Legal and Regulatory Update

ReedSmith

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NOTES FROM THE EU

EU: European Commission issues new guidelines relating to orphan medicinal products

The EU has had a regime for the promotion of the development of orphan medicinal products since 2000 when Regulation (EC) No. 141/2000 (the 'Regulation') was adopted. The Regulation provided various incentives to developers of orphan medicinal products in the EU, perhaps the most significant of which is a period of 10 years' market exclusivity for the first product for a particular indication to obtain marketing authorisation in the EU. This is significant because it is independent of any patent protection and will protect against the grant of a marketing authorisation to an effectively competing product (whether identical or similar) even if the developer of that product is willing to compile a full regulatory dossier.

The Regulation does however go on to provide certain exceptions to this market exclusivity:

- A marketing authorisation may nevertheless be granted to a competitor where the original authorisation holder consents, if it is unable to satisfy market demand or the competitive product is safer, more effective or otherwise clinically superior (Article 8(3) of the Regulation).
- The period of market exclusivity may be reduced to 6 years from 10 at the end of the fifth if the criteria for orphan designation are no longer met, in particular where the product is sufficiently profitable to justify curtailment of market exclusivity (Article 8(2) of the Regulation).

The European Commission has now published new guidance on how these exceptions are to be applied.

Guideline on aspects of the application of Article 8(2) of Regulation (EC) No. 141/2000: Review of the period of market exclusivity of orphan medicinal products[1]

The Guideline sets out the general principles and procedure whereby the period of market exclusivity for orphan medicinal products may be reduced.

Article 8(1) provides for a period of 10 years market exclusivity where a product is designated as orphan drugs and authorised throughout the Community. However, Article 8(2) stipulates that this period may be reduced to 6 years if at the end of the fifth year, it is established that the product no longer fulfils the designation criteria.

Under Article 8(2) a Member State shall inform the European Medicines Agency, advisably at the end of the fourth year of market exclusivity, that at least one of the designation criteria may not be met, providing the rationale for its doubts and justifying data. The Agency must then inform the Commission and Market Authorisation Holder who must be given at least one of the Member States' reasons and the opportunity to submit its views and data in writing.

Based on evidence from the Member State and Authorisation Holder, the Committee on Orphan Medicinal Products (COMP) will issue an opinion justifying whether or not orphan status should be maintained. If available evidence does not establish with reasonable confidence whether or not the designation criteria continue to be met, COMP must recommend that the period not be reduced.

The assessment will be done in two steps. Firstly, COMP will look to see if the original

designation criteria are fulfilled. If not, COMP will look to the other designation criteria of Article 3(1). Only if neither criteria are fulfilled may COMP recommend that the period of exclusivity be reduced.

First step With regard to the prevalence criterion, COMP's assessment will be for prevalence at the time of the review, using the same standards as for the moment of designation. Further, the sponsor is required to do a critical review of possible changes in the estimated prevalence of the condition. The Commission states that an increased survival rate because of the effect of the drug is not a reason to reduce market exclusivity.

For products designated on 'insufficient return on investment', the test is whether the marketing would generate sufficient return at the point of review. Further, the period will not be reduced if the return would be insufficient after subtraction of the incentive.

For 'the inexistence of a satisfactory method' or 'significant benefit', COMP will take into account any changes affecting the treatment of patients since authorisation. In each case, the sponsor may be asked to provide a critical review of its product at the time of review with regard to the inexistence of an alternative method or significant benefit. However, sponsors will not be required to generate new comparative data against another treatment/method that has become available since authorisation.

Second step If COMP form the opinion that the initial criteria are not met, it will look to the other designation criteria of Article 3(1).

If the initial designation was based on prevalence, COMP will look to see if the return on investment criteria is met at the time of the review, and vice versa. If COMP now view that a satisfactory method exists, it will look to the significant benefit designation criteria. However, there is normally no alternative where the initial designation was based on significant benefit.

In deciding on its recommendation, COMP will consider the extent to which the criteria are not fulfilled. For example, in the case of prevalence, only slightly exceeding the threshold may allow COMP to recommend that market exclusivity be maintained. COMP will also consider 'insufficient profitability' as an argument against a reduction.

The Commission will make their decision on the basis of the opinion of COMP within 30 days of receipt of the opinion, and only in exceptional circumstances will the Commission adopt a decision not in accordance with the opinion.

