
Legal and Regulatory Update

UK and European content is compiled and written by **Bird & Bird**, an international law firm which advises Life Sciences clients on:

- licensing intellectual property and know-how
- R&D agreements and other commercial contracts
- clinical trials
- regulatory issues
- risk management
- private equity, venture capital, joint ventures, strategic alliances, mergers & acquisitions and stock
- exchange listings
- patent & trade mark litigation
- data protection
- EU & competition law
- product liability

Bird & Bird has offices in Beijing, Brussels, Düsseldorf, Frankfurt, Helsinki, Hong Kong, London, Lyon, Madrid, Milan, Munich, Paris, Rome, Stockholm and the Hague.

US content is compiled and written by **Reed Smith LLP**, one of the leading life sciences law firms and one of the 25 largest firms worldwide with over 1000 lawyers across 14 US, four European cities and four Middle Eastern and Asian cities. A strong presence on both coasts of the United States and offices in the UK, France and Germany makes us ideally positioned to offer clients a full-service, transatlantic capability.

Reed Smith represents clients, large and small, across a great number of legal disciplines and many industry sectors. In Europe, our key industries are financial services and life sciences. Our clients include financial institutions, biotechnology and pharmaceutical companies, manufacturers, health care providers and insurers, communications companies, universities and real estate developers and government bodies on both sides of the Atlantic.

This section is intended to be a synopsis of recent legal developments and is not intended to be exhaustive. If any issue referred to in this section is to be relied on, specific advice should be sought. Please contact:

Gerry Kamstra
Bird & Bird
90 Fetter Lane
London EC4A 1JP
Tel: +44 (0)20 7415 6000
Fax: +44 (0)20 7415 6111
E-mail: Gerry.Kamstra@twobirds.com
Website: www.twobirds.com

John Wilkinson
Reed Smith
Minerva House
5 Montague Place
London SE1 9BB
Tel: +44 20 7403 2900
Fax: +44 20 7403 4221
E-mail: jwilkinson@reedsmith.com
Website: www.reedsmith.com

Legal and Regulatory Update

Journal of Commercial Biotechnology (2008) 14, 327–347. doi:10.1057/jcb.2008.31;
published online 26 August 2008

NOTES FROM THE EU

EU: Yet another new ECJ reference in relation to supplementary protection certificates for medicinal products

Council Regulation (EEC) No 1798/92 governs the creation of a supplementary protection certificate (SPC) for medicinal products, which establishes the scheme by which SPCs enable *de facto* patent term extensions in European jurisdictions of up to five years to be secured for pharmaceuticals. The reference in Case 452/07 *Health Research Inc.* concerns the time limit for filing an application for an SPC. A further reference to the European Court of Justice (ECJ) under this Regulation, and also under the corresponding Regulation (EC) No 1610/96 concerning the creation of a SPC for plant protection products, has now been made in Case C-482/07 *AHP Manufacturing BV*. This new reference concerns whether the grant of an SPC to one applicant precludes the grant of a subsequent SPC to another applicant in respect to a different basic patent.

In Case C-482/07 *AHP Manufacturing BV* The Hague District Court has referred the following questions to the ECJ for a preliminary ruling:

1. Does Council Regulation (EEC) No 1768/92 ..., and more specifically Article 3(1)(c) thereof, preclude the grant of a certificate to the holder of a basic patent for a product for which, at the time of the submission of the application for a certificate, one or more certificates have already been granted to one or more holders of one or more other basic patents?
2. Does Regulation (EC) No 1610/96 ..., and more specifically recital 17 and the second sentence of Article 3(2) thereof, give rise to a different answer to Question 1?
3. When answering the previous questions, is it relevant whether the last application submitted, like the previous application or applications, is submitted within the period prescribed by Article 7(1) of Regulation (EEC) No 1768/92 or that prescribed by Article 7(2) of Regulation (EEC) No 1768/92?
4. When answering the previous questions, is it relevant whether the period of protection afforded by the grant of a certificate pursuant to Article 13 of Regulation (EEC) No 1768/92 expires at the same time as, or at a later time than, under one or more certificates already granted for the product concerned?
5. When answering the previous questions, is it relevant that Regulation (EEC) No 1768/92 does not specify the period within which the competent authority, as referred to in Article 9(1) of that Regulation, must process the application for a certificate and ultimately grant a certificate, as a result of which a difference in the speed with which the authorities concerned in the Member States process applications may lead to differences between them as to the possibility of a certificate being granted?

The point at issue first arose in Case 181/95 *Biogen Inc v SmithKline Beecham Biologicals*. The ECJ held that different proprietors of different basic patents could each secure separate SPCs over the same medicinal product. Although such SPCs might have different expiry dates

as a result of the different basic patents expiring at different dates, they are all subject to the same constraint that they must also expire not more than 15 years after first marketing authorisation for the product. The issue of whether multiple SPCs can exist for the one product must now be, however, assessed in the light of Article 3(2) of the Plant Protection Products SPC Regulation, a provision that is also expressed to apply to the Medicinal Products SPC Regulation:

- 3(2)** The holder of more than one patent for the same product shall not be granted more than one certificate for that product. Where two or more applications concerning the same product and emanating from two or more holders of different patents are pending, however, one certificate for this product may be issued to each of these holders.

Although the second sentence of Article 3(2) allows two or more applications for SPCs concerning the same product and emanating from two or more holders of different patents to proceed where the applications are each 'pending', it does not address the situation where the applications are not 'pending' together. Such a situation can arise where one SPC having been granted on one basic patent held by one party, another SPC is only later sought by the different holder of a patent that has taken much longer to proceed to grant. On the face of Article 3(c) of the Medicinal Products SPC Regulation, which prevents the grant of an SPC where the product has already been the subject of an SPC in the same Member State, the second patentee would be prevented from seeking an SPC purely as a result of the delays of patent offices for which it was not responsible.

In the UK the Patent Office in *In the matter of Chiron Corporation's and Novo Nordisk A/S' SPC Application* [2005] RPC 24 has rejected such an unfair and arbitrary approach and held that the grant of an SPC for a product to the holder of a basic patent before

an application was lodged in relation to the same product by a different holder of a different basic patent on the basis of a common marketing authorisation did not provide a ground for rejecting the later application under Article 3(c). The only constraint was that where there were a number of patents in different hands, but protecting the same product, all holders of basic patents could be granted an SPC but only one SPC could be granted for that product to each. This new reference in Case 482/07 *Health Research Inc.* will determine whether or not the sensible approach of the UK Patent Office will prevail throughout Europe.

EC: The first reference to the ECJ on the new community regulatory data protection regime for medicinal products

The reform of European Community legislation as to medicinal products for human use by Directive 2004/27/EC as from November 2005 changed certain aspects of the regulatory data protection regime for such products and prevents an applicant for a generic authorisation relying on the clinical data filed by the originator for a certain period. The main change was to introduce a uniform '8+2+1' term of such protection where marketing authorisations were sought after the measure came into effect. It also addressed a number of issues that the previous legislation had left unclear and that had been the subject of references to the ECJ over the previous several years. Despite this, uncertainties remain and one of these is reflected in the first reference to the ECJ on this topic under the revised legislation, Case C-527/07 *Generics (UK) Ltd, Regina v Licensing Authority (acting via the Medicines and Healthcare products Regulatory Agency)*.

