BIRD & BIRD

Life Sciences Update

October 2009

A periodical update on legal and regulatory developments in the life sciences sector

In this edition, we have reported on a range of recent developments, at EU and national level, relating to pharmaceutical patent litigation, regulatory updates and recent industry news. We hope you enjoy reading this update and are happy to address any comments or questions you may have, either through your usual contact or through any of the contacts on the back page of this update.

International Life Sciences Group

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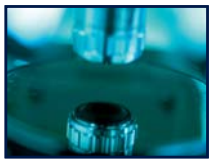
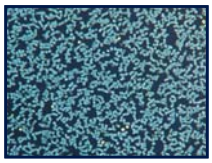
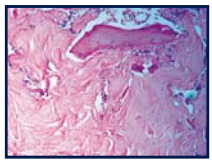
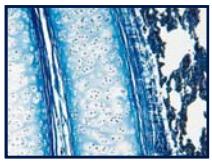
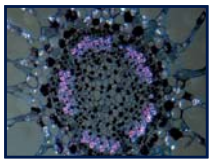
Legislative framework

Regulation 1768/92 (and Regulation 1610/96[1]) sets out the regime for granting SPCs in respect of medicinal products. SPCs provide the holder of a basic patent with an additional protection for medicinal products of up to a maximum of five years after patent expiry. The objective of SPCs is to compensate the patentee for th e lost period of effective patent protection of 20 years caused by the time taken during the life time of a patent for necessary safety and efficacy testing to be carried out to obtain marketing authorisation.

[1] The detailed rules in Article 3 (2) Regulation 1610/96, are also valid, mutatis mutandis, for the interpretation of Article 3 of Regulation 1768/92


In this case, the principal question related to the interpretation of Article 3(c) of Regulation 1768/92 in conjunction with Article 3(2) of Regulation 1610/96. Article 3(c) of Regulation 1768/92 lays down the basic rule that only one SPC per patent holder per product. Article 3(2) of Regulation 1610/96 provides that, where more applications concerning the same product and emanating from two or more holders of different basic patents are pending, one SPC for this product may be issued to each of these holders.

Background of the case

A European marketing authorisation was granted for the medicinal product "Enbrel" for the first time on 3 February 2000.

On 4 and 6 October 2000 and 30 January 2001, three SPCs were granted to three different patent holders. A further basic patent was subsequently granted to Hoffmann-La Roche, published on 2 April 2003. On 2 July 2003, Hoffmann lodged an application for an SPC for Enbrel. The Dutch patent office refused the application. On the basis of a strict interpretation of Article 3(2) of Regulation 1610/96, and the express reference therein to permitting a grant only where the SPC applications emanating from the different patent holders are pending, Hoffmann's application for an SPC was refused. The Dutch patent office found that since other SPCs for the same product had *already been granted*, other applications were no longer pending within the meaning of Article 3(2) of Regulation 1610/96.

The appeal court in The Hague decided to refer the issue to the ECJ for a preliminary ruling.

ECJ Ruling

The ECJ considered that the mere fact that SPCs have already been granted to other patent holders does not preclude the grant of an SPC to the holder of a basic patent for a product for which, at the time the SPC application is submitted, one or more SPCs have already been granted to one or more holders of one or more other basic patents.

Whilst the Dutch patent office ruled that more than one SPC applications for different patent holders could only be granted when other applications are still pending, the ECJ considered that such simultaneity of the applications could not be considered an essential condition for the grant referred to in the second sentence of Article 3(2) of Regulation 1610/96.

The ECJ considered that the strict textual interpretation of the word "pending", as had been applied by the Dutch patent office construing it as a strict condition for granting an application for an SPC to a subsequent patent holder, would effectively deprive the later applicant of the benefit provided for by SPCs. This would run contrary to the objective of the SPC Regulation. Moreover, the ECJ considered that if such a condition existed, the grant of an SPC could depend on an uncertain event which was outside the control of the applicant. As the Regulations do not contain any time limits to be taken into account by the national patent offices to reach a decision on an application, an applicant would be left solely at the discretion of national patent offices in obtaining his right to an SPC.

Clearly, the sooner a decision on an SPC application is taken by national patent offices, the less likely it is that two or more SPC applications are still pending. In other words, such condition would effectively deprive applicants of their right to an SPC in Member States where the decision-making process was efficient and would lead to disparities within the internal market. The ECJ considered that such a development would be contrary to the aim of the SPC Regulation, which was adopted to establish a uniform solution at Community level by creating a right to be obtained under the same conditions in each Member State.

The ECJ also referred to Case C-181/95 *Biogen* in which it had already been decided that the SPC Regulation did not seek to institute any preferential ranking amongst holders of national or European patents. *Biogen* had established that where a product is protected by a number of basic patents in force, which may belong to a number of patent holders, each of those patents may be designated for the purpose of the procedure for the grant of an SPC, although only one SPC may be granted for each basic patent. In *Biogen*, various patent holders had applied for SPCs simultaneously and therefore all applications would have been pending

within the meaning of Article 3(2) of Regulation 1610/96, whereas in the current case, the application was filed later, whilst the earlier application was no longer pending.

