

C/M/S/ Cameron McKenna

A Year in Pharmaceuticals – 2008

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A Year in Pharmaceuticals

New ABPI Code of Practice for Pharmaceutical Industry

More detailed requirements for pharmaceutical companies' relationships with patient groups and health professionals were incorporated into this year's revision of the ABPI *Code of Practice for the Pharmaceutical Industry* (the Code). Many of the changes relate to even greater transparency, bringing with them an increase in documentation.

The main change affecting representatives is an increase in guidance about the way that pharmaceutical companies interact with healthcare professionals (HCP). Every time a pharmaceutical company wishes to engage the services of a HCP, the details of the arrangement need to be outlined in a written agreement and although HCPs may still be used as consultants and advisers, there must be a legitimate need for the services and the basis on which they are to be paid must be properly documented.

As well as additional guidance on meetings and hospitality, therapy reviews and the provision of samples, the guidance states that declarations of sponsorship and details of grants to healthcare organisations must now accurately reflect the company's involvement; any financial support is to be for the benefit of patient care or the NHS, or for research. In addition to stating that details of any grants to healthcare organisations are now to be documented and recorded, the Code also suggests that companies might like to publicly declare when they make grants and ask the healthcare organisation to declare when support has been received. It has yet to be seen whether this will result in lists of grants being seen on company, hospital and PCT websites.

In the context of engaging the services of a HCP, companies will need to give careful consideration to the need for the service and in particular to the nature of the service. Careful scoping of projects in the context of the new provisions is likely to lead to more consideration of the practicalities of the relationship between the parties.

New Civil Sanctions for Lifesciences Companies Operating in the UK

The Regulatory Enforcement and Sanctions Act 2008 (RESA) came into force on 22 July 2008 with the key objective of allowing regulators to respond to cases of non-compliance in a more flexible, effective and proportionate manner. The provision for new civil sanctions to be imposed is likely to have significant regulatory compliance implications for lifescience companies or individuals operating in the UK in the medicines, medical devices and diagnostics sectors, and also for human tissue establishments.

RESA requires regulators granted the new powers to prepare and publish guidance about how the sanctions will be used and about how the offence to which the power in question relates is enforced. They will also be required to act in accordance with principles of transparency, accountability, proportionality and consistency and to target only cases in which action is needed.

If Ministers choose to exercise their powers in relation to UK lifesciences legislation, RESA could supplement the current enforcement powers of the MHRA and the HTA, amongst other UK regulators. These new civil sanctions would allow the MHRA and the HTA to tackle non-compliance by way of civil rather than criminal sanctions in cases where the regulator is satisfied that the person/company in question would be liable to be convicted (or in the case of "stop notices" where the regulator reasonably believes an activity presenting a serious risk of causing serious harm to human health, amongst other matters, is likely to be carried on by the person/company and is likely to involve the committing of a relevant offence).

Outcome of PPRS Negotiations

December 2008 saw the publication of the new Pharmaceutical Price Regulation Scheme (PPRS) which started on 1 January 2009. This follows the early termination of the 2005 PPRS after the upheaval of the GSK case which determined that the 2005 PPRS had the status of a contract and the OFT's 18-month study into the overall system. The new scheme is much more detailed than the 2005 PPRS, will run for a minimum of five years and will be non-contractual. The scheme aims to ensure that more patients will benefit from a wider range of innovative medicines at a fair price to the NHS and that patients will have faster access to new medicines that are clinically and cost effective.

The cost of drugs sold to the NHS will be decreased by 3.9 % in February 2009 and a further price cut of 1.9% will be introduced in January 2010. It is anticipated that, subject to discussion with the parties affected, generic substitution will be introduced from January 2010. The PPRS is accompanied by a detailed statutory scheme which applies where a company chooses not to rely on the PPRS. This has similar levels of price cut, but it will not be possible for companies to modulate price cuts across a portfolio of products.

Companies will need to come to grips with the new regime and there may be some migration between the voluntary and statutory schemes. The focus of ABPI and Department of Health negotiations will now shift to the mechanism for generic substitution to take effect from the start of 2010.

Stock Management of Pharmaceuticals

On 16 September 2008 the European Court of Justice (ECJ) ruled, in a case involving the Greek subsidiary of GSK, that dominant pharmaceutical companies cannot refuse to meet ordinary orders from wholesalers in order to limit parallel exports by those wholesalers. The ECJ case stemmed from a reference from the Athens Court of Appeal for a preliminary ruling on the application of Article 82 EC Treaty, which prohibits the abuse of a dominant position.

The ECJ held that, in principle, activity of this type can be an abuse of a dominant position on the relevant market for medicinal products. On the other hand, the ECJ held that it would be permissible for a dominant supplier to refuse to honour extraordinary orders, since this would be a reasonable and proportionate protection of its commercial interests. The ECJ left it to national courts to determine what would be regarded as 'ordinary' or 'extraordinary'.