In this case, the English High Court has referred the following questions to the ECJ for a preliminary ruling:

- (1) Where a medicinal product falling outside the scope of the Annex to Regulation

2309/93 (1) has been placed on the market in a Member State, (Austria) under its national authorisation procedure prior to the accession of that Member State to the EEA or the EC and:

- (a) that Member State has subsequently acceded to the EEA and then the EC, and as part of the conditions of its accession it has transposed into its national law the authorisation provisions of Directive 65/65 (now Directive 2001/83 (2)), no transitional provisions applying in this respect;
- (b) the product in question has remained on the market in that Member State for some years after its accession to the EEA and the EC;
- (c) following the accession of that Member State to the EEA and the EC, the marketing authorisation for the product in question has been varied by adding a new indication, and the variation was considered by the authorities of that Member State to be consistent with the requirements of Community law;
- (d) the dossier of the product in question was not updated in accordance with Directive 65/65 (now Directive 2001/83) after that Member State's accession to the EEA and the EC; and
- (e) a product containing the same active ingredient has subsequently been authorised under Article 6 of Directive 2001/83 and placed on the market in the EC;

is the medicinal product to be considered to be 'a reference medicinal product which is or has been authorised under Article 6 ... in a Member State' within the meaning of Article 10(1) of Directive 2001/83, and if so which of the above conditions is/are decisive in this respect?

- (2) In circumstances where the competent authority of a reference Member State erroneously refuses an application for a

marketing authorisation made under Article 10(1) of Directive 2001/83 in the context of the decentralised procedure provided for in that Directive, on the ground that the medicinal product referred to in Question 1 above was not a 'reference medicinal product' within the meaning of Article 10(1), what guidance, if any, does the Court of Justice think it appropriate to provide as to which circumstances the national court ought to take into consideration when it comes to determine whether the breach of Community law is a sufficiently serious breach within the meaning of the judgment in *Brasserie du Pecheur* and *Factortame*?

The first question referred in essence asks what is the starting point for the period of such protection (which is keyed to the first marketing authorisation as a medicinal product for a particular active in the Community) when the first marketing authorisation for the originator product was originally granted in a Member State before it joined the Community, but remained in force afterwards in accordance with European Community law. The second question is directed to what remedy is available to an applicant for a generic authorisation in the event that a regulatory body has wrongly refused it.

EU: Advocate General's opinion supporting parallel trade in Greek case against GSK

The long running saga of disputes between Greek exporter wholesalers and GlaxoSmithKline (GSK) following GSK's refusal of supplies for export purposes has taken a new turn. In the ECJ proceedings referred from the Greek court, *Efetiö Athinon*, the Advocate General issued his opinion on 1st April, 2008 which favours a conclusion that GSK was abusing a dominant position in refusing supplies to the exporter wholesalers (Joined Cases C-468/06 – 478/06). This

opinion goes against the trend of recent European Court and national court judgments, and also the previous opinion in the *Syfait* case given by Advocate General Francis Jacobs, and therefore comes as a surprise. The ECJ is, however, not bound to follow the opinion of the Advocate General when it adopts its full judgment in a few months' time.

In the *Syfait* case, following a complaint by various Greek wholesalers, the Hellenic Competition Commission referred questions to the ECJ for a ruling under EC law on whether GSK was abusing a dominant position by failing to meet in full all the orders that the wholesalers had placed for export purposes. The ECJ declined to give judgment on jurisdictional grounds, because it concluded that the Hellenic Competition Commission was not a court or tribunal authorised to make a reference within the meaning of Article 234 EC. Meanwhile, Advocate General Jacobs had issued his opinion (in October 2004) to the effect that it was not abusive in the circumstances of the case for GSK to refuse to supply the wholesalers in full, in order to prevent parallel trade, taking into account the specific characteristics of the pharmaceutical sector, including the pervasive regulation of price and distribution in the Member States, which were imposed on the pharmaceutical companies.

In the similar issues now raised in the proceedings referred to the ECJ by the *Efetio Athinon* (Joined Cases C-468/06 – 478/06), the ECJ was asked to rule on:

- Whether the refusal by a dominant undertaking to meet pharmaceutical wholesalers' orders in full, as a means of limiting parallel trade, constitutes *per se* an abuse of dominance, taking into account the profitability of parallel trade for wholesalers because of the price differentials resulting from state intervention; and
- Insofar as such conduct is not an abuse of dominance in every case, which factors

are relevant in assessing the possible abuse?

Advocate General Ruiz-Jarabo proposes that the ECJ should rule that a dominant undertaking which refuses to meet in full the wholesalers' orders of pharmaceutical products, in order to protect itself against the effects of parallel trade, commits an abuse of that dominant position. The Advocate General denied that GSK had put forward sufficient evidence to demonstrate economic efficiencies to justify its refusal in this particular case, but he took the view that it is possible that an undertaking could provide objective justification for such conduct by showing that the regulation of the pharmaceuticals market compels it to take such action to protect its legitimate business interests. The Advocate General, however, also stated that it is not possible to rely for such purposes on the pricing system for medicinal products (because the system allows for an element of negotiation by pharmaceutical companies with national price control authorities) nor on the impact of parallel trade on incentives to innovate. On the last point, the Advocate General rejected the idea of a causal link between the loss of income because of parallel trading and the producer's reduction of investment in research and development.

The opinion of the Advocate General takes the opposite position to the rulings of national courts in France and Spain, and also the ruling of the Hellenic Competition Commission in the *Syfait* case (in September 2006), all of which have supported the conclusion that a refusal by a dominant pharmaceutical company to supply exporter wholesalers was normally unlikely to be abusive in the economic and regulatory context of the industry. The Advocate General's present opinion is also inconsistent with the judgment of the European Court of First Instance (ECFI) also in September 2006 in *GSK v Commission* in which the ECFI quashed a decision of the European

Commission to refuse exemption under Article 81(3) EC to GSK's agreement involving a dual pricing regime in Spain whereby wholesalers were charged the national regulated price for sales for domestic consumption and a higher price on supplies for exports. In that case, the ECFI ruled that the European Commission needed to carry out a full balancing exercise under Article 81(3), *inter alia* comparing the advantages of intra-brand competition through parallel exports with the advantages of inter-brand competition at innovation level as between pharmaceuticals producers who for this purpose had an interest in protecting their revenue by limiting parallel imports. This case is also under appeal to the full ECJ.

The issues surrounding the Advocate General's present opinion are therefore very contentious. There is a rich background of economic and legal issues for the ECJ to consider, in deciding whether or not to follow the Advocate General's opinion.

EU: European Commission launches pharmaceutical investigation

The European Commission has, using its investigatory powers under Article 17 of Regulation 1/2003, launched an inquiry into competition in the pharmaceuticals sector. The inquiry has not been launched in response to any indication of specific transgressions but will examine the reasons why fewer new pharmaceuticals are being brought to the market and the apparent delay to the entry of generic pharmaceuticals.

In particular, the inquiry will look at whether pharmaceutical companies are infringing the EC Treaty's prohibition on restrictive practices (Article 81) with agreements such as patent dispute settlements. It will also examine whether the EC Treaty's ban on the abuse of a dominant market position (Article 82) has been contravened by the creation of artificial barriers to entry of the market by, for example, misuse of patent rights or vexatious litigation.

Innovation in the pharmaceutical sector is assisted by patents and other intellectual property rights. Active competition in the sector is, however, important to the public to ensure value for money on health spending. The Commission has stated that its action will complement, rather than challenge, intellectual property laws.

The Commission can use a wide range of investigative measures to gather information, including requests for information. Companies are likely to view the information sought, such as the use of intellectual property rights and litigation, as highly confidential.

The inquiry is limited to medicines for human consumption; it will take into account differing regulatory frameworks but will not question the various health schemes of the Member States. Its findings will allow any future action to be taken on the most serious competition concerns. An interim report is expected in Autumn 2008 with the final results of the inquiry planned for Spring 2009.