The outcome of this ECJ judgment is in line with the decision of the UK's IPO in its judgment of 16 November 2004 ([2004] RPC 24). However the reasoning was slightly different. The UK's IPO recognised that Article 3(2) of Regulation 1610/96 only addresses the situation where two or more applications are pending together and that this Article is merely a further interpretation of Article 3(c) of Regulation 1768/92. Therefore Article 3(2) is not applicable to the situation of successive applications for SPCs by different patent holders referring to the same product. On the basis of Article 3(c), the IPO found that where there are a number of patents in different hands, but protecting the same product, all holders of basic patents may be granted only one SPC. It should not be possible for one and the same patent holder to multiply the extent of protection under SPCs by obtaining successive SPCs.

The ECJ provides an interpretation of Article 3(2) in relation to successive SPC applications. The ECJ considers that the second sentence of Article 3(2) does not require that the applications be pending at the same time, hence there is no preferential ranking regardless of whether the applications are simultaneous or successive.

Machteld Hiemstra, The Hague

High Court's rejection of du Pont's UK paediatric SPC extension for Cozaar overturned by the Court of Appeal

In *E I du Pont Nemours & Co.'s SPC Application* ([2009] EWHC 1112 (Ch)) the High Court considered an appeal from a decision of the UK Intellectual Property Office to refuse a six month extension of a Supplementary Protection Certificate covering Cozaar (Losartan, an anti-hypertensive) under the Paediatric Regulation 1901/2006. Article 36 of the Paediatric Regulation (cross referred by Article 8 of the SPC Regulation 1768/92) requires the following at the time of the application for a six month extension:

- the inclusion in a marketing authorisation of a statement by the Competent Authority indicating compliance with the agreed Paediatric Investigation Plan (PIP) (Art 36(2)); and
- where the application for authorisation has been under Directive 2001/83, the product must be authorised in all Member States (Art 36(3))

The Paediatric Regulation amended the SPC Regulation so as to require (during a five year transitional period) applications for an extension to be filed at least six months before the expiry of the SPC (i.e. in this case by 1 March 2009). du Pont filed their application on 18 February 2009 but at that time, and indeed still at 1 March 2009, they could not comply with the conditions in Article 36. du Pont argued that it had substantively complied with the first requirement as a PIP had been complied with (only the inclusion of the statement in the marketing authorisation was missing). du Pont also argued that the second requirement had been complied with as a central authorisation for a paediatric syrup had been granted.

The High Court, in upholding the UK Intellectual Property Office's decision to refuse the the six month extension, found that an Opinion from the Paediatric Committee as to compliance with the PIP was not a satisfactory substitute for a statement from the Competent Authority; and that Article 36(3) of the Paediatric Regulation (i.e. the second condition) was to be interpreted having regard to Article 36 as a whole so that "product" meant the product defined in the updated marketing authorisation.

The judgment was appealed to the Court of Appeal ([2009] EWCA Civ 966). Jacob LJ, giving the leading judgment, held that:

- only a statement in the updated MA that the PIP has been complied with will suffice for the purposes of the first condition. The language used in the Article 36(2) was mandatory and made it clear that nothing short of this compliance statement will suffice.

A mere indication from the Paediatric Committee that the PIP had been complied with was in itself insufficient even though this was their final decision; and

- the authorisations to place the product on the market in all Member States as required by the second condition in fact refers to the need for modified MAs, updated to include the PIP compliance statement, to be in place.

As such, du Pont's application had not satisfied the requirements of Article 36.

However, where the application for a six month extension does not meet conditions set out in Article 8 of the SPC Regulation (which cross refers to the Article 36 conditions), under Article 10(3), the Comptroller shall ask the applicant to cure the "irregularity" within a stated time.

The question therefore was whether the lack of a PIP compliance statement and lack of updated MAs in all Member States amounted to an irregularity which du Pont should have been given the opportunity to cure. Jacob LJ declined to limit the scope of what might constitute an "irregularity" to only those matters which were missing from the application but which could have been produced at the time of the application or at least by the last moment on which the application could have been made. Instead Jacob gave "irregularity" a wide meaning to encompass also matters which only became capable of cure after the date of application. Taking a pragmatic view, he argued that the six month extension is a reward offered for complying with the PIP and getting the necessary updated MAs, and not for doing all of that before the application is made. Furthermore, to interpret "irregularity" more narrowly would be to put applicants at the mercy of Member States who may in fact fail to grant the updated MAs in a timely fashion.

Commenting on how late an applicant can be in supplementing its application with missing material, Jacob LJ said that in setting the Article 10(3) period, the Comptroller should take into account, inter alia, the failure to include all the materials in the application and the extent to which the applicant is guilty of unreasonable conduct or delay.

This decision now largely accords with the decision of the Dutch Patent Office to allow the extension. The Dutch Patent Office accepted (i) a PIP compliance statement dated 16 April 2009 and (ii) an end-of-procedure marketing authorisation notification dated 6 April 2009 (i.e. both dated after the 1 March 2009 deadline) from the Dutch Medicinal Evaluation Board (Competent Authority), having initially allowed du Pont to submit these documents out of time under Article 10.3 of the SPC Regulation (which requires Patent Offices to ask applicants to rectify irregularities within a stated time).

