it more consistent and coherent throughout the EU.

All sides of the industry supported the creation of a Community patent, and the creation of unified and specialised patent judiciary in Europe to replace the fragmented and expensive national court systems. These developments have been under discussion for some time, but some speakers at the 28 November hearing predicted that the specialised patent court is likely to be in place sooner than a single Community patent. A European patent court would determine pan-European judgments of EPO-granted patents, and then eventually cases on the Community patent. At present, the courts of
different EU Member States sometimes give conflicting judgments on the same issue of patent validity or infringement, as seen in 11% of the final judgments reported in the sample.

Companies, industry associations and agencies reported bottlenecks in the marketing authorisation procedures, which were alleged to be due to a lack of adequate resources in certain agencies (competent authorities). Originator companies particularly support harmonisation of marketing authorisation procedures, especially between the USA and EU, as the current differences lead to additional costs and delays.

However, how speedily the regulatory initiatives are taken forward will depend on the will of the Commission as a whole and not just the Competition Directorate-General, and more importantly on the support and priority given to such recommendations by the EU Member States. Commission Directorates-General such as Internal Markets and Enterprise and the EU Member State governments will be prime targets for lobbying by originator pharmaceutical companies on these issues.

**Parallel imports**

Although there was a question at the Commission’s presentation and hearing on 28 November from a European association of parallel traders, the Commission representatives made it clear that the current investigation does not include the issues of parallel imports in its scope. It was, however, made clear that national pricing and reimbursement procedures cause problems for all pharmaceutical companies, primarily the delays that they cause in marketing a medicinal product.

Richard Eccles, London, Morten Nissen & José Rivas Brussels

The European Commission’s Communication on the Pharmaceutical Sector

On 10 December 2008 the European Commission released a wide-ranging and significant communication on the initiatives it considers necessary to ensure that the EU pharmaceutical industry contributes to the well-being of citizens through the availability of medicines, economic growth and employment. The communication sets out 25 key objectives and is accompanied by three legislative proposals which address consumer access to reliable information about prescription-only medicines, strengthening of the EU system for pharmacovigilance and counterfeit medicines.

The Commission’s objectives are stated as:

1. To improve the availability of medicinal products for patients in need, with a particular focus on smaller markets - to be
developed in close cooperation with Member States by 2010:

2. Based on an evaluation of the European Medicines Agency (EMEA) ways to optimise the functioning of the network of EU medicines authorities - to be identified by 2010;

3. Genuinely transparent and speedy pricing and reimbursement decisions to be made possible by enhancing the application of the Transparency Directive;

4. Based on the work of the Pharmaceutical Forum, the exchange of information and cooperation among stakeholders on pricing and reimbursement to be improved;

5. Based on the agreement found in the Pharmaceutical Forum the exchange of data between Member States on relative effectiveness should be fostered in order to avoid delays in the market access of innovative treatments;

6. Ways to ensure availability and market access for generics and non-prescription medicines should be examined by 2011;

7. Launch of an in-depth monitoring of the functioning of markets in the pharmaceutical sector - as to which there is already an ongoing inquiry into the sector, the preliminary conclusions of which are reported in this newsletter;

8. An assessment of the application of the Clinical Trials Directive with a view to making, if appropriate, legislative proposals - while taking into account the global dimension of clinical trials - should be presented by the Commission by 2010;

9. Proposal to rationalise and strengthen the EU framework on pharmacovigilance to be adopted swiftly – as to which see below;

10. The Conclusions and Recommendations of the Pharmaceutical Forum's work on information to patients on diseases and treatments should be taken forward – as to which see below;

11. Measures to be taken to ensure that the information provided by the industry to those who seek it is reliable and objective;

12. Measures to reduce the potentially harmful impacts of pharmaceuticals on the European environment and public health should be proposed;

13. The proposal to prevent the entry of illegal medicinal products into the legal supply chain should be adopted swiftly – as to which see below;

14. An intensified exchange of information on illegal distribution channels in relation to counterfeit medicinal products should be proposed by 2012;

