Legal and regulatory update

Regulatory

Proposed Amendment of the Community Regulatory Framework for Medicinal Products

The European Commission published on 18th July, 2001, for discussion, its proposals for the amendment of the Community pharmaceuticals legislation. These take the form of two draft directives (a modified Community Code relating to medicinal products for human use, and a corresponding one relating to veterinary medicinal products) and a draft regulation, which would amend Regulation 2309/93 as to the centralised procedure. The proposed directives (which do not represent the final legislative proposals) are based on the consolidated Community Codes that codify existing pharmaceuticals legislation (which results in some renumbering but does not amend the legal effect of the existing legislation) and that have subsequently been adopted by the European Parliament and the Council.

The proposals include the following particular features:

- Introducing a 'fast track' registration procedure for products of significant therapeutic interest.
- Allowing a 'conditional marketing authorisation' for one year, subject to conditions as to undertaking more monitoring and clinical studies, if there is an important expected health benefit.
- Making use of the centralised procedure mandatory for all new chemical entities (NCEs), whereas at present it is optional for NCEs but obligatory for biotechnology products.
- Amending the mutual recognition procedure, which now becomes the mutual recognition and decentralised procedure, with a new arbitration system designed to reduce disagreements during the operation of that procedure as between member states.
- Introducing on a Europe-wide basis 'compassionate use' rules for medicinal products that have not yet been authorised.
- Allowing more information as to selected prescription medicines to be available at the request of patients – namely a limited relaxation of the existing ban on Direct to Consumer (DTC) advertising.
- Replacing the current five year renewal procedure by reinforced pharmacovigilance monitoring.
- Harmonising the regulatory data protection period throughout Europe for all medicinal products at 10 years, instead of as at present giving member states an option to confer only 6 years' protection on products authorised through national procedures.
- Increasing the regulatory data protection period from 10 years after first marketing authorisation in the Community to 11 years if during the first 8 years of the period an authorisation for a new indication is secured which is held, during pre-authorisation scientific evaluation, to bring a significant clinical benefit in comparison with existing therapies.

Controversially, however, the Commission has also proposed including in the amended text, at Article 10(5), the following declaration:

> Conducting the necessary tests and trials with a view to application of the present article [ie that dealing with abridged applications] to a generic medicinal product shall not be regarded as contrary to patent related rights and to supplementary protection certificates for those medicinal products

Such an attempt to provide in Europe a limited version of the 'Roche Bolar' exception under the US Waxman–Hatch Act would take effect under the patent laws of European member states. Even though there has been a trend in German and

French courts to accept that clinical trials as to safety and efficacy might be excepted from patent infringement as 'experimental use relating to the subject matter of the invention' there has been no suggestion that mere bioequivalence studies, such as those required for an abridged application, and presumably the subject of this proposal, would be so excepted.

Clinical trials

The Clinical Trials Directive was published in the *Official Journal* on 1st May, 2001, and thus member states have until 1st May, 2003, to implement its provisions in national law, although some of these can be deferred for a further year. In the UK the Department of Health and the Medicines Control Agency have published a briefing note discussing the implications of the Directive for the control of clinical trials in the UK.

On 28th June, 2001, the scientific committee of the European Agency for the Evaluation of Medicinal Products (EMEA), the Committee for Proprietary Medicinal Products (CPMP), issued a position statement on the use of placebo in clinical trials with regard to the October 2000 revision of the Declaration of Helsinki. The position statement notes that 'a strict interpretation of section 29 of the revised Declaration appears to rule out clinical trials that use a placebo arm whenever authorised therapeutic methods exist, preferring active controls'. The statement discusses the consequences of this, and concludes that

> provided that the conditions that ensure the ethical nature of placebo controlled trials are clearly understood and implemented, it is the position of the CPMP and the EMEA that continued availability of placebo-controlled trials is necessary to satisfy public health needs.

Commission rejects German provisions on pharmacovigilance

By a decision on 18th July, 2001, the Commission has rejected the provisions notified to it by Germany for reporting adverse reactions. The German provisions are stricter than those mandated under the Pharmacovigilance Directive (2000/38/EC), which Directive Germany is challenging.