Gerry Kamstra & Ewan Grist, London

English Court of Appeal overturns Patents Court decision on obviousness in *Wake Forest University Medical Services v Smith & Nephew Plc*

The validity of Wake Forest's patent (EP (UK) 0620720) was in issue in two English cases running concurrently, *Wake Forest v Smith & Nephew* [2009] EWCA Civ 848 and *Mölnlycke Health Care AB v Wake Forest* [2009] EWHC 2204. The patent related to an apparatus for closing wounds and treating infection avoiding the localised stresses on the wound of suturing. It disclosed an apparatus for sealing open wounds by maintaining reduced pressure on the wound using an open-cell polymer foam covered by a flexible polymer sheet adhered to the skin surrounding the wound.

Mölnlycke Health Care AB commenced invalidity proceedings in March 2008 and the trial was listed for July 2009. At that time Mölnlycke had not released details of any potential product and so there was no counterclaim for infringement.

Smith & Nephew released details of a new product in December 2008 and Wake Forest commenced infringement proceedings. Wake Forest made an

application for an interim injunction prohibiting the launch of Smith & Nephew's product which was granted. As a consequence of this an expedited trial was listed for March 2009. Smith & Nephew counterclaimed for invalidity citing a single piece of prior art, Bagautdinov. It was directed that the two actions should proceed in parallel as at that time Mölnlycke had not yet cited Bagautdinov but relied on other pieces of prior art as well as insufficiency and added matter attacks. In addition, Mölnlycke would not be ready for the earlier trial date.

Smith & Nephew action

The Judge held at First Instance that all the claims pleaded were invalid except claims 4, 16 and 19 which were inventive over Bagautdinov. The Judge also held claims 4, 16 and 19 were infringed by Smith & Nephew's product. The parties appealed against the validity finding.

The Court of Appeal rejected Wake Forest's appeal in relation to novelty and held that claim 1 was anticipated by Bugautdinov. The Court upheld the Judge's finding that claims 4, 16 and 19 were novel.

As to obviousness, there was no challenge in relation to the nature of the skilled addressee or their common general knowledge as set out by the Judge. The Judge adopted an "anticipation or nothing" approach in assessing obviousness. The Judge held that the teaching and purpose of Bagautdinov was directed to draining wound secretions and not to wound healing. He held that there was no indication in Bagautdinov that would have led the skilled addressee to develop Bagautdinov to produce the wound healing apparatus of the patent. As such the Judge held that Bagautdinov could not be a starting point for assessing obviousness and therefore that claims 4, 16 and 19 were not obvious.

The Court of Appeal held that the Judge had failed to carry out an overall evaluation of the evidence in assessing obviousness. It considered that the Judge had made an error of principle in failing to apply *Pozzoli*. It is an established principle that an appellate court should exercise caution in overturning a finding of fact. However, as the Judge had adopted the wrong approach in assessing the obviousness of claims 4, 16 and 19 over Bagautdinov the Court of Appeal could make its own assessment.

The Court applied the *Pozzoli* approach to assessing obviousness and held that claims 4, 16 and 19 were obvious developments of the Bagautdinov apparatus. The claims of the patent were apparatus and not process claims. It held that application of the apparatus described in Bagautdinov by the skilled addressee using its common general knowledge to seal a wound would have led to an apparatus which infringed claims 4, 16 and 19.

Mölnlycke action

Wake Forest requested the Mölnlycke trial be adjourned following the Court of Appeal's indication (before giving reasons) that it would find the patent invalid. This was rejected on the basis that a delay in considering the additional cited prior art and arguments raised in the action would cause Mölnlycke commercial uncertainty. The Judge in this case held that claims 4, 16 and 19 were novel over Bagautdinov but were obvious both over Bagautdinov and another piece of cited prior art. The Judge also held that claim 1 was invalid for added matter owing to a post-grant correction. The insufficiency attack was not made out.

Emily Peters, London

English Patents Court holds long-wear contact lens patent invalid for insufficiency in *Novartis AG & Others v Johnson & Johnson Medical Limited & Others*

In *Novartis AG & Others v Johnson & Johnson Medical Limited & Others* ([2009] EWHC 2029) the English Patents Court found that Johnson & Johnson's product infringed the Patent, but that the Patent was invalid due to insufficiency.

Background

Novartis AG ("Novartis") is the exclusive licensee of EP 0 819 258 (the "Patent") for contact lenses which may be left in the eye overnight or for several days. It brought a patent infringement action against Johnson & Johnson ("J&J") which manufactures and sells its product Acuvue Oasys in the UK. J&J contested the infringement action and counterclaimed for invalidity.

A peculiar feature of the Patent is that its claims cover not only the materials from which the contact lenses may be manufactured, but the characteristics that they should display, such as ophthalmic compatibility, corneal health, wearer comfort, and their physical properties, such as oxygen transmissibility and ion permeability.

The common general knowledge at the priority date was that the ideal long-wear contact lens would have the correct balance of properties: transmission of oxygen through the lens to the eye, hydrophillicity to allow the lens to move across the eye and wettability so that a smooth, stable and continuous tear film is formed both behind and on the front of the lens when it is worn (to allow corneal health, good vision and comfort.)