EU: Protection of dosage regimen for medicaments under the new European Patent Convention 2000

The discussion before the European Patent Office (EPO) on patentability of second medical use claims has now entered another round. In the most recent decision by the Board of Appeal T1319/04 – KOS Life Sciences Inc dated 30th April, 2008, the question of allowability of dosage regimens of medicaments was referred to the Enlarged Board of Appeal (EBA) of the EPO.

The questions referred were:

- (1) Where it is already known to use a particular medicament to treat a particular illness, can this medicament be patented under the provision of Article 53(c) and 54(5) EPC 2000 for use in a different, new and inventive treatment by therapy of the same illness?
- (2) If the answer to question (1) is yes, is such a patenting also possible where the

- only novel feature of the treatment is a new and inventive dosage regime?
- (3) Are any special considerations applicable when interpreting and applying Article 53(c) and 54(5) EPC 2000?

In the case underlying the referral, the Examining Division of the EPO had refused an application, essentially relating to the use of nicotinic acid for the manufacture of a sustained release medicament for use in the treatment by oral administration *once per day prior to sleep* of hyperlipidaemia. The Examining Division argued that the feature relating to a specific drug regimen, that is, once per day prior to sleep, reflected a medical activity excluded from patentability. The applicant lodged an appeal against this decision.

In the appeal stage, it was argued by the applicant that two decisions of the EPO (T1020/03 and G5/83) required a broad allowability of claims in second medical use format, without any restriction on which area could be novel.

The Board of Appeal found that the only feature of the invention not disclosed in the prior art was the specific dosage regimen of 'once per day prior to sleep'.

The question arising under the newly applicable Article 54(5) EPC 2000, which came into force on 13th December, 2007, was therefore whether a dosage regimen can be recognised as a specific use in a method referred to in Article 53(c) EPC 2000. New Article 54(5) EPC 2000 specifies that patentability of any substance or composition is not excluded for any specific use in a method for treatment of the human and animal body, by surgery or therapy, and diagnostic methods practised on the human or animal body.

The Board of Appeal analysed the case law available on the 'old' European Patent Convention (EPC) 1973 and came to the conclusion that, in particular, decision G5/83 uses a language which is *prima facie* broad enough to allow patenting of a substance or

composition for use in a new and inventive treatment by therapy, characterised by being *a new dosage regimen for treating the same illness with the same substance*. The question arising is therefore whether there might be sufficient reasons for giving the language used in the decision a more restricted meaning that excludes this possibility from patentability?

Additionally, there is one decision by a Board of Appeal T1020/03 that for the first time recognised a pure dosage regimen as not being excluded from patentability. The Board of Appeal, in view of this case law, saw it necessary to refer the question of allowability of second medical use claims that only differentiated from the prior art by way of a novel and inventive dosage regime to the EBA as it was an important question of law.

The considerations that should be taken into account by the EBA are that categorically denying patent protection for medicaments for use in methods of treatment where the only novel feature is a dosage regime would:

- (a) make it simpler to refuse patent applications or invalidate such patents;
- (b) avoid problems for the courts in deciding what evidence is satisfactory to show that an (old) medicament was already being manufactured and/or marketed for use in a new dosage regime;
- (c) value medical confidentiality to preserve the physician/patient relationship; and
- (d) preserve physicians' freedom to treat their patients.

Therefore, the decision of the EBA will now ultimately construe the regulations on the protection of the second medical use of medicaments with regard to a novel dosage regime. Since the protection of novel dosage regimes is critical for extending the protection of important medicaments, it will be a significant step to clarifying the options for protection before the EPO. This issue of second medical use claims for novel dosage regimes has also recently been considered by the UK Court of Appeal in *Actavis UK Ltd v Merck & Co Inc*, reported below.

UK: The Court of Appeal's recent decision on the parallel import of pharmaceutical products

Following two preliminary references to the ECJ, on 21st February, 2008, the Court of Appeal handed down the latest decision in the long running pharmaceutical parallel import case of *Boehringer Ingelheim KG and Boehringer Ingelheim Pharma KG v Swingward Limited* ([2008] EWCA Civ 83). The case essentially concerned the repackaging and over-stickering of pharmaceutical products by parallel importers.

The ECJ had previously held that whether co-branding and de-branding by parallel importers damaged the reputation of the manufacturer's trade mark for the purposes of Bristol-Myers Squibb (BMS) Condition 4 (ie no damage to the reputation of the mark) was a question of fact for the national court.

Specifically in relation to the repackaging issue, the court held that this did not, of itself, damage the reputation of manufacturer's trade marks and the mere fact that the importer had placed its own trade mark on the product alongside that of the manufacturer (the so-called co-branding), when it was plain in the circumstances that it was the *importer's* trade mark, did not damage the reputation of the manufacturer's mark unless it was done in such a way so as to damage the manufacturer's mark.

With regard to the de-branding of products, the court considered both total de-branding, where the manufacturer's trade mark was removed from the product completely and partial de-branding, typically where the product was reboxed with just the generic name displayed on the outside but leaving the manufacturer's trade mark on certain aspects of the packaging such as the blister packs or on the pills themselves.

In respect of total de-branding, the court held that there could be no trademark infringement as there was simply no 'use' of the trade mark at all.

In respect of partial de-branding however, the Claimants had argued that it was damaging to the reputation of the trade mark

that it had been partially removed, as the trade mark would have less exposure than it otherwise would have had. The court, however, rejected this argument and held that, as the trade mark owner had no right to insist that its trade mark stayed on the goods after they had been sold, in the case of partial de-branding, the continued exposure of trade mark at all after this time (albeit only partial) was more than the manufacturer had a right to insist upon. As such, the mere act of partial de-branding was not, of itself, damaging. The court did accept that de-branding could be damaging depending on the manner and form of the de-branding but this was a question of fact for the national court.

While the court concluded that the defendants' re-boxing and re-labelling of the products did not, as a question of fact, damage the reputation of the manufacturers' trade marks in this case, it stopped short of allowing the appeals due to a pending and potentially relevant reference to the ECJ by the Austrian Supreme Court in *Wellcome v Paranova* (C-276/05). The Austrian Court has asked the ECJ to consider whether the presentation of the new packaging is to be measured against the principle of minimum intervention or only against whether it is such as to damage the reputation of the trade mark and its proprietor.

Despite holding that the repackaging caused no damage to the Claimants' marks, the Court considered that the mere possibility that the ECJ may introduce what would effectively be a 6th BMS condition of minimum intervention meant that it was only right to defer its final decision until after the ECJ has given its ruling on the Austrian reference.

UK: Court of Appeal explains the limited application of the *Biogen* principle to product claims and upholds broad product claim protection for a novel enantiomer

In a judgment given on 10th April, 2008 in *H. Lundbeck A/S v Generics (UK) Limited &*

Ors, the English Court of Appeal reversed in part the decision of the Patents Court and in so doing upheld broad product claim protection for escitalopram, the (+) enantiomer of the racemate citalopram, that is responsible for the SSRI activity of citalopram.

The judgment is of especial significance because the Court of Appeal analysed the extent to which an attack of insufficiency, along the lines that had succeeded some ten years previously in the House of Lords in *Biogen v Medeva*, and that had succeeded at first instance in the Patents Court in this present case, had application to a product claim where only two synthetic routes to manufacture a product had been disclosed but the desirability of making such product was obvious. This analysis has particular authority as the leading judgment was delivered by Lord Hoffmann, who normally sits in the House of Lords, and who, when so sitting, had given the lead judgment in *Biogen*, but as to which he here concluded:

40. *Biogen* should therefore not be read as casting any doubt upon the proposition that an inventor who finds a way to make a new product is entitled to make a product claim, even if its properties could have been fully specified in advance and the desirability of making it was obvious.