The issue of what amounts to an "ordinary" or "extraordinary" order by a wholesaler has now been "federalised" by the ECJ i.e. left to national courts to decide. It is quite possible that the practice in different national courts will diverge and make stock management schemes more difficult to operate.

Patentability of Dosing Regimes, Gene Sequences and Stem Cells

2008 saw a number of significant decisions concerning the patentability of various pharmaceutical and biotech product development, including dosing regimes, gene sequences and stem cells.

a Dosing Regimes (*Actavis UK Limited v Merck & Co Inc*)

The Court of Appeal handed down a significant judgment in the case of *Actavis v Merck* in May 2008, ruling that a Swiss form claim for the use of a pharmaceutical in the manufacture of a medicament could be allowed even where the novelty lay only in a new dosing regime. Emphasising the importance of taking an approach consistent with that of the EPO where such claims are treated as novel, and not as claims to a method of administration, the Court rejected arguments that it was bound not to allow such a claim on the basis of the Court of Appeal judgment in *Bristol-Myers-Squibb v Baker Norton* and applied the cases of *Eisai (1985)* and *Genentech (2006)*.

The case provides a more consistent approach to patentability of Swiss claims across the European Patent Convention countries, and will improve the prospects of

pharmaceutical companies seeking to obtain patent protection in the UK for new applications of known substances.

b Gene Sequences (*Eli Lilly v Human Genome Sciences*)

In August 2008, the High Court held that a patent for a gene sequence and protein was invalid for lack of industrial applicability, as well as insufficiency and obviousness. Since the protein's precise function was not known at the priority date of the patent, which claimed a protein and the nucleotide coding it, the patent specification set out a list of putative uses, based on known uses of other members of the TNF ligand superfamily.

This case illustrates the difference between mechanical inventions, where satisfying the industrial applicability requirement for patentability is usually straightforward, and biotech inventions where the industrial applicability of a particular gene sequence may not necessarily be known. The discovery of such applicability may take many further years of research with the possibility that the original scientific breakthrough is left without protection. The case stresses the need for biotech companies to find a practical application with a real prospect of industrial exploitation before applying to the IPO to seek protection for their latest protein or nucleotide sequence.

c Stem Cells (WARF)

Inventions concerning products which can only be obtained by the use and destruction of human embryos cannot be patented, the European Patent Office (EPO) ruled in December 2008.

Thirteen years since an original patent application was made by the Wisconsin Alumni Research Foundation and after a long history of decisions and challenges, the EPO's highest decision-making body issued its final judgment in this month. In a restrictive interpretation of the European Patent Convention's (EPC) rules on public order and morality, the Enlarged Board of Appeal ruled that applications relating to products which could be prepared only by destroying human embryos would be refused, even if the application did not specifically describe the method involving this destruction and if a new method had been found since the application was filed which avoided such destruction.

This decision will bind the EPO unless or until the EPC or Directive is amended. Accordingly, the EPO will refuse patent applications for uses of products derived from human embryos which involve their destruction. Patent applicants for such inventions will need to file patent applications for such inventions in the patent offices of individual European jurisdictions, instead of through the central clearing house procedure of the EPO. The decision does not deal with the patentability of stem cells directly, it concerns a narrow question and the ongoing impact of the decision is questionable given that it is not possible to create human embryonic stem cells without using and destroying human embryos.

The English Courts (and perhaps others) will seek to align their laws more closely with those of the EPO, with Board of Appeal decisions being cited regularly. Following a spate of patent-friendly decisions, patentees will feel more confident in bringing proceedings in the English courts.

The issue of stem cell patentability will continue to be in the news this year. There are many pending applications relating to stem cell technologies before the EPO and with hearings in the pipeline for 2009 these applicants will be pressing the EPO for a clear answer.

Regulation of NHS Advertisements

A Code of Practice for the promotion of NHS-funded services has been issued to regulate the advertising of NHS-funded services. The new Code requires all providers of NHS-funded services to comply with applicable Advertising Standards Authority (ASA) Codes and additional NHS-specific rules; ensuring that patients have accurate

information so that they can make effective choices and receive treatment that best fits their individual needs.

The Code applies to all providers of NHS-commissioned services and the entire range of promotional activity undertaken. It sets out general principles and contains specific rules covering, amongst other issues, NHS brand/reputation protection, direct marketing to public and referring clinicians, gifts and inducements to clinicians and commissioners as well as the public, sponsorship, compliance with undertakings and complaints and enforcement. The Code is intended to regulate the level of expenditure on promotional activity by requiring open disclosure of this by providers. The enforcement of the Code will be split, with marketing communications already covered by the ASA Codes remaining under the existing regime and complaints under the NHS-specific rules being administered by the relevant commissioning PCT and/or the Strategic Health Authority.

Providers of NHS-commissioned services, together with their internal and external marketing teams, will need to familiarise themselves with the new regime. How the ASA choose to adjudicate in accordance with the NHS Promotion Code remains to be seen.