Guidelines on the application of Article 8(1) and (3) of Regulation (EC) No. 141/2000

The assessment of similarity to an authorised product under Article 8(1)[2] In assessing similarly, the Commission previously provided guidance in Commission Regulation (EC) No. 847/2000, which provided the following definitions:

- 'active substance' means a substance with physiological or pharmacological activity;
- 'similar medicinal product' means a medicinal product containing a similar active substance of substances as contained in a currently authorised orphan medicinal product, and which is intended for the same therapeutic indication;
- 'similar active substance' means an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of the same molecular structural features) and which acts via the same mechanism.

There are three components to 'similarity' within Article 8. The products will not be regarded as similar if there is a 'significant difference' within one of these components. The International Non proprietary Names (INN) may provide information regarding the similarity of the first two components.

For the assessment of 'the molecular structural features of the active substance', the applicant should demonstrate the proposed structure using evidence summarised in 'unambiguous two- and three-dimensional graphical representations', describing precisely

the active substance 'using systematic terminology', and providing WHO (World Health Organisation) reports where the substance has a recommended INN name. The applicant must give a justification if this information is not provided. He must then describe and compare the principal molecular features with the authorised product using, if he wishes, software programs and 'similarity searching'.

The 'mechanism of action of an active substance' is the interaction of a substance with a particular pharmacological target eliciting a particular pharmacodynamic effect. If the mechanism of action is not fully known, the applicant must demonstrate that 'the two active substances do not act via the same mechanisms'. The differences between two substances in terms of 'mode of administration, pharmacokinetic properties, potency, or tissue distribution of the target' are not relevant to the mechanism of action. For assessing similarity, the relevant effect is the 'primary pharmacodynamic effect'. Two substances with the same target may elicit a different effect whereas two active substances with the same effect may act at different targets.

The marketing authorisation determines the 'therapeutic indication' of a product, which has to fall within the scope of the designated orphan condition. If applying for authorisation for a second product within the same subset of the designated condition, the applicant must establish that the difference between the two subsets is 'clinically meaningful'. If there is overlap of target populations, the applicant must provide authority with an estimate of its extent.

Guidance on the procedure for the assessment of similarity and applying derogations under Article 8(3) For centralised marketing authorisation of a second product, the competent body is the European Medicines Agency. Otherwise it is the 'national competent authority'.

The application will first need to be validated by the competent body. The applicant must provide appropriate documentation on his position regarding similarity and, if appropriate, justification that one of the derogations under Article 8(3) applies. This formal check does not indicate the outcome of the application. If the application involves a generic product, similarity is assumed, so justification for one of the derogations must be provided.

For *similarity*, the applicant must submit a report in module 1.7.1 comparing the products in the context of similarity under Article 3(3) of Regulation 847/2000. He must conclude on similarity/non-similarity based on the three components giving reasons to support a claim of non-similarity.

A claim of *derogation* must be supported by information submitted in module 1.7.2. If the Authorised Holder has given consent for the second application, the applicant must provide evidence of this in a letter signed by the Authorised Holder. If the Authorised Holder is 'unable to supply sufficient quantities', the applicant must provide a report describing why, with details of the supply problems and failure to meet patients' needs. If the applicant wishes to establish that the second product is 'safer, more effective or clinically superior', he must provide a report justifying why it is clinically superior with a comparison of the products and in reference to clinical studies results and scientific literature.

Before validating the application, the competent assessing body should check which authorised products should be compared for similarity. If the body identifies a new similarity issue, the applicant must submit a report justifying the lack of similarity or one of the listed derogations. This check should be repeated before granting/amendment of marketing authorisation. For the centralised procedure, the Agency will repeat its check before the Committee for Medicinal Products for Human Use (CHMP) issues a positive opinion. If a new issue is identified by the Commission, they may refer the opinion back to the Agency for further evaluation.

The competent body will then assess similarity in parallel with the quality/safety and efficacy evaluation. If the assessment is positive, the applicant must submit a

justification for the fulfilment of a derogation. The CHMP opinion will be part of the overall opinion on quality/safety/efficacy and the applicant may ask for a re-examination of an unfavourable opinion. Applicants seeking to develop a product can request Scientific Advice from the CHMP on issues of similarity and potential fulfilment of a derogation, hence it is recommended for demonstrating the 'clinical superiority derogation'.

A national assessing body should inform the Agency of all similarity issues and their conclusions on applications to ensure consistency.