There were three grounds of attack on the validity of the three claims of the escitalopram patent in issue:

- (a) Product claims 1 and 3 lack novelty by reason of the disclosure of the racemate in the earlier published patent for citalopram;
- (b) Product claims 1 and 3 and process claim 6 are invalid for obviousness;
- (c) Product claims 1 and 3 are invalid for insufficiency because they claim the enantiomer made by any method, but the specification discloses only two ways of making it.

As to novelty, it was common ground, consistent with EPO and English case law

(in contrast, for example, to that in Germany as to this issue), that the prior disclosure of a racemate did not in itself amount to a disclosure of each of its enantiomers. It was, however, argued that claim 1, to the enantiomer, was not only for the pure enantiomer but was also for the enantiomer as an unresolved (ie unseparated) moiety of the racemate. The Court of Appeal rejected this argument and agreed with the first instance judge in holding that a claim to the enantiomer should be construed as not covering an unresolved part of the racemate.

As to obviousness, it was argued that the claim 6 process, one of the two claimed processes for producing the enantiomer, was obvious, along with another process that had not been disclosed or claimed. The evidence at trial had established the difficulty at the priority date of resolving citalopram (it had taken the patentees seven years to succeed in so doing), and the unpredictability of success of the 13 different approaches that might have been considered to resolve citalopram. It was, however, argued that claimed process had been 'obvious to try'. The Court of Appeal accepted that the trial judge had correctly stated the principle to be applied as:

The question of obviousness must be considered on the facts of each case. The court must consider the weight to be attached to any particular factor in the light of all the relevant circumstances. These may include such matters as the motive to find a solution to the problem the patent addresses, the number and extent of the possible avenues of research, the effort involved in pursuing them and the expectation of success.

The Court of Appeal then accepted that the trial judge had correctly applied this principle to the facts of the case, having first noted that there were 'a number of avenues of research' open to the skilled man seeking a solution to the problem and that therefore the skilled man would not have taken the claimed route unless satisfied that there was a 'real prospect'

that it would work, which on the evidence the trial judge found not to be established. Accordingly the Court of Appeal upheld the Patents Court judgment that neither the claimed process in issue, nor the product claims, was obvious.

As to insufficiency, the trial judge had found the escitalopram product claims to be insufficient because these were to one enantiomer of citalopram however made, when all that the patentees had discovered was one way of making that enantiomer, it being already known at the priority date that such enantiomer must exist and that either it or the other enantiomer or both must have a medicinal effect. The Court of Appeal reversed this finding. Lord Hoffmann confirmed that a product claim would usually be enabled if the specification and the common general knowledge enabled the skilled man to make it, and that for this purpose one synthetic method was enough. He explained that the *Biogen* case on which the trial judge had based his finding concerned not a claim as here simply to a novel product but to a type of ‘product by process’ claim to ‘a molecule identified partly by the way it has been made ... and partly by what it does...’. Such claim was to a class of products that satisfied the relevant conditions, one of which was that the molecule had been produced by recombinant DNA technology. Lord Hoffmann went on to observe:

34. ... But the specification in *Biogen* described only one method of making the molecule by recombinant technology and disclosed no general principle. It was easy to contemplate other methods about which the specification said nothing and which would owe nothing to the matter disclosed.

35. In my opinion, therefore, the decision in *Biogen* is limited to the form of claim which the House of Lords was there considering and cannot be extended to an ordinary product claim in which the product is not defined by a class of processes of manufacture. It is true that the House in

Biogen indorsed the general principle stated by the Board of Appeal in T409/91 *Fuel Oils/EXXON* [1994] OJ EPO, that – the extent of the patent monopoly, as defined by the claims, should correspond to the technical contribution to the art in order for it to be supported or justified.

36. The judge said that in holding claim 1 insufficient, he was applying this principle. But then he treated the relevant “technical contribution to the art” as being the inventive step, namely a way of making the enantiomer. That, I respectfully consider, was a mistake. When a product claim satisfies the requirements of section 11 1 1 of the 1977 Act, the technical contribution to the art is the *product* and not the process by which it was made, even if that process was the only inventive step.

Lord Hoffmann then went on to explain how this approach was consistent with EPO case law, and also with the public policy justification for product claims as demonstrated by the approach to these throughout history by the courts and the legislature.

Lord Justice Jacob agreed with Lord Hoffmann’s conclusions but added several valuable observations of his own. In particular he pointed out that careful thinking was called for in considering claims to desirable ends, giving the following example of one type of product claim that could still be attacked as being insufficient:

61. So, for example, if a man finds a particular way of making a new substance which is 10 times harder than diamond, he cannot just claim ‘a substance which is 10 times harder than diamond’. He can claim his particular method and he can claim the actual new substance produced by his method, either by specifying its composition and structure or, if that cannot be done, by reference to the method ... but no more. The reason he cannot claim more is that he has not enabled more – he has claimed the entire class of products which have the

known desirable properties yet he has only enabled one member of that class. Such a case is to be contrasted with the present where the desirable end is indeed fully enabled – that which makes it desirable forms no part of the claim limitation.

Thus, the *Biogen* principle still has application to product claims in certain circumstances, but not, it would seem, to product claims drawn in terms of conventionally chemical terminology, such as that in issue in the present case.

UK: House of Lords upholds validity of Angiotech's drug eluting stent patent and agrees with the approach of the Dutch courts on inventive step in preference to that of the lower English courts

In its recent judgment in *Conor Medsystems v Angiotech Pharmaceuticals* the House of Lords has reversed judgments of the Patents Court in 2006 and the Court of Appeal early in 2007, that had both found the UK designation of EP 0 706 376 B, Angiotech's patent for a stent coated with the drug taxol, to be obvious and thus invalid for lacking inventive step. In so doing it agreed with, and quoted various passages from, a decision of the District Court of The Hague that had rejected the attack of lack of inventive step in respect to the Dutch designation of the patent. In contrast to some of its other decisions in the patent field the judgment of the House of Lords in this case is an exercise in judicial restraint and will be a disappointment for those who were looking for new statements of principle as to the law of obviousness, perhaps in recognition of the dangers of so doing given the irreducible subjectivity of obviousness determinations. Instead it focuses on the specific issue in this case with which the House of Lords disagreed with the lower English courts. But in so doing, it also makes an important contribution to the debate as to the relevance of attacks on

inventive step based on an 'obvious to try' approach.

Conor were no longer a party to the action, the parties having settled as between them their disputes under these patents in the summer of 2007. In order that Angiotech could secure the opportunity in the House of Lords to try to reverse the decision of the Court of Appeal and restore their patent, they, however, had to pay for the UK Patent Office to instruct counsel to argue Conor's case in its place. The Angiotech patent was directed to providing a solution to the problem of restenosis, a condition encountered with ordinary stents (tubular metal scaffolds inserted into an artery to keep it open) where the injury caused to the inner layer of an artery by their insertion could produce an exaggerated healing response that restored the original constriction in the artery that the stent was meant to treat.

The lead judgment of the House of Lords was given, as has become usual in their judgments in patent cases, by Lord Hoffmann, who recognised that although it was inevitable in the present system of litigation in Europe that national courts would occasionally make inconsistent decisions on differing national designations of a European patent (especially where dealing with questions of degree as arose with obviousness), it was undesirable that there be differences as between them in principle, as had been the case here. He identified the principle in this case as being how one identified the concept embodied in the invention for the purposes of determining inventive step. In essence, the lower English courts had erred by so formulating the inventive concept as to incorporate insufficiency type concerns (based on the failure of the specification to set out data showing that the invention did actually provide the promised benefit, that of preventing restenosis), in their analysis of inventive step:

19 ... the invention is the product specified in a claim and the patentee is entitled to

have the question of obviousness determined by reference to his claim and not to some vague paraphrase based upon the extent of his disclosure in the description. There is no requirement in the EPC or the statute that the specification must demonstrate by experiment that the invention will work or explain why it will work ...

