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Introduction

Welcome to the 2012 edition of our Life Sciences and Healthcare e-zine.

I am the Consultant of the Clinical Advisory Group here at William Fry and work alongside associates Sinéad Keavey, Aimée Lenehan, Mark O'Shaughnessy, and solicitor Ruth Finnerty. We specialise in advising healthcare professionals on their practice, including the defence of claims and at disciplinary hearings. There are reports at the moment that the Government is considering ways of reducing costs in medical negligence cases. In this edition, Aimée Lenehan and I look at the proposals understood to be before the Government and highlight a number of alternative cost-saving measures already in place.

Also included in this edition are updates on developments of interest in the IP, competition law and regulatory fields, including reports on a number of decisions of the European Court of Justice. We also continue to update you on life sciences transactions in which William Fry has advised and in this regard we include a report on BioMarin's acquisition of Pfizer's plant in Co Cork, making it the first time the company has located biopharmaceutical production outside of the United States.

We hope you find this e-zine informative. If you have any queries or comments, please let me or your usual William Fry contact know.

Margaret Muldowney
Consultant

Acquisition of Pfizer Plant by BioMarin

William Fry advised BioMarin Pharmaceutical Inc in relation to its acquisition of Pfizer's Shanbally plant in Cork. BioMarin plans to occupy the Shanbally plant in a phased transition pending results of its ongoing clinical study for a treatment for MPS IVA, also known as Morquio A Syndrome.

BioMarin, which was founded in 1997, develops and commercialises innovative biopharmaceuticals for patients with severe and/or life-threatening diseases. Since its inception, the company has received approval for four breakthrough products. BioMarin is headquartered in Novato, California, with subsidiary offices in the United Kingdom, Europe, Latin America, the Middle East, and Asia Pacific.

BioMarin completed its purchase of the Shanbally plant in August 2011. The acquisition of the Shanbally plant will greatly expand BioMarin's manufacturing capacity and is the first time the company has located biopharmaceutical production outside of the United States.

William Fry advised BioMarin on all aspects of the asset purchase, including in relation to the corporate, property and environmental aspects of the transaction.

Contributed by: Laura Dunne

Proposal for a Medical Injuries Assessment Board

Last year reports were that the Government was considering proposals to allocate responsibility for the assessment of damages in medical negligence claims to a state body, rather than having such issues fought through the courts. No decision has yet been made by the Government.

If implemented, it is estimated that these radical proposals would save the State up to €50 million over three years and would remove delays in medical negligence cases.

Little detail is available, but reports suggest that either a medical injuries assessment board, similar to the Injuries Board, would be set up, or the task of assessing damages would be given to the Injuries Board. Major savings have already been achieved by the Injuries Board in personal injuries actions.

If the proposed new entity is to deal solely with the assessment of damages in medical claims, the potential to reduce costs and save time could be limited. While in some instances it is clear from the outset that liability is not really an issue, for the most part medical negligence claims require a detailed analysis of the patient's allegations, with the input of expert opinion, before a decision can be made to defend or settle.

Assessing damages, including for example future care costs and loss of earnings, is a complex and time consuming part of a significant number of medical negligence claims. However, many cases do not include claims for such damages.

Reform of the system is needed. Nonetheless, a number of initiatives in the last decade have introduced strategies to significantly reduce the length and expense of these actions. Such initiatives include:

- **The Civil Liability and Courts Act 2004:** The Act reduced the time within which a claimant can sue; set deadlines for the filing of pleadings; and provided the option of mediation. The objectives of the Act included the saving of time and reduction of costs.
- **The Working Group on Medical Negligence and Periodic Payments:** The Working Group was established by the President of the High Court on 18 February 2010. In its first report in October 2010, it recommended a facility for periodic payment orders. These recommendations have not yet been implemented. The Group is now looking at the conduct of medical negligence claims in order to identify shortcomings and improve the system. As with its first report we can expect that the Group will look to the "UK experience". The UK has a pre-action protocol to resolve claims without resorting to litigation, or at least at an early stage in the proceedings. The protocol encourages openness when something has "gone wrong" with a patient's treatment. It sets strict timelines for the delivery of medical records, the issuing of proceedings, and the exchange of expert reports. It also sets out best practice for handling complaints.
- **Mediation:** This is not suitable in every claim but should not be overlooked as an effective method for reducing costs and time spent in litigation.
- **The State Claims Agency:** The Government empowered the State Claims Agency (SCA) in 2002 to handle the defence of clinical claims against public and voluntary and certain private hospitals. This has resulted in significant savings as it avoids the need for multiple insurers and lawyers. The SCA has its own dedicated team of experienced claims handlers to advise on such claims, including advising on the assessment of damages.