For applying the derogation based on 'inability to supply sufficient quantities', the applicant must provide a supporting report to the competent assessing body who will then circulate the report to Member States for comment and provide the Authorised Holder with the opportunity to provide written comments. The assessing body will then issue a position on the fulfilment of the derogation which, if part of the centralised procedure, forms part of the CHMP opinion.

Where marketing authorisation applications are received at the same time, under the centralised procedure, an opinion will not be necessary where the procedures remain in parallel. Where a product is under assessment by the Commission, a national authorisation may grant marketing authorisation as there is no authorised product.

EU: Implementation of the joint technology initiative innovative medicines

The objectives of the IMI Joint Undertaking are to significantly improve the efficiency and effectiveness of the drug development process.[3] There are, however, a number of particular objectives. These include supporting 'pre-competitive pharmaceutical research and development' through a co-ordinated approach to overcoming identified bottlenecks in the drug development process, as well as supporting the implementation of research priorities as outlined by the Research Agenda of the Joint Technology Initiative on Innovative Medicines ('Research Activities'), notably by awarding grants following competitive calls for proposals. The Initiative also aims at ensuring that its activities are complementary with Decision No. 1982/2006/EC of the European Parliament and Council concerning the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007–2013) ('Seventh Framework Programme'). Further, particular objectives include increasing the research investment in the biopharmaceutical sector and promoting the involvement of small- and medium-sized enterprises.

The IMI Joint Undertaking is established for a period up to 31 December 2017 with interim evaluations carried out by 31 December 2010 and 31 December 2013 concerning the quality and efficiency of the IMI Joint Undertaking, and progress towards the objectives set.

The founding members of the IMI Joint Undertaking are the European Community, represented by the Commission, and the European Federation of Pharmaceutical Industries and Associations ('EFPIA'), subject to providing the requisite funding. Applications for new membership must be made to the Governing Board.

The three bodies are the Governing Board, the Executive Director, and the Scientific Committee. The Governing Board has overall responsibility for the operations of the IMI Joint Undertaking and shall oversee the implementation of its activities. The Executive Director, as chief executive, has responsibility for the day-to-day management of the IMI Joint Undertaking in accordance with the decisions of the Governing Board. The Scientific Committee is representative of academics, patient organisations, industry and regulatory bodies. The Scientific Committee is purely advisory to the Governing Board. Moreover, there shall be the IMI States Representative Group – consisting of a

representative from each EC Member State and each country associated to the Seventh Framework Programme – which will also fulfil an advisory role. A Stakeholder Forum shall be convened at least once a year to be informed upon the activities of the IMI Joint Undertaking (Article 9, Statutes).

The maximum EC contribution to the running costs and Research Activities shall be 1000 million euro. The resources of the IMI Joint Undertaking shall come from Members' financial contributions, any revenue generated by the IMI Joint Undertaking, as well as any other financial contributions, resources and revenues. Running costs shall be financed by the Members. The founding members shall contribute on an equal level, each of them not exceeding 4 per cent of the total financial contribution provided by the Community. Any unused amount may be put towards Research Activities. Any other member shall contribute in proportion to its total contribution towards the Research Activities.

Research Activities shall be financed through three avenues. Firstly, by non-monetary contributions by the research-based pharmaceutical companies that are a member of EFPIA, with resources (such as personnel, equipment, consumables, and so on) at least equal to the financial contribution of the Community. Secondly, by a matching financial contribution of the Community from the Seventh Framework Programme entered to the budget of the IMI Joint Undertaking. Finally, through contributions from members as hitherto outlined.

The IMI Joint Undertaking shall support prospective research activities following open and competitive calls for project proposals, independent evaluation, and the conclusion of grant agreements and project agreements.

The grant agreement shall set up the appropriate arrangements for the implementation of research activities and the appropriate financial arrangements and rules relating to intellectual property rights. It shall also govern the relationship between the selected consortium and the IMI Joint Undertaking. The project agreement shall be concluded between consortium members to set up the appropriate arrangements for setting up the grant agreement and govern the relationship between the participants in a project.

A number of listed legal entities are eligible for funding. These include micro-, small- and medium-sized enterprises within the meaning of Commission Recommendation 2003/361/EC, legal entities established as non-profit public bodies under national law, intergovernmental organisations, which have legal personality under international law, as well as any specialised agencies set up by such organisations, legal entities established under EC law, legal entities established as non-profit organisations which carry out research or technological development as one of their main objectives, secondary and higher education establishments, and non-profit qualified patients organisations.