There were cases, such as *T 1329/04* in the EPO, where patents were found to lack inventive step because they disclosed nothing more than speculation that did not go beyond what was obvious. But these were far from the facts of this case, where there was some teaching in the specification, based on a particular assay, indicating that it was advantageous to use taxol to prevent or treat restenosis, and so passed the threshold test of making the invention plausible:

37 ... there is ... no reason as a matter of principle why, if a specification passes the threshold test of disclosing enough to make the invention plausible, the question of obviousness should be subject to a different test according to the amount of evidence which the patentee presents to justify a conclusion that his patent will work. ...

Here the claim in issue was to a stent coated with taxol, the novelty of which was unchallenged. The alleged inventiveness lay not in discovering how to make it but in the claim that such a product would have a particular property, namely, the prevention or treatment of restenosis. Thus the relevant question was whether it was obvious to use a taxol coated stent for this purpose, but the lower English courts had failed to address this.

The correct test that they should have applied, according to Lord Hoffmann, was whether it could be shown on the basis of the prior art 'that the skilled person would have an expectation of success sufficient to induce him to incorporate taxol in a drug eluting stent?' Lord Hoffmann inferred from other observations in the English judgment at first instance that the trial judge would have

answered this question in the negative and so rejected the attack, a view which accorded with his own on the basis of the prior art references themselves and the expert evidence that had been before the judge.

Another member of the House of Lords, Lord Walker, although agreeing, as with other members of the House, with Lord Hoffmann, added some observations on the relevance of the 'obvious to try' approach, as to which Lord Hoffmann had observed that the notion was useful only in cases in which there was fair expectation of success, and that how much of an expectation would be needed depended upon the particular facts of the case. Lord Walker pointed out that the expression's origins lay in a 40-year-old case (*Johns-Manville Corporation's Patent*) that was concerned with 'a fairly low tech process' and observed that with the increase since then in the volume of high-technology research, especially in the fields of pharmaceuticals and biotechnology, the expression had taken on a life of its own. He then, however, quoted some observations by the retired Patents Court Judge, Sir Hugh Laddie, as to the problems with this approach, and by Lord Justice Jacob, in the Court of Appeal in this case, as to its limited application. Although Lord Walker did not endorse these in terms, it would seem that these opinions are viewed sympathetically by the House of Lords, and that it will be rare that an inventive step attack based on an 'obvious to try' approach will succeed in the English courts in future.

The wider consequences of this decision of the House of Lords may however be limited because there has already (with the exception of this particular case, where insufficiency considerations impermissibly crept into an inventive step analysis), been a discernable shift in approach on the part of the English Patents Court and the Court of Appeal, especially in the pharmaceuticals and medical device areas, which have become increasingly reluctant to hold patents invalid for lack of inventive step.

UK: Court of Appeal decides 'settled' EPO case law trumps UK precedent on Swiss-type claim to a new dosage regime

Summary

The Court of Appeal has decided in the case of *Actavis UK Ltd v Merck & Co Inc* [2008] EWCA Civ 444, that a Swiss-type claim can be patentable where the novelty is only conferred by a new dosage regime or form of administration of a substance. This is surprising because previously, the same court had found such a claim to lack patentability (*Bristol-Myers Squibb v Baker Norton* [2001] RPC 1). Accordingly, the court has created a further exception to the rules of binding precedent (*stare decisis*), where the precedent is contrary to 'settled' EPO law.

Background and facts

The case turned on the validity of Claim 1 of Merck's patent. This claimed the use of finasteride for the treatment of androgenic alopecia ('male pattern baldness' (MPB)) administered in the amount of about 0.05–1.0 mg per day. At the filing date of the patent, finasteride was already known to be useful in treating benign prostatic hyperplasia and had been proposed for treating MPB, but with a daily dosage of 5 mg or more.

At first instance, Mr Justice Warren had found the invention non-obvious, but had revoked the patent on the basis of the decision in *BMS*. Merck appealed and Actavis cross-appealed on obviousness.

The handing down of the judgment from the Court of Appeal was delayed due to a decision from the 'Technical Board of Appeal' (TBA) of the EPO in T/1319/04 – *KOS Life Sciences Inc*, which had referred questions on the very point of patentability of dosing regimes to the EBA. The Court of Appeal invited the parties to make written submissions in relation to this decision.

Court of Appeal decision

Despite the TBA reference in *KOS*, the Court of Appeal decided to hand down a final judgment.

The Court of Appeal distinguished the facts of *BMS* from the present case on the basis that there was no clear ratio that a Swiss-type claim lacked novelty if the only difference between it and the prior art was a new dosage regime for a known medical condition. Further, unlike in *BMS*, there was no disclosure in the prior art of the exact feature of the dosing-regime claimed.

The Court went on to hold that even if it was wrong on that, the *BMS* approach was not in line with that of the EPO, which permitted Swiss-type claims where the novelty is conferred only by a new dosing regime under Article 52(4) of the EPC, as they were not to methods of medical treatment. Indeed, the Court of Appeal held that this position is 'settled' at the Board of Appeal level and that the UK Courts should strive to follow 'settled' EPO jurisprudence, although it is not binding in the same way as decisions from the ECJ. The 'special circumstances arising from the creation of the European patent system and the central importance given to decisions of the Boards of Appeal' required the court to recognise a further but limited exception to the rules of binding precedent laid down in *Young v Bristol Aeroplane Co Ltd* (1944) KB 718, decided at a time when 'international influences' had little significance in our law.

The Court of Appeal did not accept Actavis' submissions that the pending reference in *KOS* demonstrated that the Court was 'wrong in saying that the position as regards new dosage regimes conferring novelty was settled in the EPO'. The Court of Appeal agreed with Merck that the *KOS* reference made no difference at all as it involved a question under EPC 2000 that was not applicable to this case. The Court of Appeal noted that it was possible that the EBA would rule that the existing EPO approach to novel dosing regimes was wrong, but this was unlikely. In the circumstances,

the court decided it would stand over the hearing on permission to appeal until after the EBA decision in KOS.

On obviousness, the Court of Appeal held that no error of principle had been demonstrated. The Court of Appeal held that Mr Justice Warren had been correct to accept Merck's argument that by the priority date of the patent, published research meant that, in the two-month period before the priority date of the patent, the landscape had changed so much that the skilled person would not have considered using finasteride for MPB, and so 'would never get to investigate suitable dosages forms for he would think there are none'. Mr Justice Warren had held that, absent the new published research, the patent would have been obvious.

Conclusion and comment

The position is on hold pending KOS. Although this is a reference under EPC 2000, it is clear from the TBA that they consider it the same as under EPC 1973, that is, EPC 2000 merely sought to enshrine the case law evolved by the EBA.

Lord Justice Jacob, however, did comment on the judgment that despite holding that such claims are allowable, they will nearly always be obvious as '... it is standard practice to investigate appropriate dosage regimes'.

The case is of further interest as the Court of Appeal has in effect said that it is free to follow EPO case law where it is considered to be 'settled' at the Board of Appeal level, despite conflict with previous decisions of its own. This raises the question – when is EPO case law 'settled'? The answer to this is not straightforward as there is no rule of binding precedent in the EPO system. As a consequence, conflicting decisions can arise and indeed there are such conflicting decisions from the EPO on the very issue of whether novelty can be conferred by a new dosing regime. A House of Lords decision would therefore be welcomed on this issue.