Further change is needed and, given the current fiscal environment, is to be expected and welcomed. However, further reductions in costs and delays can be achieved by utilising fully the strategies already available to practitioners, of which the above are but a few examples. It remains to be seen whether the establishment of a medical injuries assessment board, and in respect of which it has to be emphasised there is little available detail, in itself, would achieve the twofold objectives of the exchequer.

Contributed by: Margaret Muldowney; Aimée Lenehan

European Court Rules on Patentability of Stem Cells

The EU's top court has decided that, for the purposes of patent law at least, human life begins at fertilisation.

The European Court of Justice made its ruling in a reference from a German court on the interpretation of the EU Biotechnology Directive. The reference was made in proceedings brought by Greenpeace seeking the annulment in Germany of a patent held by Professor Dr Brüstle, a director of the Institute for Reconstructive Neurobiology at Bonn University. Dr Brüstle's patent related to neural precursor cells, the production of such cells from embryonic stem cells, and the use of such cells for the treatment of neurological conditions. Greenpeace grounded its case for annulment of the patent on the Biotechnology Directive which excludes from patentability "*the uses of human embryos for industrial or commercial purposes*".

The European Court was asked to interpret the concept of the "human embryo" for the purpose of ascertaining the scope of the prohibition on patentability. Focusing on the commencement of the process of development of a human being, it held that the concept includes: (i) a human ovum after fertilisation; (ii) a non-fertilised human ovum into which the nucleus from a mature human cell has been transplanted (i.e., a clone); and (iii) a non-fertilised human ovum the division and development of which has been stimulated by artificial means. The Court noted that while the latter two types of organism have not, strictly speaking, been the object of fertilisation, they are nevertheless capable of commencing the process of development of a human being.

Dr Brüstle's patent concerned stem cells obtained from a human embryo at the blastocyst stage (i.e., the stage the embryo reaches five days after fertilisation). The European Court left it to the German Court to decide whether such cells are capable of commencing the process of development of a human being and so fall within the concept of a "human embryo" for the purposes of the Directive.

Moreover, the European Court held that the use of human embryos for scientific research falls within the prohibition on the patentability of embryos used for industrial or commercial purposes. The grant of a patent, it stated, implies its industrial or commercial application. The only exception to the prohibition on patentability is the use of the embryo for therapeutic or diagnostic purposes which benefit the embryo itself.

Finally, the Court concluded that an invention cannot be patented where the implementation of the invention requires either the prior destruction of human embryos or their use as base material, even if the application for the patent does not mention the use of embryos. The fact that the destruction of the embryos may have occurred at a stage long before the implementation of the invention is irrelevant.

The decision has been welcomed by those opposed to stem cell research. However, others have expressed concern about the potential adverse effect it may have on medical and scientific research in the EU. Investors may decide to invest in a jurisdiction where there are fewer, or less stringent, restrictions on the patenting of stem cells, such as America or Asia. Researchers may decide to base themselves in a jurisdiction where they can capitalise on their research by patenting it. While stem cell treatments can still be developed in the EU outside the patent system on a non-commercial basis, the attraction to investors and researchers of a jurisdiction offering patent protection cannot be underestimated.

Contributed by: John Magee

The Highs and the Lows – What Happens When Drug Patents Expire?

A drug which is protected by a patent may not be copied for a certain period of time (usually 20 years). After this period of time, the market is opened to cheaper generics and the former patent holder inevitably faces a dramatic reduction (possibly up to 80%) in sales revenue. Jobs can be lost and the local community and wider economy can also suffer.