15. Within IMPACT (the WHO International Medical Products Anti-Counterfeiting Task Force), third countries developing and enforcing legislation against counterfeit medicinal products should be assisted by the Commission:
16. To improve international cooperation in the field of pandemics, existing bilateral and multilateral relations with third countries should be strengthened and extended:

17. The regulatory cooperation with the US, Japan and Canada within existing confidentiality arrangements, focusing on safety monitoring should be intensified:

18. Mutually agreed mechanisms for inspections in third countries should be proposed to these three countries by 2010:

19. Bilateral cooperation to be strengthened, including the field of research, with Russia, India and China, focusing on clinical trials and the manufacture of active ingredients:

20. Training and information sharing procedures with these three countries should be fostered:

21. International harmonisation at ICH and the promotion of the use of international standards by third countries beyond the US and Japan should be further developed:

22. Using TEC (EU-US Transatlantic Economic Council) areas for simplification and convergence of rules between the US and the EU and engaging in upstream regulatory dialogue for major legislative proposals should be pursued:

23. The EU should work towards the implementation and enforcement of the WTO framework in its bilateral and multilateral contacts, including bilateral Free Trade Agreements (FTAs), in particular as regards the protection of intellectual property rights:

24. The effects of the implementation of the Regulation on Advanced Therapies should be assessed and reviewed by 2012; and

25. A report on the use of ‘-omics’ technologies in pharmaceutical research and development should be submitted by 2010 and the question of whether new Community instruments are needed to support their development should be explored with stakeholders.

The first legislative proposal is a draft Directive amending Directive 2001/83/EC which inter alia would allow marketing authorisation holders to disseminate, either directly or indirectly through a third party, information to the general public on prescription medicines. Such information could not be disseminated over the radio or on television but may be provided by unsolicited health-related publications, websites and by way of written answers to questions from the public. The draft Directive is accompanied by a draft Regulation adopting the changes in Directive 2001/83/EC for the purposes of centrally authorised products under Regulation 726/2004.

The second legislative proposal is a draft Directive amending Directive 2001/83/EC which inter alia would allow, after the granting of a marketing authorisation, national competent authorities to require a
marketing authorisation holder to conduct a post-authorisation safety study if there are concerns about the risks of an authorised medicinal product. There are other provisions relating to transparency and communication of safety issues and clarification of responsibilities for pharmacovigilance. The draft Directive is accompanied by a draft Regulation adopting similar changes into Regulation 726/2004.

The third legislative proposal, and last so far, is a draft Directive that would amend Directive 2001/83/EC inter alia by requiring greater verification and inspection procedures for medicinal products entering into the EU and into the distribution chain in the EU.

The next stage for these legislative proposals will be a discussion in the European Parliament.

**Gerry Kamstra**  
London

---

**UK: The Association of the British Pharmaceutical Industry and the Department of Health reach final agreement on the new Pharmaceutical Price Regulation Scheme**

As reported in our July newsletter, the ABPI and the DoH have been negotiating a revised version of the voluntary agreement regulating the price of licensed branded medicines in the UK, the Pharmaceutical Price Regulation Scheme (PPRS). In July an “outline” agreement was reached and on 19 November a final version of the revised PPRS was announced. The 127 page text of the new agreement is available at the DoH website.

The new PPRS will start on 1 January 2009 and will run for a minimum of five years. As before, it is non-contractual and voluntary and it will remain the scheme for the Four Nations of the UK. Any manufacturer or supplier may apply to join the scheme (ie not just members of the ABPI) and if it does so any statutory scheme under the National Health Services Act 2006 may not be applied against it.