The finding that the patent was obvious two months before the priority date but not

at the priority date due to intervening publications having changed the common general knowledge is also of interest, not least because it raises the possibility of deliberate steps being taken by patentees to muddy the waters in the months preceding the filing of a prospective patent application.

UK: High Court allows appeal against aspects of the process used by the National Institute of Clinical Excellence in formulating their guidance on Alzheimer's drugs

In 2007, the first court challenge was made against the guidance by National Institute of Clinical Excellence (NICE) (established by the NICE (Establishment and Constitution) Order 1999), over what drugs should be available for prescription on the National Health Service (NHS), and on how the High Court had largely rejected the challenge to NICE's recommendation that three Alzheimer's drugs should not be prescribed on the NHS for mild cases of Alzheimer's disease, but should be prescribed for moderately severe cases of the disease only. On 1st May, 2008 the English Court of Appeal reversed a significant aspect of the High Court judgment, relating to the procedural fairness of NICE's assessment system, and the nature of the access to be given to consultees of the economic model used to assess the cost-effectiveness of the drugs. Although it was not asked to reverse the determination originally made by NICE, the effect of the judgment is to mandate the release to the consultees of information that would enable them to make further representations to NICE with a view to its making a further determination about the circumstances in which the drugs in issue should be prescribed.

The Court of Appeal held that NICE had acted unfairly by only making available to consultees (namely the companies whose drugs were the subject of the assessment), a read-only version of the economic model,

in the form of an Excel spreadsheet, rather than the fully executable model that had been requested and that would have allowed changes to be made to the inputs or assumptions on which the model was based in order to test its robustness or reliability. NICE had sought to justify its refusal to provide the fully executable model on two grounds – the first that had been provided to it by a third party on terms of confidentiality which precluded its wider dissemination, and the second that its use would result in extra work and delay. The Court of Appeal rejected both reasons. The economic model had been commissioned for the purposes of NICE's appraisal process and paid for, the confidentiality provisions in the commissioning agreement were in general terms only and did not restrict the use or disclosure of the model, and in any case any disclosure of the fully executable model by NICE to consultees could be made subject to standard undertakings of confidentiality. As for the second objection, a possible extra two or three months in the context of a 2.5-year appraisal process, as had been the case here, did not weigh heavily in the balance in deciding whether procedural fairness required release of the fully executable version of the model to consultees.

The Netherlands: Dutch Patent and Research & Development Box

Introduction

The Dutch Government stimulates innovation and R&D activities through corporate income tax incentives in the Dutch Patent and Research & Development Box (the '*Patent Box*'). In the Patent Box, all profits allocable to self-developed intangible assets that are patented or qualifying research & development activities are subject to a special tax regime at a rate of 10 per cent. The profits covered include royalty income and capital gains upon the (partial) disposal of the assets less their depreciation costs. Trade marks and similar assets do not fall within the scope of this special tax regime.

Patent Box – conditions

The Patent Box applies, provided certain conditions are satisfied:

- The company (taxpayer) applies the Dutch Patent Box regime to its patented intangible asset or intangible assets that results from certain research & development projects (see below).
- The Patent Box regime must be elected in the corporate income tax return.
- The patent must be self-developed and not acquired from third parties on the market (but acquired intangible assets that are embedded in the ultimate patent are not excluded).
- The patent or research & development project contributes to at least 30 per cent of the total profits realised from the intangible asset.
- Under the Patent Box, the costs of producing the intangible assets are deductible in the year covered. Conversely, the income realised with the intangible assets is taxed in the Patent Box at the reduced rate of 10 per cent to the extent the income exceeds (threshold) the total amount of production costs of all elected Patent Box intangible assets (on an ongoing basis). In addition, the maximum amount of income from the intangible assets taxed at the reduced rate of 10 per cent is capped at four times the total amount of the production costs of the elected Patent Box intangible assets (on an ongoing basis).
- Income not exceeding the threshold and income exceeding this capped amount will be taxed at the statutory rate of 25.5 per cent.
- Intangible assets patented prior to 1st January, 2007 do not qualify for the Dutch Patent Box.

Research & Development – conditions

Intangible assets that are not patented are also available for the Patent Box provided the

intangible assets are the result of certain qualifying research & development projects. The threshold is set at €100,000 and the cap at €400,000. This expansion of the Patent Box tax rate applies from 1st January, 2008 and promotes smaller research & development projects and activities.

Dutch double taxation treaties

If the Dutch owner of the intangible assets begins to license its intellectual property, it will generally generate royalty income under the license agreements from the licensee. Apart from EU Member States, most countries levy royalty withholding tax on payments of the royalties to a foreign licensor at rates of up to 30 per cent. The Netherlands has a wide tax treaty network that provides for reduced royalty withholding tax rates reducing the tax leakage on royalty income to just 0–15 per cent withholding tax on royalties paid to licensors that are tax resident in the Netherlands. This makes the Netherlands an attractive jurisdiction to own intangible assets (intellectual property rights) and operate (license) the intangible assets out of the Netherlands at the same time.

Conclusion

The combination between this low tax regime in the Dutch Patent Box and the reduced withholding tax rates for royalties under the widespread Dutch double taxation treaties makes the Netherlands an attractive option for establishing R&D centres.

© Bird & Bird

NOTES FROM THE US

INTELLECTUAL PROPERTY

Application of doctrine of patent exhaustion to method claims

Concerning an area of law that had not been considered since 1942, the US Supreme Court held in *Quanta Computer, Inc. v LG*

Electronics, Inc. (9 June 2008) that the doctrine of patent exhaustion applies to method claims, namely that methods can be ‘embodied’ in a product, the sale of which exhausts patent rights. While the subject matter of the patent was in the electronics field, this decision will have an impact upon patent owners in the biotechnology field seeking to license the same patent to multiple parties at different levels in the supply chain, potentially restricting that practice.

The respondent, ‘LG Electronics Inc.’ (LGE), possessed three computer technology ‘method patents’ (the ‘LGE Patents’) that related to the operation of a computer. LGE licensed these patents to ‘Intel Corporation’ (Intel) that entitled Intel to manufacture and sell microprocessors and chipsets using the LGE Patents. LGE and Intel entered into two agreements: a licence agreement and a master agreement. The licence agreement entitled Intel to ‘make, use, sell (directly or indirectly), offer to sell, import or otherwise dispose of its own products practising the LGE Patents. Nevertheless certain limitations were imposed insofar as no licence should be ‘granted by either party hereto ... to any third party for the combination of Licensed Products of either party with items, components, or the like acquired ... from sources other than a party hereto, or for the use, import, offer for sale or sale of such combination’. Moreover, the master agreement meanwhile stipulated that written notice was required that LGE had not licensed the customer to use its patents. ‘Quanta Computer, Inc’. (Quanta) subsequently purchased the chips from Intel and combined Intel’s chips with non-Intel products in ways that practised the LGE Patents. LGE consequently filed against Quanta for patent infringement.

The District Court granted summary judgment to Quanta, but in a subsequent judgment held that patent exhaustion only applies to apparatus or composition-of-matter claims that describe a physical object, and not process or method claims that describe operations to make or use a product. The

Court of Appeals for the Federal Circuit affirmed in part and reversed in part. It agreed that the doctrine of exhaustion did not apply to method claims, but concluded in the alternative that the licence agreement between LGE and Intel did not allow Intel to sell Intel products to Quanta for use in combination with non-Intel products. Moreover, it was held that the 'notice' Intel agreed to send to its customers imposed a 'condition' on the sale that the patent exhaustion doctrine would not apply.