The active ingredient in Lipitor, the best selling prescription drug in history, is produced here by Pfizer. Lipitor came off patent protection in the US in November 2011 and Irish patent protection is due to

expire in May of this year. Sanofi's blood thinning drug Plavix is also to lose its protection this year, while Eli Lilly's anti-psychotic drug Zyprexa came off patent in April 2011.

The pharmaceutical sector is hugely important to the Irish economy. It employs over 24,500 people directly and almost the same number indirectly. It accounted for €56.8 billion of exports in 2010, representing 63.55% of our total merchandise exports. Furthermore, it has invested over €7 billion in the State in the last ten years and pays the Exchequer almost €3 billion in taxes on an annual basis.

Given the importance of the sector to our economy, it is no surprise that concerns have been raised about the potential impact of what is known in the industry as the "patent cliff". Many fear that drug companies may close their manufacturing bases here as generic producers in India and China take over production. Even if drug companies continue to manufacture in Ireland, the export value of the drugs produced will be significantly reduced. While it is true that the "man on the street" will have access to cheaper medicines, this may come at a significant cost to the broader economy.

The more optimistic amongst us, however, take the view that drug companies will rise to the challenge and seek alternative sources of revenue through the development of new markets and specialised products. In the US, for instance, when Lipitor lost its patent protection, Pfizer responded by setting up a direct mail service and implementing discounts and incentives for patients, insurers and companies that process prescriptions. Such incentives were designed to ensure that Lipitor would be as cheap, if not cheaper, than the generics. Pfizer is itself manufacturing a generic version of the drug, Atorvastatin, and distributing it through another company, Watson Pharmaceuticals.

While manufacturing facilities located in Ireland may be closed in the coming years and jobs may be lost, the Irish Pharmaceutical and Healthcare Association expects that new jobs may be created by an increase in the number of clinical trials conducted in Ireland. Undoubtedly, our 12.5% corporation tax rate, dubbed Ireland's "oil" by our Minister for Finance, coupled with decreasing labour costs, an educated workforce and a Commercial Court renowned for its speedy resolution of patent disputes, will continue to draw the large drug companies to our shores.

Contributed by: Mary Drennan

Name of Repackager Not Required on Pharmaceuticals

The European Court of Justice has ruled that it is not necessary to include the name of a repackager on repackaged pharmaceuticals. The preliminary ruling was delivered in joined trade mark infringement proceedings referred to the European Court by the Danish courts.

The pharmaceuticals at issue in the main proceedings were manufactured by Merck Sharp & Dohme, which also held the trade marks rights in the goods. The pharmaceuticals were imported into Denmark by two parallel importers authorised to market and sell the goods there. These "marketing authorisation holders" then outsourced the repackaging of the pharmaceuticals to group companies. However, the repackaging was stated to have been carried out by the marketing authorisation holders. Merck challenged, before the Danish courts, the practice of not naming the repackager on the packaging of the pharmaceuticals, alleging that it infringed its trade mark rights. The Danish courts then asked the European Court for guidance on the correct interpretation of the relevant provisions of the EU Trade Mark Directive.

The Directive provides that trade mark rights are exhausted when a trade marked product is put on the market in the EU with the trade mark owner's consent. However, such rights are not exhausted where there are legitimate reasons for a trade mark owner to oppose further commercialisation of the goods in question.

The Court found that the lack of the name of the repackager on pharmaceuticals is not a legitimate basis to oppose further commercialisation. It stated that as the marketing authorisation holder is the entity with ultimate responsibility for repackaging, it is sufficient, from a consumer protection perspective, that the name of this entity be provided. The interests of the trade mark owner are safeguarded as he/she can enforce his/her rights directly against the marketing authorisation holder. Further, the use of the name of the marketing authorisation holder avoids giving consumers the impression that the goods have been repackaged by the trade mark owner.

While the decision provides clarity on the rights of trade mark owners as regards repackaged pharmaceutical goods, it was not an unexpected or surprising ruling. It is in line with the industry norm that a marketing authorisation holder is ultimately responsible for the actions of the repackager it authorises to repackage imported goods.