The IMI Joint Undertaking shall adopt its general rules governing intellectual property policy to be incorporated in grant agreements and project agreements. The objective of such a policy is defined as 'to promote knowledge creation, together with its disclosure and exploitation, to achieve fair allocation of rights, to reward innovation, and to achieve a broad participation of private and public entities … in projects'.

The policy shall reflect the following principles. These are firstly, that each participant in a project shall remain the owner of that intellectual property it introduces and generates in that project unless otherwise mutually agreed in writing by participants in a project. The terms and conditions shall be outlined in the grant and project agreements. The second principle is that participants shall undertake to disseminate and allow the use of results and intellectual property generated by the project under terms and conditions defined in the grant and project agreements, subject to the protection of intellectual property rights, confidentiality obligations and legitimate interests of the owners.

Finally, the Regulation and Statutes detail other administrative matters, including

employment matters, financial auditing procedures, and responsibilities concerning the establishment and initial operation of the IMI Joint Undertaking.

EU: Latest European Court ruling fails to resolve parallel trade uncertainty[4]

The European Court of Justice (ECJ)[5] has again refused to set down clear guidance on the legality of refusal by pharma companies to fill export orders from parallel traders. The ongoing legal battle between drug wholesalers and pharma companies about restrictions on parallel trade enters a new phase of uncertainty following the most recent ruling by the ECJ in a case brought against pharma giant GlaxoSmithKline (GSK) by a group of Greek wholesalers.

Parallel trade comes about where wholesalers take advantage of different reimbursement prices for the same drugs prevailing in different EU Member States by buying drugs and shipping them from low price countries to high price countries.

The most recent ruling (itself in a case which has kept the parties in litigation for 8 years already) is the latest episode in a series of exchanges between national European courts and competition regulators, the EC and the ECJ. Unfortunately, the implication of the ruling is that this particular series still has a long time to run.

In his earlier advisory opinion to the Court in this case,[6] the European Advocate General had clearly not been impressed with the string of familiar arguments advanced by GSK. These are essentially that drug companies' refusal to supply parallel traders for export is justified by differential national reimbursement prices imposed on the drug companies by state social security authorities, rather than set by the drug companies; that parallel trade unfairly impinges on a fair return on the substantial R&D required to bring a drug to market; that restrictions on drug exports were needed to ensure adequacy of national supply in each country; and that parallel trade serves only to line the pockets of the parallel traders rather than serving the interests of consumers.

As expected, the European Court did not dissent from the views of its Advocate General. To do otherwise would have been to open up a new exception to the much promoted imperative of completing the European internal free market by vigorously attacking any obstacle placed in the way of inter-state trade. It would have taken a very brave court indeed to do this.

However, in a significant move towards the position advanced by the pharma companies, the Court held that pharma companies can refuse to supply 'unusual' orders from wholesalers. But to prevent the drug companies from jumping to the conclusion that any export order at all could be 'unusual', the Court also made it clear that a refusal to supply based only on the fact that the order was for export rather than domestic sale would be unlawful. It was for the national courts to decide what was unusual in the light of previous 'regular commercial practice'.

The Court relied on two previous cases, both over 30 years old, as authority for this idea. One admittedly is one of the leading cases in the area of abusive refusal to supply. However, in a judgment in that case running to over 300 paragraphs, one really needs to look hard to identify the two sentences the Court relied on in the GSK case. The other case cited by the Court concerned a refusal to supply petrol in a fuel shortage, where it was held to be not abusive for BP to supply less fuel to an occasional customer than to a regular customer. It is difficult to see how this forms a compelling analogy to GSK's case.

One might speculate that the Court felt that it had two difficult alternatives from which to choose. The Court did not want to make the pharma industry – among the most vibrant sectors in the EU – a new wide exception to its crusade to complete the internal market. However, perhaps a degree of sympathy for the fact that the national pricing differentials at the root of the problem are not the pharma companies' fault left the Court with a desire to leave the door slightly ajar.