Marketing authorisations granted for the first European orphan drugs

Although some 50 or so Orphan Drug Designations have been awarded under the new European Orphan Drugs legislation, the first pharmaceuticals so designated to be granted a marketing authorisation received this on 3rd August, 2001. The products in question were enzyme replacement therapies for Fabry's disease – Transkaryotic Therapies' Replagal (agalsidase alpha) and Genzyme General's Fabrazyme (agalsidase beta). However, because they proceeded in parallel both products will benefit from the 10 years' exclusivity conferred in Europe on orphan drugs against 'similar medicinal products' for the same therapeutic indications – an unusual situation, which may not happen again.

Intellectual property

Biotechnology Directive

The European Court of Justice (ECJ) has rejected the challenge mounted by the Dutch Government, and supported by the governments of Italy and Norway, to the legality of the Directive on the legal protection of biotechnological inventions. By its Judgment of 9th October, 2001, it accepted the recommendation from Advocate General Jacobs of 14th June, 2001, and rejected pleas as to:

- incorrect legal basis, it having been suggested that, especially in the light of the European Patent Convention (EPC) it did not fall within the definition of measures for approximation of the provisions laid down by law, regulation or administrative action in member states that have as their object the establishment and functioning of the internal market;
- breaching the principles of subsidiarity;
- having not only failed to remove legal

ambiguities described in the recitals, but having made them worse, given the provisions both as to *ordre public*, and as to the patentability of plant varieties;
- incompatibility with obligations under international treaties, notably TRIPs, the Agreement on Technical Barriers to Trade, the EPC and the Convention on Biological Diversity;
- the incompatibility of Article 5(2) with human dignity;
- the procedure by which the Directive was adopted.

The Commission has announced that it will be proceeding against those member states that had not transposed the Directive into national law. The only countries that have so far fully implemented the Directive are Denmark, Finland and Ireland. The UK has implemented most of it, but not as yet those provisions dealing with the interrelation with plant variety rights.

European Parliament Resolution on the patenting of *BRCA1* and *BRCA2* genes

On 4th October, 2001, the European Parliament passed a resolution criticising the European Patent Office (EPO) for granting patents relating to human genes in general and to the *BRCA1* and *BRCA2* ('breast cancer') genes in particular. The EPO has countered, in a statement of 17th October, pointing out that such patenting is envisaged in the Biotechnology Directive, which the European Parliament approved. The patents in question have been granted to Myriad Genetics and it is understood that several oppositions to the patents have been filed with the EPO.

Parallel imports and trade marks

Judgment is currently awaited from the ECJ in two sets of proceedings concerning the use of trade marks to prevent parallel imports, and in which Advocates General have given opinions – Case C-414/99 *Davidoff* concerning international exhaustion, from England, and joined Cases C-443/99 *Merck, Sharpe & Dohme v Paranova* from Denmark and Case C-143/00 *Glaxo & ors v Dowelhurst & anr*, from England. The *Davidoff* case, concerning the extent to which consent to import into the Community can be inferred from the circumstances in which the product was first placed on the market outside the Community, is of less direct immediate relevance to the biosciences sector in view of the regulatory constraints which preclude the ready marketing of products imported from outside the Community. The joined *Merck & Glaxo* cases give the ECJ, having not long ago given judgment in the rebranding parallel imports case of Case C-379/97 *Pharmacia & Upjohn v Paranova,* yet another opportunity to revisit its parallel imports case law in relation to repackaging. In these joined cases Advocate General Jacobs recommended in Case C-443/99 *Merck, Sharp & Dohme* on 12th July, 2001, that:

> Article 7(2) of the First Council Directive of 21 December 1988 to approximate the laws of the Member States relating to trade marks (89/104/EEC) does not entitle a trade mark owner to oppose the marketing of a pharmaceutical product put on the market under his trade mark where the importer has repackaged it and reaffixed the trade mark and has complied with the other requirements set forth in the Court of Justice judgment in Joined Cases C-427/93, C-429/93 and C-436/93 *Bristol-Myers Squibb and Others* (the product inside the packaging must not be affected, the manufacturer and origin must be clearly indicated, the reputation of the trade mark or its owner must not be damaged as a consequence of poor packaging, and the trade mark owner must be given notice before the repackaged pharmaceutical product is put on sale) if such repackaging and reaffixing of the trade mark are reasonably required to enable the importer to obtain effective access to the market of the importing Member State (or to a significant part of it) and in so far as other, less intrusive, methods of repackaging will not enable him to obtain effective access to that market (or to a significant part of it); for that purpose account must be taken not only of obstacles which exist in law – such as the regulatory requirements of the importing Member State – but also of obstacles which exist in fact, including resistance of consumers, for example to over-stickered

boxes, which is such as to affect prescription or dispensing practice.

In Case C-143/00 *Boehringer Ingelheim and Others*:

(1) Neither Articles 28 and 30 EC nor Article 7(2) of the First Council Directive of 21 December 1988 to approximate the laws of the Member States relating to trade marks (89/104/EEC) precludes a trade mark owner from using his trade mark rights to prevent the parallel importer of a pharmaceutical product from repackaging that product provided that such use of his rights does not contribute to the artificial partitioning of the markets between Member States or otherwise constitute a disguised restriction on trade between Member States. A trade mark owner who uses his trade mark rights to prevent a parallel importer from necessary repackaging contributes to such artificial partitioning.
(2) Repackaging is necessary if it is reasonably required to enable the importer to obtain effective access to the market of the importing Member State (or to a significant part of it) and in so far as other, less intrusive, methods of repackaging will not enable him to obtain effective access to that market (or to a significant part of it); for that purpose account must be taken not only of obstacles which exist in law – such as the regulatory requirements of the importing Member State – but also of obstacles which exist in fact, including resistance of consumers, for example to over-stickered boxes, which is such as to affect prescription or dispensing practice.
(3) A parallel importer intending to market repackaged goods bearing a trade mark must in all circumstances give the owner of the trade mark reasonable advance notice. Three to four weeks' notice will normally be regarded as reasonable. A parallel importer who has failed to give the trade mark owner reasonable advance notice cannot rely on Article 30 EC or on Article 7(2) of the Directive in proceedings brought against him for infringement.

In each of the two joined cases Advocate General Jacobs recommends to the ECJ taking the opportunity to further define to what extent repackaging and reaffixing of the trade mark are necessary and thus permitted – it must be 'reasonably required to enable the importer to obtain effective access to the market of the importing Member State (or to a significant part of it)' and 'for that purpose account must be taken not only of obstacles which exist in law – such as the regulatory requirements of the importing Member State – but also of obstacles which exist in fact, including resistance of consumers, for example to over-stickered boxes, which is such as to affect prescription or dispensing practice.' Moreover, in the *Glaxo* case Advocate General Jacobs rejects the criticisms made of the recent development of EC law in this area by Mr Justice Laddie in his Judgement referring the questions to the ECJ.

Competition law

Commission orders IMS to license copyright

IMS Health (IMS), the world's leading supplier of pharmaceutical sales information, has been ordered by the European Commission that it must license to competitors under the copyright in its so-called '1860 brick structure' for collecting pharmaceutical sales data. Competitor companies in Germany last year had been refused licences by IMS to use the system for gathering regional sales information after IMS had secured injunctions against them. The Commission concluded that IMS's refusal to grant licences constituted abuse of a dominant market position, and has now, in the exceptional circumstances of this case, imposed interim measures forcing IMS to provide licences on non-discriminatory, commercially reasonable terms. On 10th August, 2001, the Court of First Instance of the European Community suspended the interim decision of the Commission that IMS should license its competitors to use the system pending a full hearing of the application by IMS for the order for interim relief. The suspension was granted on a number of grounds including the potentially serious economic

consequences for IMS of the decision of the Commission to fix the terms for a compulsory licence, and the serious encroachment on IMS's property rights. While the Court reviewed briefly the case put forward by the Commission for interim measures to be adopted and identified some weaknesses in it, it remains to be seen whether the interim measures will be adopted at the full hearing.