The Patent seeks to describe a lens which will have the correct balance of all the required characteristics. However, J&J claimed that the Patent failed to explain how to manufacture a product with these characteristics.

Priority

J&J first contested the priority date of the Patent. If the earliest priority date was disallowed, they had two extra pieces of prior art which could invalidate the patent for lack of novelty.

The Patent claimed priority from three earlier applications. The first and second priority documents disclosed materials claimed in the Patent to make contact lenses. However they did not disclose the additional characteristics required by the Patent. An earlier document can found a claim to priority where it discloses the "same invention". This means that "the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole" (Article 87(1) EPC.) J&J argued that these documents could not be used to claim priority as they did not disclose the same invention. Novartis argued that the integers of the claims of the Patent could have multiple priority dates.

The possibility of partial and multiple priorities is addressed in Article 88(2) EPC: "Multiple priorities may be claimed in respect of a European patent application. [...] Where multiple priorities are claimed, time limits which run from the date of priority shall run from the earliest date." This provision has been interpreted in decision G02/98 by the Enlarged Board to mean that, where the claims are for integers A and B, multiple priorities are not allowed, whereas they are possible for an A or B claim.

The judge was therefore required to decide whether the claims could be divided into a limited number of clearly defined alternative subject-matters, some of which are disclosed and enabled by the first and second priority documents. He found that the features of the lenses listed in the claims could not be considered separate from each other. The additional characteristics are essential features of the invention and are not disclosed in the first and second priority documents. The Patent was therefore only entitled to priority from the date of the third priority document. This meant that the extra prior art asserted by J&J could be considered as it was disclosed before the newly established priority date of the Patent.

Novelty

J&J therefore claimed that the Patent lacked novelty under s 2(3) of the Patents Act 1977, on the basis of five of prior disclosures (Hopken, Domschke, Chang, Lai and Koegh). The test that must be applied in considering an allegation of anticipation was explained by the House of Lords in *Synthon v SmithKine Beecham* [2005] UKHL 59; [2006] RPC 10. The prior art must both constitute a prior disclosure and be enabling.

To constitute a prior disclosure the prior art must contain a clear description of, or clear instructions to make, something that would necessarily infringe the patentee's

claim if carried out after the grant of the patentee's patent. In respect of the disclosure, both parties agreed that there is insufficient information to determine whether the lenses in the prior art do or do not satisfy the requirements of the claim, without specific tests being carried out. The judge was therefore unable to conclusively decide that a prior disclosure had been made, so the lack of novelty attack was unsuccessful.

The issue of enablement was considered later in terms of sufficiency of the Patent.

Obviousness

The judge found that the patent was not obvious over the common general knowledge, as asserted by the defendants: "I am satisfied it was not obvious how to make a silicon hydrogel lens which was opthalmically compatible over a period of extended wear in the light of the common general knowledge at the priority date."

He also found that the patent was not obvious over the other prior art. J&J's claim for invalidity due to obviousness therefore also failed.

Insufficiency

J&J claimed, under section 72 of the Patents Act 1977, that the teaching of the Patent did not provide sufficient information for the person skilled in the art to make lenses falling within the claims without undue experimentation. The Patent should therefore be invalid for insufficiency as it does not provide a solution to the known problem of identifying a suitable material from which to make a lens which will meet the functional requirement of ophthalmic compatibility over a period of extended wear.

The judge agreed with J&J's argument that the description provides little or no practical assistance to the skilled person faced with this problem. He noted that there is no teaching in the Patent of a principle of manufacture and that the claimants themselves had acknowledged that it would only be possible to ascertain whether a product falls within the scope of the claims by carrying out a trial over a test period.

Infringement

The judge held that had the patent been valid the Acuvue Oasys lens would have fallen within the scope of claims 1 and 24, but not claims 8 or 11.

In claim 1, J&J only argued that their product did not infringe one of the elements of the claim: the oxygen permeability levels. The judge found that Novartis had shown that the Oasys lens infringed this part of the claim. Claim 24 required the product to have a hydrophilic surface, and the judge found that this was the case for the Oasys lens.

Claim 8 and 11 cover a polymeric material comprised of a plurality of co-continuous phases, at least one being an oxyperm phase (permeable to oxygen) and at least one other being an ionoperm phase (permeable to ions and water). The judge found that Novartis had not conclusively shown that the Oasys product fell within these claims.

Amy Williams, London

English Patents Court agrees with Dutch but not German court in *Occlutech GmbH v AGA Medical Corp and Another*

The English Patents Court was the third court in Europe to adjudicate on infringement *Occlutech GmbH v AGA Medical Corp and Another* [2009] EWHC 2013 (Ch).

Having reached diametrically opposed views on the construction of claim 1 of AGA's patent, the German court held Occlutech to infringe whilst the Dutch court found no infringement. The English judge agreed with the latter.