With about 4 billion euro of parallel trade annually, one might think that there is an awful lot of 'regular commercial practice' which parallel traders can use to justify their export orders. One might also ask whether it would still be normal commercial practice for a parallel trader to request an increase in supplies of 5, or 10, or 20 per cent – measured over a month, a year or perhaps the history of the trader's relationship with the relevant drug manufacturer. What about the case of a parallel trader who currently trades in one drug, but seeing differentials falling away, switches his request for supply to similar volumes of another drug manufactured by the same supplier?

The truth is that although pharma companies are likely to hail the judgment a major step forward, it may in practice be difficult to convince national courts that large orders for export from existing traders are unusual within the meaning of today's judgment, given the already widespread nature of parallel trade. The judgment will, however, at the same time provide support to those national courts and competition authorities – such as the French Competition Council – who have shown sympathy with the more fundamental arguments raised by the pharma companies.

Likely reaction by pharma companies will be to pursue their existing progression down the supply chain. As the courts continue to fail to resolve the uncertainty about how the law regulates drug distribution, pharma companies are likely to attempt to gain more security by acquiring more and more direct ownership and control of distribution. Even this, however, is not a complete answer. A refusal to supply a third-party distributor can still be abusive even where the supplier has established its own internal distribution system – particularly where the supplier was previously trading with the third-party distributor. This difficulty for the drug companies may also then lead to a temptation to leverage the existing legal obligation to satisfy demand in each national market by canny planning of creation and utilisation of production capacity so as to ensure that in a given geography, available supply does not exceed local demand. So we might see some cases where drug manufacturers argue that they simply do not have sufficient production capacity to be in a position to guarantee supply in the various EU Member States although at the same time feeding demand for export orders.

In summary, it would appear that the ECJ has sidestepped the key issue which will result in more litigation and more uncertainty in the market as to the permissible scope of parallel trade.

UK: Lessons to be learned in drafting intellectual property licence agreements

The English High Court has considered the rules of interpretation when dealing with ambiguous drafting within a formal commercial agreement. In *Oxonica Energy Limited v Neuftec Limited [2008] EWHC 2127*,[7] the High Court adopted the modern approach of looking at the context in which an ambiguous phrase is used rather than applying a literal interpretation of the words used. The judge also held that the contra proferentem rule should generally apply in a 'take it or leave it' situation where one party is effectively unable to influence the drafting of the terms of the agreement.

The case concerned Neuftec Limited ('Neuftec') who possessed know-how of considerable value concerning additives for diesel fuel for which it had filed an international patent application under the Patent Cooperation Treaty ('PCT application'). Neuftec was granted national patents in a number of other countries. Oxonica Energy Limited ('Oxonica'), a nanotechnology company, was approached by Neuftec during the development of the fuel additives, primarily to help to solve a problem in the manufacture of the small particles necessary in the creation of the additives and thus make the product commercially useful.

On 7 December 2001, the parties entered into an exclusive licence and know-how agreement. The agreement required Oxonica to pay royalties to Neuftec in respect of the manufacture, use, sale or other exploitation of the 'Licensed Products', which are defined as 'any product, process or use falling within the scope of the claims in the Licensed Application or Licensed Patent'. The phrase 'Licensed Application' was defined as the PCT application and as 'any continuation, continuation-in-part or divisional applications thereof as well as foreign counterparts and re-issues thereof'; and 'Licensed Patent' was defined as 'any patent issuing from the Licensed Application thereof as well as foreign counterparts and re-issues thereof'.

Oxonica used and exploited the know-how passed to it under the licence agreement and developed a commercial fuel additive called 'Envirox'. It also made the necessary royalty payments to Neuftec as per the licence agreement.

However in June 2006, Oxonica sought to supply a variation of Envirox called Envirox 2 (a fuel additive Oxonica could supply from a different source), to a Turkish oil company with which it was hoping to contract with on terms which would have involved supplying large quantities of the fuel additive. If Oxonica supplied Envirox, this would have attracted large royalty payments for Neuftec. The fuel additive, Envirox 2, fell within the claims of the PCT application but outside the more limited claims in some of the granted national patents. As a result, Oxonica refused to pay royalties on sales in countries where patents with the more limited claims had been granted. The question arose as to whether Envirox 2 was a Licensed Product within the meaning of the licence agreement. Oxonica brought proceedings and sued for a declaration that it was not; and that therefore sales of Envirox 2 did not attract royalties under the licence agreement. Neuftec counterclaimed for an audit in respect of sales of Envirox 2 and payment of all royalty sums due under the licence agreement.