GlaxoSmithKline appeals Commission ruling on dual pricing

On 23rd July, 2001, Glaxo Wellcome plc appealed against the Commission decision of 8th May, 2001, which had found that its Spanish dual pricing policy was contrary to Article 81(1) EC Treaty since it restricted parallel imports and exports to other states. Glaxo Wellcome contends in its appeal that its Spanish conditions of sale do not constitute an agreement and have no restrictive object or effect. They also contend that the conditions of sale compensate for a market irregularity caused by the setting of prices by the Spanish authorities, or alternatively that the conditions are exempted under Article 81(3). Meanwhile the Commission has started investigating Pfizer's dual pricing policy in Spain, details of which were notified to the Commission in May after its ruling against Glaxo Wellcome.

Information Commissioner's guidance on uses and disclosure of medical data: Report on Commissioner's consultation day

In May 2001, the Information Commissioner issued draft guidance on the impact of the Data Protection Act 1998 on the use and disclosure of medical data for consultation. (A copy of the guidance is available from www.dataprotection.gov.uk under Guidance, Drafts for Consultation.) Although the guidance was triggered by increasing requests for advice from public sector healthcare providers, it also covers use of medical data in private sector healthcare and in clinical trials and other research. The guidance is concerned only with what the Commissioner terms 'threshold issues' – that is compliance with the obligation to process personal data fairly and lawfully and for specified and lawful purposes (the first and second data protection principles). The Commissioner asked for comments on the Code to be submitted by the end of August 2001 and, on 19th October, 2001, held a workshop in Manchester to explain the responses she had received, to allow presentations by interested parties and to allow for discussion.

There were presentations from the Imperial Cancer Research Fund (on the challenge posed by the legislation to epidemiology), the Association of Community Health Councils of England and Wales (ACHEW), the General Medical Council (GMC) and the NHS Executive (Confidentiality Issues Unit). Overall, there was a consensus that more information should be given to patients about the uses made of their information and that in, at least some situations, the aim should be to obtain explicit, informed consent to the use of patient personal data. Beyond this, views diverged widely.

The Imperial Cancer Research Fund highlighted the difficulties that informed consent would impose on epidemiology: the act of seeking consent would add to the cost of research, would impose administrative burdens and would quite possibly skew the statistical significance of research. As the research was non-invasive and did not lead to the release of identifiable information, the Fund suggested that these additional constraints were inappropriate and proposed that dispensations from the Act should be introduced for epidemiology. The Fund felt that this difficulty was unique to epidemiology and that the Act would pose far fewer problems for clinical trials where informed consent was already a requirement.

ACHEW took the opposite position, highlighting examples of disclosure of patient data that caused them to receive

complaints, and arguing that informed consent was the only basis on which to move forward. ACHEW even questioned whether consent should be sought for the use of anonymous data (which falls outside the scope of data protection legislation).

The GMC explained the background to its guidance on confidentiality, issued in 2000. The guidance concluded that implied consent would satisfy the clinician's duty of confidence, where the patient was aware of the uses to which information would be put and of his or her ability to object and did not exercise this right. The GMC had concluded, in the course of drawing up its guidance, that there was little clarity as to what could be done with patient data, despite the importance of the issues, and that guidance would need to be developed taking into account law, ethics, principles and practicalities.

The Confidentiality Issues Unit at the NHS Executive stated that its goal was to obtain informed consent for more uses of medical data. The speaker outlined the difficulties of obtaining fully informed consent in an organisation the size of the NHS. There was to be a three to five year plan to achieve this goal. In the meanwhile, regulations made under Section 60 of the Health and Social Care Act 2001 (which allows for the overriding of patient confidentiality in specified situations) may provide a lawful basis for processing.

The workshops considered whether guidance should be issued on other aspects of data protection (to which the consensus was yes), how best patients should be kept informed, what issues were of concern to patients and to clinicians in relation to research, what issues arose out of the sharing of data for crime and disorder or social services purposes and when encryption or other anonymising techniques might be used.

The Assistant Commissioner responsible for the guidance indicated that the next stage would be for the Commissioner to consult with more patients' groups prior to reissuing the guidance later this year/early next year. The Commissioner would also consider issuing guidance on other areas of the Act and on developing the guidance to cover suggested standards and best practice.