Contributed by: David Cullen; John Magee

European Court Decision Underlines Strict Approach to Bans on Internet Sales

In the recent *Pierre Fabre* case, the European Court of Justice ruled that a clause in a selective distribution agreement banning the online sale of cosmetics breached Article 101 of the Treaty on the Functioning of the European Union (TFEU). This decision confirms that an absolute ban on internet sales contravenes EU competition rules unless it can be objectively justified.

The French company, Pierre Fabre Dermo-Cosmétique SAS (Pierre Fabre), used a selective distribution system which required sales of certain cosmetics and personal care products to be made in the presence of a qualified pharmacist. This effectively banned internet sales of the products by resellers. The French Competition Authority condemned the ban as contrary to competition law and imposed a fine of €17,000 on Pierre Fabre.

Pierre Fabre appealed to the Paris Court of Appeal which subsequently made a preliminary reference to the European Court asking it to consider the legality of internet sales bans in selective distribution agreements.

The European Court confirmed that a ban on internet sales in a selective distribution network amounts to a restriction of competition contrary to Article 101(1) TFEU. The Court acknowledged that a ban could be justified in an appropriate case if it had a legitimate aim and the restriction went no further than was objectively necessary. However, potential justifications are strictly reviewed. The Court disagreed with Pierre Fabre that the ban in question was necessary to protect consumers stipulating that in a previous case it had dismissed as a valid justification the need to advise customers on the use of non-prescription medicines. The Court also noted that Pierre Fabre had failed to demonstrate to the French Competition Authority in what way 'face to face' contact with a pharmacist would protect customers, particularly since any negative effects of the relevant product would only become apparent after use and in this event the customer would generally consult a doctor. Further, the Court also held that the protection of a prestigious brand image does not justify a restriction on competition.

The Court went on to consider whether an internet sales ban could benefit from the EU block exemption for vertical agreements (VBE). The VBE exempts selective distribution agreements from the application of Article 101(1) TFEU. However, the exemption does not extend to restrictions on sales to end users by members of a selective distribution system operating at the retail level of trade. Accordingly, the Court held that restrictions on internet sales to consumers are similarly excluded from the protection of the VBE. On the other hand, the VBE does allow for the possibility of prohibiting a distributor from operating out of an unauthorised place of establishment. However, the Court declined to characterise an internet sales ban as equivalent to a prohibition from operating out of an unauthorised place of establishment within the meaning of the VBE.

Although the French Competition Authority previously found that Pierre Fabre had failed to demonstrate that it could benefit from an individual exemption under Article 101(3) TFEU, the European Court did not have adequate information to consider the point and ultimately it will be for the Paris Court of Appeal to examine whether the conditions for an individual exemption are satisfied.

The *Pierre Fabre* case serves as a reminder of the strict approach to bans on internet sales. Competition law does not outlaw such a ban where, for example, it is necessary for the protection of the health and safety of the users of a potentially dangerous or complex product. However, maintaining a prestigious image is not a legitimate aim for restricting competition and manufacturers should be alert to the risks of seeking to protect brand profile through the prevention of online sales.

Contributed by: Cormac Little

Supplementary Protection Certificates: A Positive Spin on a Negative Term

A recent decision of the European Court of Justice provides welcome news for the manufacturers of paediatric medicines. The decision was delivered in a case concerning the duration of supplementary protection certificates (SPCs), which can extend patent protection for medicinal products by up to five years. Once a patent is applied for, it begins to expire. However, medicinal products cannot be commercialised until the patent holder receives marketing authorisation, a process that can take up to 15 years. Where certain conditions are met, an SPC extension is granted in order to compensate pharmaceutical companies for the loss of patent protection pending marketing authorisation. The term of an SPC is the period of time from patent application to the grant of marketing authorisation less five years, and subject to a maximum term of five years. A 2006 EU Regulation introduced a six month extension to the SPC period in order to encourage patent holders to conduct research into medicinal products for paediatric use. The “paediatric extension”, as it is known, may only be granted to the holder of an SPC.