The patent claimed medical devices made of braided metal (typically Nitinol), whereby the devices when implanted have a generally dumbbell shape *"...characterised in that clamps (15) are adapted to clamp the strands at the opposed ends of the device."* The judge held the Occlutech devices did not infringe based on the construction of the word *"clamps"* and the phrase *"opposed ends of*

the device." He was not convinced that the patentee had made a "dictionary definition" in the specification for the word clamp. Although the specification referred to alternative methods of securing the ends, they were specified as alternatives only. It was not apparent to him why the patentee should intend to exclude such alternatives. However, the drafting of claim 1 was *"so clear that the actual wording cannot be ignored...and the relevant words cannot be extended beyond their natural wording..."* Instead of a clamp, the Occlutech devices were welded. Although welding was listed as an alternative to clamping in the specification, the word "clamp" within the claim did not extend to welding. Further, the Occlutech devices did not infringe as they were welded at only one end. Although not welded at *"opposed ends of the device"* the argument presented by AGA was that the Occlutech devices achieved the same functionality as the claimed invention. The judge was not convinced: *"[t]o adopt this approach is not successfully to adopt a purposive construction of the patent; it is to go way beyond what seems clearly to be a specific limitation, deliberately included, even though one cannot glean why that limitation might be there."* Accordingly, the Occultech devices do not infringe the UK patent.

The Düsseldorf Higher Regional Court construed claim 1 of the corresponding German designation of the patent wholly differently. Welding was included within claim 1 and a ring positioned over the welding of the Occlutech devices fulfilled the same purpose as a clamp. Although the court agreed that claim 1 described clamping at either end *"the average skilled person will not content himself with this mere linguistic understanding."* The technically meaningful understanding of the claim would not limit the skilled reader to two clamps or welds. Accordingly, the Occlutech devices infringe the German AGA patent.

The UK AGA patent was found valid by the English judge. The only prior art document was a Boston Scientific patent disclosing a knitted stent. Each of the braided metal, dumbbell shape, and clamping of claim 1 were not obvious and moreover when in combination there was a clear inventive step.

Jennifer Jones , London

Regulatory

New Commission Regulation (EC) No 668/2009 on certification of quality and non-clinical data relating to advanced therapy medicinal products

Article 18 of Regulation (EC) No 1394/2007 on Advanced Therapy Medicinal Products (ATMP) provides that Small and Medium-sized Enterprises (SMEs) developing an ATMP may submit to the European Medicines Agency (EMEA) all relevant quality and, where available, non-clinical data required in accordance with modules 3 and 4 of Annex I to Directive 2001/83/EC on the Community code relating to medicinal products for human use, for scientific evaluation and certification.

Provisions for the evaluation and certification of such data have been laid down by the European Commission in its Regulation (EC) No 668/2009, published on 25 July 2009 in the Official Journal of the European Union.

The certification procedure aims at giving the SMEs an incentive to develop ATMPs

regardless of any future application for marketing authorisation. It could, nevertheless, facilitate the evaluation of any future application for a clinical trial authorisation or a marketing authorisation application, provided that these applications are based on the same data.

Requirements

In order to be eligible for this new procedure, *applicants* must be (i) a micro, small or medium-sized enterprise, within the meaning of Recommendation 2003/361/EC, (ii) developing an ATMP and (iii) established in the Community.

To be valid, an *application* must contain:

(a) All information necessary to demonstrate the applicant meets all the requirements set out above;

(b) Indication as to the type and nature of the data submitted;

(c) Reference to any applications for certification previously submitted for the same product and related information;

(d) The relevant fee as provided for in Council Regulation (EC) No 297/95. According to the EMEA Rules for the implementation of Regulation (EC) No 297/95, the fees for this procedure will amount to €56,600 for the evaluation of an application relating to quality and non-clinical data and €37,700 for the evaluation of an application relating to quality data, respectively;

(e) The data referred to in module 3 of Part I of Annex I to Directive 2001/83/EC which is submitted for certification[2]; and

(f) Where the application relates to both quality data and non-clinical data, the data referred to in module 4 of Part I of Annex I to Directive 2001/83/EC which is submitted for certification[3].

In case of applications for certification relating to combined ATMP[4], additional requirements will apply in relation to the conformity of the medical device or active implantable medical device contained in the combined product with the essential requirements laid down in the relevant EU legislation[5].

In the CAT[6] Draft Procedural Advice (DPA) on the certification procedure, currently under consultation, further guidance on the procedure, timelines and dossier structure that SMEs should fulfill in order for the EMEA to issue its appropriate certificate are provided. According to this document, prior to the submission of the application for certification, the SME's status shall have been obtained by the applicant and a letter of intent, stating the reasons for the product being classified as ATMP, shall have been sent to the EMEA (i.e. CAT Secretariat) at the latest four months prior to submission.

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[2] For the purposes of compliance with this requirement, the application shall contain at least the following data: (a) general information and information related to the starting and raw materials; (b) manufacturing process of the active substance(s), with the exception of data on process validation; (c) characterisation of the active substance(s), limited to the data necessary to adequately describe the active substance(s); (d) control of active substance(s), with the exception of data on the validation of the assays; (e) description and composition of the finished product.

[3] For the purposes of the compliance with this requirement, the application shall contain at least the following data: (a) primary pharmacodynamic data supporting the rationale for the proposed therapeutic use; (b) pharmacokinetics bio-distribution data, if relevant to corroborate the primary pharmacodynamic data; (c) at least one toxicity study.