The High Court found in favour of Neuftec. It dismissed Oxonica's claim and allowed the counterclaim. Therefore, royalties were payable under the licence agreement on all sales of Envirox 2. The judgment set out a number of practical issues which led to this outcome. These include:

Commercial agreement – Must look at the context

The judge found that by applying settled principles in relation to the interpretation of ambiguous formal commercial agreements, the licence agreement was to be construed so that Licensed Products referred to things falling within the scope of the claims of the Licensed Application or Licensed Patent *as the context required*. The context qualification also applied to the definitions of Licensed Application and Licensed Patent. On the facts of the case, royalties were payable on anything falling within the scope of the claims of the PCT application as filed and nothing else. In those circumstances, Envirox 2 was a Licensed Product and attracted royalties.

- *Draftspersons lack of legal knowledge*
  The judge criticised the lack of good knowledge of international patent law in the draftsperson. He found a number of phrases to illustrate the ambiguity within the terms of the licence agreement, including:
- *Patent application*
  This definition could have two meanings: (1) the legal state of affairs constituted when a person requested the competent authority to grant him a patent and that request is still outstanding, or (2) the content of the documents which that person filed with a view to initiating the above.
  The first was an institutional fact and was temporal by nature. It ceased to exist as soon as the application was withdrawn, refused, or granted. The second was a historical fact that remained no matter what the Patent Office did. Furthermore, the expression patent 'application' was often employed without being conscious

of its ambiguity; there are many examples in the Patents Act 1977 where it is used in one or other sense and the particular meaning had to be determined from the context.

- *International patent application*
  The judge noted that there was no such thing as an international patent. Patents are national, so whoever wished to be granted a patent had to request it from the competent national authority. An 'international patent application' was a preliminary procedure conducted on the international plane which would give you extra time before committing to the expense of national patent applications. Such international patent applications could not be refused as such and conferred no patent monopoly. They did not convert automatically into a national application.
- *Mixed patent and know-how licences*
  The judge found that the term 'Know how' could be defined as all the information possessed by a licensor which a licensee would like to have in order to help him get started. In practice the information would consist of miscellaneous items, some of which were trivial in isolation. Conversely, nobody would grant a know-how licence under which the licensee did not have to pay royalties unless he used all of the know-how, for then the licensee might abstain from using one bit of the know-how and so avoid having to pay royalties on the rest. Therefore, it was often difficult to draft an acceptable royalty clause. A method often used in mixed patent and know-how licences when defining what was to count as use of the innovation (for the purposes of computing royalties) was to use the claims of a patent.
- *Licensed Application*
  This definition was stated to mean the PCT application and 'any continuation, continuation-in-part or divisional applications thereof as well as foreign counterparts and re-issues thereof'. The judge commented that these are technical expressions used in American patent law, yet this was an agreement governed by English law and signed at a time when the only patent application that existed was a PCT application claiming priority from two former British applications. Strictly speaking, there could never be any continuation or continuation-in-part 'thereof', nor any re-issue of the Licensed Application.
- *Licensed Products*
  The key expression in the licence agreement was 'Any product, process or use falling within the scope of the claims in the Licensed Application or Licensed Patent'. The ambiguity started with 'or'. In English it was used to connect two or more conditions, the satisfaction of any one of which would suffice. Sometimes the context showed that the alternatives were mutually exclusive, at other times that they were not. The word 'or' could not do the work by itself and context was vital.
  Here, Oxonica argued 'Licensed Products' meant: 'the claims in the Licensed Application or Licensed Patent, as the case may be', and denied that both could exist at the same time and place. For each territory at any given point in time, it argued that the inventor was either in possession of an application or a granted patent, but never both.
  On the other hand Neuftec contended that 'Licensed Products' meant those products covered by: 'the claims in the Licensed Application or Licensed Patent, or any of those'. Thus, it was enough if a product fell within a claim of the PCT application, even if it did not fall within any claim of the granted patents, because the licence agreement was also a know-how licence and the claims of the PCT application could have been chosen as a convenient yardstick to indicate royalty-bearing products. The phrase 'or Licensed Patent' was put in to cover the possible

case where a granted patent had even wider claims than the PCT application.