LGE contended that, because method patents are linked not to a tangible article but to a process, they can never be exhausted through a sale. While the Supreme Court acknowledged it is true that a patented method cannot be sold in the same way as an article or device, methods may nonetheless be 'embodied' in a product, the sale of which exhausts patent rights. The precedents used by the Supreme Court do not differentiate transactions involving embodiments of patented methods or processes from those involving patented apparatuses or materials. Indeed to eliminate exhaustion for method patents would seriously undermine the exhaustion doctrine as patentees seeking to avoid patent exhaustion could simply draft their patent claims to describe a method rather than an apparatus.

The Supreme Court next considered the extent to which a product must embody a patent in order to trigger exhaustion. To trigger exhaustion the product must embody the essential features of the patent – namely that they carry out 'all the inventive processes' when combined 'according to their design' with standard components. Moreover, even products that partially practise a patent may still exhaust that patent. Indeed the Supreme Court affirmed that while each Intel microprocessor and chipset practises thousands of individual patents, the exhaustion analysis is not altered by the fact that more than one patent is practised by the same product. While the sale of a product embodying patent A would not exhaust patent B, a product

practising patent A while substantially embodying patent B does not prevent exhaustion of patent B.

Finally, the Supreme Court addressed the issue of whether the sale of the Intel products to Quanta exhausted LGE's patent rights. LGE maintained that there was no authorised sale because the licence agreement did not permit Intel to sell its products for use in combination with non-Intel products to practise the LGE Patents. Nevertheless the Supreme Court construed the licence agreement to authorise Intel to sell products that practised the LGE Patents, namely because there were no conditions limiting Intel's authority to sell products substantially embodying the patents – as these products did.

REGULATORY

FDA to exempt early-stage drugs from GMP regulations

The Food and Drug Administration (FDA) has amended §210.2 (21 CFR 210.2) to exempt most Phase 1 investigational drugs from complying with the 'good manufacturing practice' (GMP) requirements in parts 210 and 211 (21 CFR Parts 210 and 211), to be effective from 15th September, 2008. The exemption shall not apply to investigational drug products manufactured by, or for, a sponsor and available for use in Phase 2 or 3 studies and used in any subsequent Phase 1 study by the same sponsor. Even though part 211 shall be disapplied for certain drugs, the drugs shall still be subject to section 501(a)(2)(B) of the 'Federal Food, Drug and Cosmetic Act' (FDCA). Such drugs include recombinant and nonrecombinant therapeutic products, vaccine products, allergenic products, *in vivo* diagnostics, plasma derivative products, blood and blood products, gene therapy products and so forth, which are all subject to the GMP requirements contained in section 501(a)(2)(B) FDCA.

The FDA states that it has taken this action to focus a manufacturer's effort on applying

GMP that is appropriate and meaningful for the manufacture of the earliest stage investigational drug products intended for use in Phase 1 clinical trials while ensuring safety and quality. The FDA hopes this will streamline the drug development process.

The FDA provides several reasons to justify this exemption. First, investigational drugs remain subject to section 501(a)(2)(B) FDCA which stipulates that a drug is adulterated if 'the facilities or controls used for, its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practices to assure that such drug meets the requirements as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess'.

Secondly, the FDA continues to oversee the investigational drugs used in Phase 1 trials through its existing authority. Information must be submitted informing the FDA of the steps that the manufacturer is taking to ensure the safety and quality of the investigational drug. Moreover, the FDA has various powers: it can place the investigational drug on clinical hold if the study subjects are exposed to unreasonable and significant risk; and it can terminate the trial if methods, facilities and controls used for manufacturing, processing or packaging are inadequate to establish and maintain appropriate standards of identity, strength, quality and purity as needed for subject safety. Consequently, the FDA retains the ability to take appropriate actions to address manufacturing issues, for instance to initiate an action to seize an investigational drug.

Thirdly, the FDA believes that many of the issues presented by investigational drugs in Phase 1 trials are different to larger Phase 2 or 3 trials. Many of the requirements contained in the part 211 regulations do not apply to the conditions under which many of the investigational drugs for use in Phase 1 clinical trials are produced. For instance, concerns underlying the regulations' requirement for a

fully validated manufacturing process, rotation of the stock for drug product containers, the repackaging and relabelling of drug products, and separate packaging and production areas are generally not concerns in Phase 1 trials.

This rule shall affect drug manufacturers, chemical manufacturers and laboratories that manufacture drugs on a small scale for use in Phase 1 trials. The FDA anticipates that the rule should reduce the documentation created by drug manufacturers that produce in-house investigational drugs, and, in some cases, should reduce the amount of component and product testing. Some chemical manufacturers and laboratories that do not supply the pharmaceutical industry may, however, experience a slight increase in documentation if they have not written standard operating procedures or if they need to modify existing methods of documentation. Nevertheless the rule should not require more information than is already collected as part of standard laboratory practices.

Overall the FDA anticipates that the impact shall be negligible on companies, potentially even reducing the compliance burden for some. While exempting products from part 211, the FDA has produced companion guidance clarifying on how to manufacture Phase 1 investigational drugs under GMP which, in its opinion, do not include recommendations that would increase the burden of compliance on such companies.

FDA plans for national electronic health information surveillance system

The FDA has announced plans for a national electronic health information surveillance system to track the performance and safety of medical products once they are on the market (<http://www.fda.gov/oc/initiatives/advance/sentinel>). The Centers for Medicare and Medicaid Services announced similar proposals to share prescription drug claims data for Part D Medicare enrollees with other government agencies. Although the specific details of the plan have not been finalised, the so-called 'Sentinel System' would provide the

FDA with access to a broad range of publicly and privately maintained health data sources.

The Sentinel system has been under consideration for some time. Health and Human Services Secretary Mike Leavitt asked the FDA to explore launching such a programme back in 2005, the Institute of Medicine recommended the institution of such a programme in 2006, and Congress passed legislation in autumn 2007 that required the creation of a drug-monitoring programme.

It has been reported that Sentinel will allow access to data from more than 25 million Medicare drug benefit beneficiaries (*Washington Post*, 23rd May, 2008), and there have been discussions with private insurers about allowing their data to be included in Sentinel. Wellpoint has said it plans to contract with the FDA to provide such data, possessing 35 million members itself (*Bloomberg/Boston Globe*, 23rd May, 2008).

Currently the FDA uses voluntary self-reporting to discover adverse reactions that, according to the *Los Angeles Times*, reveal an estimated 1–10 per cent of problems with drugs and medical devices. In addition to improving detection of adverse reactions, it is hoped that the scheme will help reduce the \$900m spent on treat outcomes of adverse drug events each year.

There are potential problems with the proposed Sentinel system. Most importantly, Medicare collects data only when a doctor, hospital or other medical provider is seeking payment. These are called ‘claims data’ which are far less accurate than actual patient health records. Moreover, sometimes patients suffer problems after receiving drugs because they are unwell, not because the drugs are to blame. A further problem lies in the fact that Medicare beneficiaries use an average of 28 prescriptions in a year, compared with an average among all Americans of 16 prescriptions. Sorting out which medicine caused any single problem could be difficult in these circumstances. Finally, there are some concerns within the pharmaceutical industry that the analysis of data will not be as rigorous as a clinical trial.

PRODUCT LIABILITY

Riegel v Medtronic, Inc.

In the Riegel decision (20 February 2008), the Supreme Court readily held that the express pre-emption provision of the Medical Device Amendments to the FDCA pre-empts state law claims seeking damages for injuries caused by medical devices that received ‘premarket approval’ (PMA) from the FDA. In a marked contrast to the fractured *Medtronic, Inc. v Lohr*, 518 US 470 (1996) decision involving the same pre-emption statute and a 510(k)-cleared device, seven justices joined the majority opinion, authored by Justice Scalia, while Justice Stevens wrote a short concurrence and Justice Ginsburg was the sole dissenter. It is safe to say Riegel is a landmark decision that flatly rejected the small number of minority view cases involving PMA devices.