[4] "Combined advanced therapy medicinal product" means an advanced therapy medicinal product that fulfils the following conditions: (i) it must incorporate, as an integral part of the product, one or more medical devices within the meaning of Article 1(2)(a) of Directive 93/42/EEC or one or more active implantable medical devices within the meaning of Article 1(2)(c) of Directive 90/385/EEC, and (ii) its cellular or tissue part must contain viable cells or tissues, or (iii) its cellular or tissue part containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to (see article 2(1)(d) of ATMP Regulation).

[5] See Council Directive 93/42/EEC of 14 June 1993 concerning medical devices and Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices, respectively.

[6] Committee for Advanced Therapies.

Scope

The CAT is responsible for evaluating applications for certification. Interaction between the EMEA and the relevant notified bodies may be necessary in cases of combined ATMPs, which in same cases may also lead to an "extension" of the ordinary timeframe for such a procedure (i.e. 90-days procedure to be possibly extended, via a clock-stop, in case additional information is needed). The possibility for the CAT to request site visits of the premises where the ATMP concerned is being developed has also been provided. If the applicant accepts the conduct of a site visit, it shall be carried out by inspectors from the Member States who hold the appropriate qualifications.

According to the DPA, the evaluation performed under Article 18 of the ATMP Regulation is intended to certify that each submitted study complies with the relevant scientific and technical requirement set out in the Annex I to Directive 2001/83/EC and adequately follows state-of-the-art scientific standards and guidelines.

For these reasons, the scientific and technical requirements followed by the CAT when assessing the data submitted for certification, will be the same applicable to the evaluation of a marketing authorisation. Not all sections as defined by part I of Annex I to Directive 2001/83/EC may however be completed for the application for certification.

Moreover, in order to distinguish between this new procedure and existing procedures (namely, scientific advice procedure), it is provided that the certification procedure will focus only on scientific evaluation of existing experimental data (quality/non-clinical). No advice as to further development of the product will be provided. In case the latter information is needed the appropriate procedure should have to be applied for (i.e. scientific advice).

In the same vein, a certificate is not intended to conclude either on the benefit/risk profile of the product or on the adequacy of the studies submitted for the product to be further developed in a clinical trial. The latter is the scope of a separate procedure, under the responsibility of the National Competent Authorities where the clinical trial will be conducted.

The Commission Regulation does not provide for any time limit for an application for certification to be submitted. An application for the certification can therefore legally be submitted at any time of the development of an ATMP. However, the DPA appears to be more restrictive in this regard when providing that a minimum quality and where available non-clinical data package will have to be submitted to allow for certification.

Outcome

If appropriate on the basis of the evaluation, the EMEA will issue a certificate identifying the quality and, where applicable, non-clinical data submitted and the corresponding testing methodologies followed by the applicant, which have been found acceptable in terms of regulatory compliance and scientific robustness. This certificate will not be binding with regard to any future regulatory procedure and all relevant data, even if already certified, and should be submitted again for the purpose of any future regulatory procedure.

In principle, the certificate should help EU SMEs to increase profits out of the R&D performed (e.g. by selling at a more profitable price their early-stage products or by attracting interested investors).

In practice, the actual value of the Certificate will mostly depend on: (i) the stage of development of the ATMP at the time when the Certificate was issued and (ii) any additional changes introduced to the ATMP after the Certificate was firstly issued.

In this regard, the DPA addresses a clear reminder to applicants that if a certificate is granted during early development its relevance/validity is likely to be limited.

Applicants may wish to follow the DPA of the CAT, according to which the optimum time point to apply for the certification procedure is when the ATMP has reached a level of sufficient development with respect to quality and non-clinical data.

Indeed, although from a legal point of view nothing prevents applicants from requesting certification of their data very early in the development of their products

and to "update" their certificate as much as they might consider it necessary, the fee requested for each procedure as well as the "minimum" data requirements could act as serious deterrents to use this procedure too soon or too recurrently.

Furthermore, the fact that a list of "issues" as regards compliance with the above mentioned scientific and technical requirements for future consideration by the Applicant may be included in the evaluation report attached to the certificate as well as the possibility for the EMEA to issue a "refusal letter" whenever the opinion is negative, might also have an impact on the decision of a company as to if and when an application for certification should be submitted.

In a subsequent development relating to ATMPs, Commission Directive 2009/120/EC of 14 September 2009 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use as regards advanced therapy medicinal products, published in the Official Journal of 15 September 2009, and to be implemented no later than 5 April 2010, amends Annex I to Directive 2001/83/EC as regards ATMPs. It updates the definitions and detailed scientific and technical requirements for gene therapy medicinal products and somatic cell therapy medicinal products and establishes detailed scientific and technical requirements for tissue engineered products, as well as for advanced therapy medicinal products containing devices and combined advanced therapy medicinal products.

Mauro Turrini, Italy

Medical devices transferred to a new authority in Finland from November 2009

Monitoring the manufacture and marketing of medical devices will become part of the National Supervisory Authority for Welfare and Health, i.e. Valvira, as of 1 November 2009.

Valvira was established as a result of the merger of the National Product Control Agency for Welfare and Health (STTV) and the National Authority for Medicolegal Affairs (TEO) on 1 January 2009. Valvira (www.valvira.fi) shall improve the management of health risks in the environment as well as legal protection and the quality of services in social welfare and health care.