EC's Proposal on Counterfeit Medicines for Human Use

In March 2008, the European Commission released a public consultation on proposals for tackling counterfeit medicine. The Commission was of the opinion that the rise in counterfeit medicines has been caused by uncertainty as to the subjects of pharmaceutical legislation and guidance, shortcomings in product integrity, and lack of compliance with pharmaceutical legislation and guidance.

The UK government response to the consultation was published in May. Although the UK government generally supported the Commission's proposals, it asked for further information on how the proposed schemes would operate in practice.

December 2008 saw the European Commission adopt the proposal which includes a number of measures to provide the maximum level of assurance that only high-quality medicines are sold within the legal supply chain. It is intended that this will be achieved through attaching safety-features to genuine products to help identify those which are false, listing wholesale distributors who have undergone inspection in a database managed by the EMEA and subjecting them to mandatory audits by purchasers, and improving the control at the EU borders through which false medicinal products could enter.

The legal proposal will now be debated in the European Parliament, representing citizens and in the Council, representing Member States. The fact that the Czech Republic, whose EU Presidency will be responsible for ensuring the proposal's debate among Member States, have emphasised their commitment to this proposal, suggests that it is likely to be dealt with as a priority and its adoption expedited. The legal proposal, however, can become law at the earliest 18 months following adoption and publications by the European Parliament and Council, meaning that the effects of any new legislation are unlikely to be seen until 2011.

European Commission Pharmaceutical Sector Enquiry

To much fanfare the European Commission published its preliminary report in the Pharmaceutical Sector Inquiry in November 2008. Although the report is work in progress, the Commission claims to be 'shocked' that originator companies use patent rights and other legal measures to delay entry by generic companies and it is clear that the Commission wishes to remove these barriers to generic entry. In doing so, the Commission will explore the fine line between the existence of rights and when enforcement of those rights infringes competition law.

The Directorate General for Competition within the Commission is expected to bring infringement proceedings in specific cases. It can also be expected to issue guidelines, a form of 'soft' law, on some areas of concern. Other measures, such as patent and

regulatory regime reforms would require wider support in the Commission and from Member States and would not be such a quick gain. Yet even if outcomes are uncertain and slow, the Commission has certainly gained the industry's attention in 2008 and this will continue throughout 2009.

Submissions on the interim report are to be provided by the end of January 2009. The final report had been expected in Spring 2009 but the Commission is now talking in terms of Spring/Summer.

Repackaging of Pharmaceuticals

Two important decisions from 2008 have significantly changed the legal landscape surrounding the repackaging of pharmaceutical products by parallel importers.

In its second decision in *Boehringer Ingelheim v Swingward*, dated 21 February 2008, the Court of Appeal applied the second judgment of the ECJ in the same proceedings. The reference to the ECJ was intended to clarify the application of the fourth of the famous *Bristol-Myers Squibb* conditions. When repackaging products for the purpose of parallel trade within the European Union, parallel importers of pharmaceutical products must comply with the BMS conditions in order to avoid infringing the brand-owner's trade marks.

Under BMS condition 4, repackaging will be infringing unless the presentation of the repackaged product is not such as to be liable to damage the reputation of the trade mark and of its owner. The claimant brand-owners argued that "damage" should be interpreted broadly, to include dilution of the mark, and in particular that co-branding and partial de-branding should be regarded as damaging in principle.

The Court of Appeal disagreed, finding that the ECJ's decision was that damage only occurs where the repackaging damages the mark's ability to guarantee the origin of a product. This is a question of fact for the court in each case. In this case, there was no damage caused by the partial removal of the brand-owner's marks from their products after they had been put on the market. Nor was the application by the parallel trader of their own marks to the products in combination with the brand-owners' marks damaging.

The Court of Appeal refrained from making a final decision in this case, however, pending the ECJ's decision in *Wellcome v Paranova*. This decision was published on 22 December 2008. The main question referred was whether, when repackaging pharmaceutical products for the purpose of parallel imports within the European Union, there was a principle of "minimum intervention". Wellcome had argued that repackaging should be regarded as infringing unless it caused as little prejudice as possible to the trade mark consistent with gaining effective market access to the Member State of importation. If upheld, this would effectively have created a new BMS condition with which parallel importers would have had to comply in order to avoid infringing brand-owners' trade marks.

The ECJ rejected this submission. BMS condition 1 already requires that repackaging is only permissible where it is necessary in order to gain effective market access for the parallel imported goods. However, this condition only relates to the fact of repackaging. There is no additional condition, relating to the manner and style of repackaging, such that only the minimum intervention is permissible. The criterion under which to assess the manner and style of repackaging is that set out at BMS condition 4: whether the repackaging is damaging to the reputation of the trade mark and its owner.

Although the effect of the decisions in *Boehringer and Wellcome* may increase the extent to which parallel traders repackage parallel imported pharmaceuticals, since damage is a question of fact, there are still likely to be disputes concerning the effect of any particular style of repackaging, and national courts may differ in their approach. Greater focus may also be given to the "necessity" test, before any considerations of damage come into question.

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