Company/commercial law

Case law: Breach of Restrictive Covenant: *Ward Evans Financial Services Ltd v (1) Iain Fox (2) Alan Phillips (2001)*/CA/References: Lawtel 30/07/2001; [2001] EWCA Civ 1243

Summary

Employees who set up a competing company but left it dormant while still in employment were in breach of an agreement that imposed a restriction on employees holding material interests in another company in circumstances where holding such shares impaired the employees' ability to act in the best interests of their employer.

Facts

F and P worked as independent financial advisers for the claimant employers (WE). After having implemented a pension scheme for a company (C), both employees decided to set up a company called Fidelius, which C then used to implement its pension scheme. WE argued that by doing so F and P were in breach of their trust and confidentiality written agreement with WE as they were competing directly with WE and that they had secured one of their clients. WE sought damages for breach of their employment contract, on the grounds that F and P could not have any material interest in another company, which would damage their ability to work in WE's best interests. At first instance, the trial judge held that F and P were not in breach of their agreements. WE appealed.

Decision

F and P were found to be in breach of their agreements, as their material interest in Fidelius clearly impaired their ability to

work for WE's best interests. Furthermore, their interest in Fidelius had been generated while working for WE and neither of the employees had revealed its actions to WE. The Court of Appeal allowed the appeal on the ground that the High Court Judge had not taken into account the issues related to a separate clause in the agreement.

Breach of confidence and resulting damages: *Edward John Giles v Roderick Middleton Rhind (2001)* unreported

Facts

Two shareholders in a company (G and R) had entered into a shareholder's agreement, whereby they had agreed certain confidentiality undertakings between themselves regarding information concerning the company, Surrey Foods Limited (SF). At first instance it was found that R had breached his confidentiality obligations, by redirecting one of SF's clients towards his own company. The loss of this business had driven SF into liquidation and as a consequence the proceedings that SF had undertaken against R had been discontinued. Under this action, G sought to recover from R the loss in value of his shares, and other benefits that he claimed he would have otherwise continued to enjoy. The preliminary issue centred around whether G could successfully claim damages for any of the above loss following the House of Lords decision in *Johnson v Gore Wood & Co (2001)* 2 WLR 72 (where it was held that the bringing of a claim in later proceedings was, in principle, an abuse of process).

Decision

It was held that had SF not lost the contract, G would not have suffered any losses in his shares or in the monies he would have received. Thereon, G's losses were reflective of SF's losses, and so had SF recovered, G would have done so too. Consequently, in the light of the decision in Johnson (*supra*), G's claim failed. This decision was reached with reluctance, as it left a wrong without a remedy.

Restrictive Covenant: *John Michael Lapthorne v Eurofi Ltd (2001)*/ Reference: [2001] EWCA Civ 993, CA

Facts

E, a business providing financial consultancy, and L (self-employed consultant) entered into a consultancy agreement, whereby L agreed to (a) promote, develop and extend E's business; (b) secure contracts between E and clients for the provisions of services; (c) provide his services solely to E's clients; (d) only take on work from non-clients of E if E agreed in writing and in the event of his income being below £12,000 in a 12 month period (clause 3(a)); and (e) E would be entitled to invoice and retain, for its own benefit, fees for its own services (clause 3(b)).

E contended that L was in breach under the terms of the consultancy agreement, as he had provided services to E's clients for his own benefit. The main issues at stake were that L had breached the agreement and had failed to comply with his fiduciary duty, by providing services to E's clients without E's consent. At first instance the judge had found that L was not in breach of his covenant where an individual was no longer one of E's clients. However, by offering his services to another individual while being one of E's clients, L was in breach, although the restrictive covenants were unenforceable because it was unreasonably in restraint of trade. E appealed against the judge's decision and submitted that he was wrong to conclude that restrictive covenants were unenforceable in restraint of trade.

Decision

It was held that the contract between E and L was neither one of employment or services, therefore L was not compelled to

devote himself entirely to consulting for E and E was under no obligation to provide continuous work to L. With regard to his fiduciary duty, the Court of Appeal concluded that it did not apply to either of the clients in question. Finally, because clause 3(b) was too widely drawn it became a restraint of trade, and so it could not protect E's business interests or be enforceable against L.