As reported in the previous Life Sciences Update, the Finnish Medicines Agency ("Fimea"), a new state authority for medicines in Finland, will start running its operations on 1 November 2009 as well. In connection with the establishment of Fimea, the Finnish National Agency for Medicines (the "NAM") will be abolished and the activities will be transferred from the capital Helsinki to the city of Kuopio located about 400 kilometers from Helsinki.

Fimea will handle the present tasks of the NAM associated with authorisation and supervision of medicinal products. However, as part of the reorganisation of the administration of health care and social welfare in Finland, the functions of the Medical Devices Department of the NAM will be transferred to Valvira.

Ella Mikkola, Finland

Industry

Judgment of the European Court of Justice in the GSK dual pricing case

The European Court of Justice ("ECJ") has given judgment on the appeals of the European Commission, GSK and two trade associations against the judgment of the European Court of First Instance ("ECFI") in the GSK dual pricing parallel exports case, *Joined Cases C-501/06P, C-515/06P and C-519/06P, GlaxoSmithKline Services Unlimited, formerly Glaxo Wellcome plc v Commission and Commission, EAEPC and Aseprofar v GlaxoSmithKline Services Unlimited, formerly Glaxo Wellcome plc*.

The ECJ has dismissed all of the appeals. This means that the European Commission's decision of May 2001 that the Spanish dual pricing arrangement of GSK (then Glaxo Wellcome) infringes Article 81(1), is upheld. However, the annulment of the Commission's decision to refuse exemption under Article 81(3) is confirmed. In this respect the ECFI's judgment is now upheld by the ECJ.

The dual pricing scheme was contained in GSK sales conditions providing for dual pricing for supplies in Spain, with a higher price being charged for sales for exports, so as to avoid the low prices imposed by Spanish regulation for the domestic market. The case is of considerable interest on a number of levels, especially the statements in the ECFI judgment concerning the importance of assessing the full economic and regulatory context of the pharmaceutical sector as regards the eligibility of an agreement in the pharmaceutical sector for Article 81(3) exemption. The Article 81(3) exemptions criteria can be applied where, broadly speaking, the benefits of an agreement through improved efficiency and benefits to consumers outweigh the disadvantages of the agreement's restrictive effects.

The ECFI also went further in the context of the Article 81(1) assessment, stating that some disadvantage to consumers must be shown in order for the agreement to infringe Article 81(1) by *object*. However, it is noteworthy that the ECJ has held that an agreement that impedes parallel exports is to be treated generally as having a restrictive *object* and as therefore infringing Article 81(1) without need to assess the existence of any restrictive *effect*. The ECJ stated that issues of consumer disadvantage fall to be considered only as part of the Article 81(3) assessment. (The ECJ thus followed the Opinion of the Advocate General Trstenjak of June 2009, as summarised in the July issue of this Bulletin).

Glaxo Wellcome notified its conditions for the sale of products to wholesalers in Spain to the European Commission in 1998, seeking Article 81(3) exemption. These sales conditions required higher prices for products to be exported, though Glaxo Wellcome argued that this was in reality a single price for all sales in Spain subject to reductions in prices imposed by regulation for sales for domestic consumption (reimbursed by the Spanish health authorities). The company aimed to prevent "export" of the artificially low price imposed by regulation on the Spanish market, in order to preserve revenue for future research and development. The European Commission found that the arrangement infringed Article 81(1) and refused Article 81(3) exemption, stating that *"a pricing policy which makes it economically uninteresting for wholesalers to indulge in parallel trade must be considered to be at least as effective as an outright contractual export ban"*. GSK argued that parallel trade primarily benefitted parallel traders rather than the consumers of the healthcare system of the importing state, whilst reducing manufacturers' capacity to finance R&D. The Commission concluded that Glaxo Wellcome had failed to prove any causal link between parallel trade and R&D investments, or that parallel trade had disrupted its distribution system or, most importantly, that the exemption criteria of Article 81(3) were fulfilled.

On appeal, the ECFI concluded that the contractual conditions did not have the *object* of restricting parallel trade, but did have the *effect* of restricting competition. The ECFI concluded that a finding of a restriction by *object* would require an indication of a reduction of the welfare of consumers, in terms of price. It also

concluded that the Commission had been wrong to reject GSK's arguments in favour of Article 81(3) exemption concerning the strong levels of pharmaceutical sector competition of innovation, the need for sufficient levels of profitability for R&D investment (innovation), and the need for such profits to be generated globally despite the significant differences between Member States' health systems and price controls. Therefore, the ECFI annulled the Commission's rejection of GSK's Article 81(3) application. It held that the Commission was required to undertake a prospective analysis to determine whether the disadvantages to intra-brand competition were offset by efficiency advantages through improved inter-brand competition at the innovation level. The ECFI held that the Competition should balance the restrictive effects of the agreement against the evidence of likelihood of the Article 81(3) arguments being fulfilled.