The contra proferentem rule

Neuftec also argued that because the document had been drafted by Oxonica's solicitors it should be interpreted contra proferentem. The judge quoted Lord Mustill in *Tam Wing Cheun v Bank of Credit and Commerce Hong Kong Ltd [1996] 2 BCLC 69, 77*, where 'the basis of the contra proferentem principle is that the person who puts forward the wording of a proposed agreement may be assumed to have looked after his own interests, so that if words leave room for doubt about whether he is intended to have a particular benefit there is reason to suppose he is not'. The judge said that the contra proferentem rule was not to be used save as a last resort. In the present case, the main drafting effort had been undertaken by Oxonica's solicitors, but it is clear that Neuftec was not obliged to take it or leave it and had involvement with the drafting. The maxim was not applicable in this case, even as a last resort.

The judge said that although there were strengths and weaknesses to both sides of the argument, it was Neuftec's interpretation which made the most business sense. Its main weakness was that the definition of 'Licensed Application' covered not only the PCT application, but also continuation applications, but that problem could be resolved. The key was that there were two different contexts in the licence agreement in which 'Licensed Products' was employed:

- Clause 2.1, which gave Oxonica the exclusive licence to exploit the Licensed Products.
- Clause 4, which imposed an obligation to pay royalties based on sales of Licensed Products.

As these contexts are not the same, it was possible that the wording operated differently in each case. The purpose of the first context was to give Oxonica the exclusive licence to exploit Neuftec's intellectual property, including know-how and any technology falling within the claims of the PCT application as filed and any other patent applications and patents claiming priority from the PCT application. For that purpose, the language employed by the draftsman was intelligible.

The judge said that the purpose of the second context was to define the class of royalty-bearing products. In some licences there was intended to be an exact correlation between the two, in the sense that the licensee must pay if he did something that was covered by the intellectual property right, but not otherwise. But that was by no means invariably the aim, and in some mixed licences it might not be practicable or desirable. That was the case here.

The judge said that, on a literal reading, no royalties would have been payable unless the product fell within the scope of claims of all of those aforementioned things. The paradoxical and absurd result would have been that the more applications and patents there were, the more likely it would be that Neuftec would get no royalties.

Having regard to the context, the judge concluded that royalties were payable on things falling within the scope of claims of the PCT application as filed, and nothing else.

Practical points of the case

This case illustrates the pitfalls of drafting a contract although relying too heavily on precedent agreements/clauses without having a good understanding of the underlying law. The results of the ambiguities in this case were costly litigation and uncertainty.

NOTES FROM THE UNITED STATES

A guide to the PhRMA revised Code on interactions with healthcare professionals

On 10 July 2008, the Pharmaceutical Research and Manufacturers of America ('PhRMA')

issued a revised Code on Interactions with Healthcare Professionals ('HCPs') (the 'PhRMA Code').[8] The revised PhRMA Code, which becomes effective January 2009, contains several key changes that will impact significantly the sales and marketing efforts of pharmaceutical companies that choose to comply. The most important revisions are those relating to sales representatives' ability to provide meals and logo items to HCPs. Specifically, the revised Code prohibits sales representatives from paying for off-site or restaurant meals for HCPs and their staff and prohibits the use of branded 'reminder' items, such as mugs, notepads or pens. The following paper contains a description of these and other revisions and also details the potential impact of the revised Code on the pharmaceutical industry.

The revised Code explicitly prohibits practice-related items of minimal value, such as pens, notepads, mugs or similar 'reminder' items that are branded with the company's name or logo. Whereas the original Code permitted companies to provide HCPs and their staff with branded reminder items, the revised Code allows only practice-related items that relate to a patient's disease or are intended to educate the patient about treatment. Accordingly, educational items such as textbooks, subscriptions to relevant scientific journals or copies of clinical treatment guidelines are permitted, as are anatomical models, informational sheets and brochures, patient self-assessment and tracking tools or written materials that inform patients about adherence to medicine regimens, healthy lifestyle choices or the availability of patient assistance programmes (all capped at a US$100 value). In addition, unlike the original PhRMA Code, the revised Code states it is inappropriate for companies to offer HCPs medical equipment such as stethoscopes because the equipment is primarily designed for patient treatment and not for education.

The updated Code restricts sales representatives or their direct supervisors from taking an HCP and/or his or her staff to a meal at a restaurant. Sales representatives may continue to host meals accompanied by informational sessions in an office or hospital setting; however, off-site meals are no longer allowed. As with the original Code, take-out meals or 'dine and dash' programmes continue to be prohibited. Note, however, that this revision does not impact the ability of an individual acting on behalf of a company who is *not* a sales representative or direct supervisor from providing an off-site or restaurant meal.