Under the new scheme the DoH and the ABPI have committed to a number of specific policy initiatives aimed at encouraging and rewarding innovation and assisting the uptake of cost-effective new medicines. These will include initiatives:

- Establish a single unified horizon scanning process to identify new technologies in development by industry;
- Address the anomaly whereby the funding direction of the DoH does not apply to National Institute of Clinical Excellence (NICE) technology appraisal recommendations (on purchasing of products) which are subsequently updated in a clinical guideline and update good practice guidance;
- Pilot the use of prescribing incentive schemes to promote uptake of innovative products;
- Explore how to optimise use of existing levers such as Payment
by Results to further improve uptake; and
• Publish metrics on the uptake of clinical and cost effective medicines at local, national and international level.
There are two new provisions in the 2009 PPRS that will help implement a pricing system that better reflects value to patients:
• Flexible pricing: A system of flexible pricing will be introduced. This system will continue to allow a company to set an initial launch price for a new active substance. In addition there will be flexibility for companies to increase or decrease this original list price as either further evidence or new indications change the value that the medicine provides to NHS patients. Flexible pricing will only apply when medicines are subject to NICE appraisal: a review by NICE will be required to determine whether the revised price provides value to the NHS and should receive a positive recommendation for use. NICE will not negotiate or publicly set or indicate prices; and
• Patient access schemes: These are schemes agreed between the DoH and a pharmaceutical company for consideration in the context of a NICE appraisal. These schemes are aimed at improving patient access to a medicine which has not initially been assessed as cost or clinically effective by NICE. The new PPRS sets out arrangements for patient access schemes (though subject to certain conditions to ensure that they are implemented sensibly and that the cumulative burden on the NHS is manageable).

The ABPI and DH have agreed that the experience of the flexible pricing and the patient access schemes should be reviewed by 2011.
With regard to pricing in general, the new PPRS preserves a company’s ability to set the prices of new active substances. It will also preserve companies’ ability to modulate prices (i.e. change the prices of its product portfolio) under conditions that are mutually agreed.

The new scheme includes provisions for price cuts. These cuts have been re-negotiated since the “outline” agreement announced earlier in the year. The first change relates to measures linking the price of non-patent protected branded drugs to the price of any equivalent generic (also referred to as “the wedge”). These will no longer be introduced following the re-negotiation. The price cuts in NHS primary and secondary care will instead be delivered by the following combined measures:
(i) A 3.9% price cut will be introduced in February 2009. Members of the scheme may achieve this cut by modulation (i.e change the prices of their NHS portfolio so as to equate to this):
(ii) Subject to discussion with affected parties, the DoH will introduce generic substitution (i.e pharmacists will be able to dispense a generic drug against a prescription for the branded medicine, unless the GP has
ticked a box indicating that only the brand medicine can be dispensed). In addition, certain exemptions from these arrangements on clinical grounds will be agreed, subject to consultation. This measure will not be introduced before January 2010 because of the discussions and system changes required:

(iii) There will be further price adjustments in each year, starting in 2010, aimed at ensuring that the reductions of 5% originally envisaged by the DoH are delivered over the course of the new scheme, as set out in the table below: and

(iv) Companies with sales of £5m or less in 2007 will be exempt from the price adjustments. The first £5m of sales will be exempt for companies of up to £25m sales in 2007.

As the precise effect of generic substitution is unknown, the expected savings have been modelled. Including assumptions about the proportion of prescriptions GPs will tick to exclude substitution. When the assumptions on generic substitution savings are combined with the price cuts in the table, it is thought unlikely that exactly 5% will be delivered. Therefore, the agreement includes a provision by which either the DoH or the ABPI will be able to call for a review to be undertaken of the savings being delivered with a view to adjustments being made to correct any under- or over-delivery of 5% over the term of the new scheme.

The second change over the “outline” agreement announced earlier this year relates to a potential additional price cut of 2% if the drugs bill growth exceeds 6.7% in 2008 or 2009. This will no longer form part of the new scheme. The DoH and the ABPI have agreed that there will instead be an additional price cut of 1% in January 2010. The additional price cut will not be contingent on growth in the drugs bill.