Merck Sharp & Dohme challenged the German Patent Office’s refusal to grant an SPC for the drug Januvia, which is used in the treatment or prevention of diabetes. The period between the date of grant of the patent for Januvia and the date of the grant of marketing authorisation was less than five years, which meant that the term of any potential SPC would be a negative term. However, Merck sought the SPC to allow it to apply for the paediatric extension.

The German Federal Patent Court referred the matter to the European Court of Justice for clarification. The Court noted that the pre-conditions to the grant of an SPC do not require that the SPC be of a positive duration. It also noted that while an SPC of a negative duration serves no purpose of itself, it may be of use to the holder of a basic patent who wishes to apply for the paediatric extension. The refusal of an SPC can thus jeopardise the objectives of the paediatric extension, namely to compensate the effort made to evaluate the paediatric effects of the medicinal product at issue. As the paediatric extension may be of benefit where the negative duration of the SPC is not more than six months, it follows that the grant of an SPC cannot be refused by reason only of the fact that its duration is not positive.

The Court also held that where the duration of an SPC is negative, it cannot be rounded to zero. It is only in the case where the period between lodging the basic patent application and the date of the first marketing authorisation is exactly five years that an SPC can have a duration equal to zero. Where the SPC is negative, the date the paediatric extension starts to run is determined by deducting from the patent expiry date the difference between five years and the duration of the period which elapsed between the lodging of the patent application and the grant of the first marketing authorisation.

The decision is a positive development for both patent holders and paediatric medicine in general as it rewards the efforts of those involved in evaluating the paediatric effects of medicinal products. It also provides welcome clarification as regards the duration of SPCs and the paediatric extension.

Contributed by: Mary Drennan

Pharmaceutical Regulatory News

Legislation to Provide for Generic Substitution of Prescribed Drugs and Medicines

The Government is expected to introduce legislation providing for a system of reference pricing and generic substitution for prescribed drugs and medicines under the General Medical Services (GMS) scheme and community drug schemes. The Department of Health has confirmed that it is preparing the Health (Pricing and Supply of Medicines) Bill which is due to be published this year. The Bill is intended to promote price competition among suppliers and to increase the scope for savings for patients through the greater use of generic medicines.

Biosimilar Guidelines Overhaul

The European Medicines Agency has recently published a concept paper recommending a review of its guideline on Similar Biological Medicinal Products published in 2005. The paper advises that the guideline should be revisited in light of how biosimilars are currently being developed. The concept paper identifies a number of issues for consideration including:

- whether the principles of biosimilarity should be clearer
- whether a definition of “biosimilar” should be introduced as the term is often used in an inappropriate way
- the equivalence of efficacy and safety aspects
- the possibility of having the same pharmaceutical form, strength and route of administration for biosimilar products and reference medicinal products
- the utility of the current guideline lists of references, some of which are outdated

Once feedback is received on the concept paper, a revised draft guideline is expected to be released later in the year for further consultation.

European Medicines Agency: Electronic Submission of Information on Medicines

The European Medicines Agency’s new system of electronic submission of information on medicines is being introduced on a phased basis. The purpose of the new initiative is to create a list of all medicines authorised and registered in the EU, to identify medicines accurately and to strengthen the EU safety monitoring system for medicines.

The first phase was the publication in July 2011 of the format for the notification of the electronic submission of medicinal product information. The format lists all of the data elements required. The format was updated in September 2011 to include the XML Schema Definition (XSD) for the individual data elements.

Phase two involved electronic submission by marketing authorisation holders using tools developed in-house by pharmaceutical companies or software vendors. It is expected that by the end of January 2012 marketing authorisation holders will be able to use data-entry and submission tools provided by EMA.

Phase three involves EMA, with the assistance of a contractor, processing and validating the information submitted to ensure that it is accurate and up to date.

It is intended that the final phase will be carried out in 2014 and will involve updating the July 2011 notification format in line with the International Organisation for Standardisation (ISO) Identification of Medicinal Products standards. Marketing authorisation holders will not be required to resubmit data previously provided, but may be asked to provide updates based on additional ISO data elements not included in the July 2011 format.

Contributed by: Mary Drennan; John Magee