In Riegel, the court first concluded that FDA’s PMA imposes ‘specific requirements applicable to a device’, and that federal law forbids manufacturers from deviating from FDA-approved ‘design specifications, manufacturing processes, labelling, or any other at-tribute.’ It also concluded that common law negligence and strict liability claims impose state ‘requirements’ as that term is ordinarily understood when used in pre-emption statutes, and that the Riegel plaintiff’s tort claims were pre-empted because they sought to impose state requirements on the relevant medical device that were ‘different from, or in addition to’, the federal requirements.

At the same time, the court was careful to note the limits of Riegel – namely, that the case did not present claims in which the state duties were ‘parallel’ to, rather than different from, or in addition to, federal requirements. Given that many plaintiffs frame their allegations precisely this way – as mirroring rather than supplementing federal requirements – further litigation over the scope of this theoretical pre-emption ‘exception’ is likely.

Apart from the ‘parallel’ claim exception, Justice Ginsburg’s dissent includes a footnote that plaintiffs also may try to exploit. Footnote 1 of her dissent states: ‘The court’s holding does not reach an important issue outside the bounds of this case: the pre-emptive effect of § 360k(a) where evidence of a medical device’s defect comes to light only after the device receives premarket approval’. Plaintiffs undoubtedly will argue that the circumstances of their cases fit within this footnote and that pre-emption thus does not apply. If taken at face value, Justice Ginsburg’s footnote would swallow the court’s holding, given that covered medical devices cannot be sold before PMA is granted, and allegations of product defect ordinarily would only crop up after approval. The majority opinion, however, contains no indication that the express pre-emption clause is without force in a case where the ‘defect comes to light only after premarket approval’. The facts of Riegel itself also undermine this assertion, in that the plaintiff’s allegations were that the FDA granted PMA to the device in question, and then the device malfunctioned during an operation on plaintiff; the plaintiff did not contend that the manufacturer (or the FDA) knew of a device ‘defect’ prior to PMA. Ultimately, this passing comment in dissent should merit little deference or attention.

Other aspects of the majority opinion also are interesting. To begin with, the court made no mention of the Circuit split that its decision resolved, citing neither majority view cases – save the Second Circuit’s decision under review – nor the minority view case, *Goodlin v Medtronic, Inc.*, 167 F.3d 1367 (11th Cir. 1999). Since the court seemingly viewed the issue as a relatively straightforward statutory construction exercise, there certainly was no need for it to rely on or address any of the circuit level decisions. At the same time, the majority view pre-emption cases contain a wealth of analysis and involve application of the pre-emption statute in various circumstances, and some discussion of them would not have been out of place.

In addition, the majority opinion made no mention of the ‘presumption against pre-emption’, a concept discussed only by Justice Ginsburg in her dissent. As Justice Ginsburg noted, some of the court’s earlier cases have stated that in divining Congressional intent regarding preemption, the analysis ‘starts with the assumption’ that pre-emption was not intended. If the presumption against pre-emption is viewed, however, as a principle of statutory construction that comes into play only when the statutory language is ambiguous – and does not when the Congressional intent to pre-empt is ‘clear and manifest’ – the court’s silence is less mysterious. The majority found nothing ambiguous about the MDA’s express pre-emption provision, and viewed the plain statutory language as ample proof of Congressional intent.

The court was also seemingly not troubled by arguments premised on 21 C.F.R. § 814.39. Plaintiffs argue that this regulation gives manufacturers room to freely revise their labels and deviate from the warning language mandated through the PMA process. In fact, the Solicitor General addressed this issue, including in a supplemental letter to the court in January 2008, that attached a proposed rule to amend 21 C.F.R. § 814.39(d) and clarify the ‘agency’s longstanding view’ that manufacturers have no discretion to implement changes without the FDA’s consent. In the end, plaintiff’s arguments about the meaning of 21 C.F.R. § 814.39 went entirely unmentioned. The court instead cited to 21 C.F.R. § 814.39 for the proposition that applicants who wish to deviate from FDA-mandated requirements must obtain FDA approval for a PMA supplement detailing the change.

The Riegel decision was issued just over two months following the oral argument, which was held on 4th December, 2007. Some of the questions posed by the Justices during the argument foreshadowed the opinions about whether juries engage in the same kind of balancing inquiry undertaken by the FDA

during the PMA process, and how the medical device approval process and pre-emption inquiry differ from those applicable to drugs.

In terms of what Riegel may indicate for future life sciences pre-emption cases, it is safe to assume that medical device product liability plaintiffs will attempt to position their claims as relying on standards that simply 'parallel' federal requirements, even when they in fact are not. Existing majority view authorities do provide some help in dealing with supposedly 'parallel' allegations, however. For example, in *McMullen v Medtronic, Inc.*, 421 F.3d 482, 488-89 (7th Cir. 2006), the court examined whether plaintiff's state law claims were the 'genuine equivalent' of the FDA-imposed federal requirements, concluded they were not actually parallel, and upheld express pre-emption.

In other cases, such as the Second Circuit's opinion in *Riegel v Medtronic, Inc.*, 451 F.3d 104, 123 (2d Cir. 2006), as well as *Gilleon v Medtronic, Inc.*, 2002 WL 31300694 (N.D. Cal. 2002), and *Carey v Shiley, Inc.*, 32 F. Supp. 2d 1093, 1106-07 (S.D. Iowa 1998), courts have recognised that any 'parallel' exception to express pre-emption is narrow, applying only where the defendant's alleged noncompliance resulted in a device physically different from the one the FDA approved, or with labelling other than what the FDA approved. If a plaintiff's allegations depend on supposedly 'parallel' duties falling outside these narrow areas, implied pre-emption principles and *Buckman Co. v Plaintiffs' Legal Comm.*, 531 US 341, 352 (2001), may have application. See *Cupek v Medtronic, Inc.*, 405 F.3d 421, 424 (6th Cir. 2005) (claims that manufacturer should have recalled product earlier and failed to comply with specified reporting and other federal regulations were 'disguised fraud on the FDA' claims and pre-

empted); *Webster v Pacesetter, Inc.*, 259 F. Supp. 2d 27, 36, 39 (D.D.C. 2003)

(allegations that defendant failed to properly investigate and report to the FDA did not support warning or fraud claims but rather were pre-empted under Buckman).

Furthermore, the FDCA contains a 'no private right of action clause', 21 U.S.C. § 337(a), which also limits plaintiffs' ability to sue directly for alleged FDCA violations. See *Kemp v Medtronic*, 231 F.3d 216, 235-36 (6th Cir. 2000) (noncompliance claims violate no private right of action clause).

Finally, since the majority was careful to adhere closely to the MDA express pre-emption statute, on the surface the case has limited application to the prescription drug context that rests on different pre-emption principles. Some aspects of Riegel nevertheless may have significance outside the medical device context. In statements made by the court not relevant to the immediate decision, the majority stated that because the FDA's position on pre-emption has changed over time, the agency's position might only warrant a reduced amount of deference. Since plaintiffs argue that the agency's position on pre-emption in the drug context likewise has changed over time, arguments regarding reduced deference may resurface in the Supreme Court's other pre-emption cases. On the other hand, even the sole dissenter, Justice Ginsburg, made seemingly positive references to implied conflict pre-emption, arguing that 'a medical device manufacturer may have a dispositive defence if it can identify an actual conflict between the plaintiff's theory of the case and the FDA's' approval requirements, even as she rejected express pre-emption.

© Reed Smith