<table>
<thead>
<tr>
<th>Date</th>
<th>Price adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 2009</td>
<td>-3.9%</td>
</tr>
<tr>
<td>January 2010</td>
<td>-1.9%</td>
</tr>
<tr>
<td>January 2011</td>
<td>+0.1%</td>
</tr>
<tr>
<td>January 2012</td>
<td>+0.2%</td>
</tr>
<tr>
<td>January 2013</td>
<td>+0.2%</td>
</tr>
</tbody>
</table>

As in the 2005 scheme, the new scheme provides a framework for imposing reasonable limits on the profits to be made from the supply of medicines to the NHS, with annual financial returns required from members (AFRs). The new scheme takes account of developments and changes agreed in negotiations, specifically the need to encourage research and development. Accordingly there is an increase in the R&D allowance to a maximum of 30% of NHS sales.

Gerry Kamstra
London
Finland: Extension of generic substitution and introduction of a reference price system in 2009

A number of blockbusters will become subject to generic substitution in Finland earlier than in many other European countries, i.e. whilst valid product patents are still in force in other European countries. This is the result of new legislation coming into force on 1 January 2009. The most significant amendments will enter into force on 1 April 2009.

As reported in our October 2008 Life Sciences Update, product patents for medicines were first adopted in Finland in 1995. A large number of patented medicines in Finland are protected, and will remain so until 2019, by the process patent only. In 2006, the Medicines Act (Section 57(c)) was amended to bring the Finnish system, i.e. the effect of the combination of the patent protection and generic substitution, closer to that of other countries: so far generic substitution has not been applied to pharmaceutical products that are protected by a valid process patent or SPC in Finland and by valid product patents or SPCs in at least five other EEA countries.

Section 57(c) will be abolished in 2009. As a result of the new legislation enacted by the Finnish Parliament in November 2008, at the same time a reference price system for medicinal products will be introduced in Finland in 2009.

Ella Mikkola
Helsinki

Belgium: Recent amendments to the reimbursement regime for (generic) medicinal products

Several provisions of the Law of 14 July 1994 on mandatory healthcare and indemnities insurance (“the Law”) have recently been amended by the legislator¹. Both the regime for the inscription as reimbursable products and the regime of price revision for reimbursable products² have been amended.

The intention of the Belgian legislator is to address the issue of medicinal products’ availability by guaranteeing the sound functioning of the reference reimbursement system. The former regime provided that the applicant for reimbursement had to make the product available on the market within the three months following the entry into force of the reimbursement decision. The basic rule under the new regime provides

¹ See Draft legislation laying down various provisions. Parliamentary Documents, 2008-2009, nr 52-1608/001
² Respectively ruled by Articles 72bis and 35 ter of the Law.
that the product must be available on the date of entry into force of the reimbursement decision. However, a new paragraph is inserted, which provides that, where the applicant cannot comply with the obligation to make the product immediately available, it must warn the competent authority in relation to Healthcare Insurance (RIZIV/INAMI), which then registers the product on a list for a maximum of one year, without prejudice to the reimbursement decision. If the product is still unavailable on the first day of the twelfth month following the entry into force of the reimbursement, the product is deleted from the list.

The law provides examples of causes of unavailability but these are not exhaustive. Unavailability may result from the registration suspension, from force majeure or from the existence of a dispute concerning the right to commercialise a product where the main active substance is supposedly protected by a patent. In such circumstances, the product is by right reinserted in the list as from the end of the unavailability. The law does not indicate any maximum duration of such suspension, which means it cannot be precluded that the suspension could last longer than twelve months. It has to be noted that the Belgian legislator chose a pro-generic approach.

The preparatory documents of the amending statute also state that the explicit wording of the “Euro-Bolar” provision, as far as its applicability to the price-fixing and reimbursement procedure is concerned, has been considered as unnecessary, given that the current regulatory framework does not prohibit the preparation and introduction of applications for price-fixing and reimbursement before the patent expiry date.

The impact of the amendment to the Law on case law is important to consider. Under the previous regime, the Belgian courts admitted that the imminence of the entry of the newly reimbursable product on the market justified a summary procedure. The urgent character of the matter being sufficiently established. As a consequence of the new regime, the urgent character of the action will be more difficult to demonstrate.