The most interesting aspect of the ECJ judgment is the ruling on GSK's claims that the ECFI had interpreted Article 81(1) incorrectly in finding that the agreement had an anti-competitive effect. GSK argued that the agreement could not have the effect of restricting competition in the sense of reducing consumer welfare, against the background that parallel importers retained most of the margins for themselves (as between the prevailing price levels in the Member States of export (Spain) and import). By contrast, the Commission argued in its appeal that the ECFI's findings concerning restrictive effect showed that the agreement actually had a restrictive *object* and that the ECFI had misinterpreted the term "object" in Article 81(1). The European Commission and the trade associations also appealed against the ECFI's annulment of the Commission's rejection of GSK's application for Article 81(3) exemption.

The ECJ stated that in order to assess the anti-competitive nature or object of an agreement, it is necessary to consider the content of its provisions, the objectives it seeks to attain and the economic and legal context of the agreement. The ECJ treated it as an established principle that agreements aiming to prevent or limit parallel exports have the object of restricting competition contrary to Article 81(1), as has been held by the ECJ in several previous cases. Further, the ECJ stated that there is nothing in Article 81(1) to indicate that agreements must deprive consumers of certain advantages in order to have an anti-competitive object, as had been stated by the ECFI. Rather, Article 81EC aims to protect not only the interests of competitors or of consumers, but also the structure of the market. Therefore the ECFI had committed an error of law in failing to conclude that GSK's agreements had such an anti-competitive object.

On the basis that the ECFI did find that the agreement infringed Article 81(1) (albeit by means of its restrictive *effect*), and on the basis that the anti-competitive object and effect of an agreement are not cumulative but alternative conditions for assessing whether an agreement is within the scope of Article 81, the ECJ concluded that GSK's claim that the agreement did not have an anti-competitive effect was unfounded.

The European Commission and the trade association appellants made various further claims to the effect that the European Commission had committed errors of law or reasoning in relation to the application of Article 81(3). The Commission alleged that the ECFI had misapplied the case law relating to the allocation of the burden of proof and the standard of proof and the causal link necessary for the application of Article 81(3), as between the restrictive features of the agreement and the claimed advantages or efficiencies in terms of research and development or innovation.

In its judgment on the Article 81(3) claims, the ECJ stated that the ECFI's role as an appeal court carrying out a review of the European Commission's decision must be limited to verifying whether the rules on procedure and on the statement of reasons have been complied with, whether the facts have been accurately stated and whether there has been any manifest error of assessment or misuse of powers. The ECFI could carry out only a limited review of the merits of the case and it was not for the ECFI to substitute its economic assessment for that of the Commission. The ECJ concluded on each of the Commission's (and the appellant trade associations') claims that the content of

the ECFI's judgment did not reveal any error of law or inadequate reasoning.

The ECJ held that the Commission had erroneously failed to take into account the specific structural features of the pharmaceutical sector highlighted by GSK in its notification, and that the Commission had failed to demonstrate whether or not GSK's sales conditions would entail a gain in efficiency of competition. It accordingly held that the European Commission's assessment had been insufficient for Article 81(3) purposes.

With regard to the benefits of the arrangement for the financing of R&D, the ECJ specifically held that, contrary to the Commission's assertions, the existence of an objective advantage for Article 81(3) purposes did not require that all of the funding resulting from the operation of the GSK sales conditions must be invested in R&D. The ECFI had been entitled to conclude that it was sufficient that part of the increase in profits resulting from the restriction of parallel exports would go to R&D expenditure.

The ECJ rejected the Commission's further claim that the ECFI had created a new category of reviewable error ("lack of serious examination") which is outside the scope of a proper review in an Article 81(3) context. Rather, the ECJ concluded that the ECFI had merely found that the Commission had not taken into account all of GSK's factual arguments and relevant evidence. The Commission's examination was held not to be sufficient to support the conclusions it had reached, by reference to GSK's claims concerning the need for R&D to be funded globally despite the differing price and regulatory controls as between the Member States.

Comment

The judgment of the ECJ re-establishes the case law prior to the ECFI judgment, that restrictions of parallel trade, in particular parallel exports, will generally be regarded as a per se infringement of Article 81(1), as a restriction of competition by object. This avoids any need to assess the existence of any anti-competitive effects of such an agreement.

As regards the application of the Article 81(3) exemptions criteria to an agreement restricting parallel exports, the ECJ confirmed the ruling of the ECFI that a prospective analysis of the efficiencies and other advantages of such an agreement (in terms of R&D and innovation) needs to be made as against the disadvantages of the restrictive effects of such an agreement. For this purpose, a court or body applying Article 81(3) to such an agreement needs to balance the benefits to inter-brand competition at innovation level with the restrictions of competition at intra-brand level, by comparing the benefits to R&D funding (resulting from the restriction of parallel trade) with the loss of choice of alternative supplies which can result from the restriction of parallel imports. Most significantly, the ECJ has confirmed that the specific legal and economic context of the pharmaceutical sector should not be taken into account in assessing whether an agreement has the *object* of restricting competition under Article 81(1), but rather is relevant in the application of Article 81(3).

The result of the ECJ's judgment in relation to GSK's sales conditions is that there is still no valid European Commission decision on GSK's notification for exemption. The Commission is now supposed to reassess its original decision even though, since the introduction of the "modernisation", self-assessment regime as from May 2004, the Commission no longer operates a notification-based system of Article 81(3) decisions.

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