The revised Code prohibits manufacturers from providing entertainment or recreational items to HCPs, including tickets to the theatre or sporting events, sporting equipment, or leisure or vacation trips, even if provided in connection with an HCP's engagement as a speaker or consultant or whether the entertainment or recreation is secondary to an educational purpose. (The original Code permitted entertainment or recreation for HCPs where the HCPs provided legitimate consulting, advisory board or speaker training services.)

The revised Code's provisions on consultants and speakers remain substantially unchanged. However, the revised Code does add that compensation and reimbursement of expenses should be based on fair market value and, as noted above, that recreational or entertainment events cannot be provided to consultants or speakers in connection with their respective events.

The guidelines for funding Continual Medical Education ('CME') also remain predominately unchanged. However, the revised Code explicitly recommends that companies separate grant-making functions from sales and marketing functions and follow the standards for commercial support of CME established by the Accreditation Council for Continuing Medical Education or other accrediting bodies.

The PhRMA Code now contemplates that companies may decide to publicly announce their support of the Code and complete an annual certification (signed by the CEO and/or Chief Compliance Officer) that they have appropriate policies and procedures. The PhRMA website will identify those companies that commit to abide by the Code and

provide information for companies' Chief Compliance Officers. In addition, PhRMA will direct complaints about company conduct to the Chief Compliance Officer. Finally, the revised PhRMA Code encourages companies to seek external verification or audits of policies and procedures that comport with the Code.

The revised Code instructs companies to provide training on applicable laws, regulations, and industry standards as they pertain to interactions between HCPs and that companies train representatives to ensure general science and product-specific knowledge that is consistent with FDA requirements. Additionally, the PhRMA Code provides that companies periodically assess representatives' compliance with company policies and provide updates or additional training as needed.

The revised Code obligates companies to require HCPs who act as speakers or consultants on their behalf and who serve as members of a formulary or clinical guideline committee to disclose this relationship to the committee. Importantly, a committee may require the speaker or consultant to recuse himself or herself from decisions relating to the related company's products. The revised Code further recommends that companies require this disclosure to last for at least 2 years beyond the termination of the speaker or consulting arrangement with the company.

According to the revised Code, if companies opt to use non-patient identified prescriber data (that is to determine safety and risk information, to conduct research, to track adverse events, to focus marketing, and so on), they should (1) respect the confidential nature of the prescriber data, (2) develop policies regarding the use of the data, (3) educate employees and agents about those policies, (4) maintain an internal contact person to handle inquiries regarding the use of the data and (5) identify disciplinary action for misuse of such data. Additionally, the revised Code recommends that companies honour requests from HCPs who ask that their individual prescriber data not be made available to sales representatives.

With regard to the impact on the pharmaceutical industry, companies that decide to comply with the revised PhRMA Code will need to amend their compliance policies and procedures by January 2009. In addition to the operational challenges associated with revising, approving and distributing policies and procedures, companies will need to update – and roll-out – updated training programmes. As a practical matter, pharmaceutical companies that do business in California and Nevada will likely have to adopt the PhRMA changes to ensure adherence to those states' legal requirements that drug companies have comprehensive compliance programmes. In addition, the PhRMA Code revisions may signal a change to what have long been standard sales and detailing efforts. For example, the restrictions on off-site meals and branded reminder items foreclose very common industry sales and marketing practices. Although less common to begin with, entertainment activities are likely to diminish or to be eliminated entirely. Another significant adjustment for certain companies relates to the separation of grant-making and sales functions. Companies that desire to comply with the revised Code but currently combine these functions will have to restructure their operations.

NOTES

1. Commission Communication C. (2008) 4051 final of 17 September 2008.
2. Commission Communication C. (2008) 4077 final of 19 September 2008.
3. Council Regulation (EC) No. 73/2008.
4. This summary was first published in *European Pharmaceutical Contractor*.
5. Joined Cases C-468/06 to C-478/06 *Sot. Lelos kai Sia EE and others v. GlaxoSmithKline AEVE Farmakeftikon Proionton* (16 September 2008).
6. Legal & Regulatory Update (2008). *Journal of Commercial Biotechnology* **14**, 327–347.
7. [2008] EWHC 2127 (5 September 2008).
8. http://www.phrma.org/code_on_interactions_with_healthcare_professionals/.