Nicolas Carbonnelle & Marc Martens, Brussels

UK: SFO’s price fixing prosecution of pharmaceutical companies rejected

A prosecution brought by the Serious Fraud Office (“SFO”) alleging that a number of pharmaceutical companies had conspired to defraud the NHS of £120m by fixing the prices of various drugs has been abandoned after the Court of Appeal refused the SFO permission to appeal.

Those charged with the offences included Goldshield, Kent Pharmaceuticals Ltd, Norton Healthcare Ltd, Generics (UK) Ltd and Ranbaxy (UK) Ltd. The charges related to alleged price fixing cartels concerning the supply of the commonly prescribed drug warfarin and penicillin-based antibiotics on the NHS.
The prosecution, which resulted from the SFO’s investigation codenamed Operation Holbein, was originally halted in July 2008 by the High Court after the House of Lords held in a separate case in March 2008 that cartels could not be prosecuted on a common law charge of conspiracy to defraud unless there were aggravating factors and “mere price fixing” without any aggravating conduct was not an offence until the Enterprise Act 2002 made it so. The alleged offences occurred between 1996 and 2001 and so pre-dated the Act.

The SFO was ordered to pay costs. It is thought that Operation Holbein may have cost as much as £40m over the course of its 6 year duration.

Ewan Grist
London

Italy: the new Code of Professional Conduct for the pharmaceutical industry

Farmindustria, the Italian Pharmaceutical Industry Association, has recently published the 2008 edition of its “Code of Professional Conduct” (hereinafter, the “New Code”). The Code, compliance with which is compulsory for affiliated companies, represents the commitment of the industry not only to abide by specific laws in force but also “to operate on the basis of transparent standards of conduct that regulate the various circumstances in which corporate activities take place”.

The New Code does not substantially amend the previous Code with the exception of provisions concerning “relationships with patient associations” (Section 4.5 of the New Code). A few minor changes are also introduced in relation to “scholarships and scientific consultancy” and “clinical trials and drug-related studies” set out in Sections 4.1 and 4.3 respectively.

As to the industry’s “relationship with patient associations”, Farmindustria implements in Italy, without major changes the “EFPIA Code on relationships between the pharmaceutical industry and patient organisations” (hereinafter, the “EFPIA Code”) of 5 October 2007. In particular, the EFPIA Code, which is due to be implemented by all national pharmaceutical industry associations affiliated to EFPIA, sets out the standards which must apply (in a manner compatible with national laws and regulations and in a way that is no less rigorous than the provisions contained therein) to relationships between EFPIA member companies (and their subsidiaries/contracted third parties) and patient organisations which operate in Europe.

In particular, Section 4.5 provides that any form of economic support, whether direct or indirect, by the pharmaceutical company towards a patient association must comply
with the following criteria:

i) A specific and preliminary agreement aimed at regulating the amount of financing and the reasons for its disbursement must be reached. For this reason, each pharmaceutical company must develop a standard internal procedure for the approval of such agreements;

ii) The public utilisation by a pharmaceutical company of the logo or material owned by a patient association must be authorised in advance by the Association. In order to acquire such authorisation, the objectives for and the manner of using such logos and materials must be clearly defined;

iii) Any form of sponsorship by pharmaceutical companies vis-à-vis the patient associations must be transparent and without promotional objectives;

iv) No company can request to be the sole financier of a patient association;

v) In all cases in which travel or other forms of hospitality are provided, the provisions set out under Subsection 3 of the Code on conferences and congresses shall apply (i.e. hospitality of modest value); and

vi) The pharmaceutical companies must include on their own website a list of those patient associations that are supported by them.

According to EFPIA strategy, a review of the Code itself, and subsequently all of its national implementations, will be initiated before the end of 2010.

Mauro Turrini
Milan/Rome
This update gives general information only as at the date of first publication and is not intended to give a comprehensive analysis. It should not be used as a substitute for legal or other professional advice, which should be obtained in specific circumstances.