**ES- TEVA PHARMA & RATHIOPHARMA ESPAÑA v. LA ROCHE AG**

**Teva Pharma S.L.U. & Ratiopharma España S.A. v. F. Hoffmann La Roche AG, Provincial Court of Barcelona, Section 15, Spain, 22 May 2017, Appeal Docket Number: 739/2015.**

In May 2017, Section 15 of the Barcelona Court of Appeals declared the nullity of patent ES 2.083.348 (ES 348), the Spanish part of patent EP 0.694.547 B1 (EP 547), owned by La Roche AG, due to lack of inventive step. Patent ES 348 protects the drug valganciclovir (monoester L-valinate of ganciclovir) and its salts, a process for preparing that compound and the use of the compound for the preparation of pharmaceutical compositions for the treatment of antivirals and related diseases. Valganciclovir is a prodrug of ganciclovir whose oral bioavailability is much higher than that of ganciclovir.

Teva Pharma S.L.U. (hereinafter, “Teva”) and Ratiopharma España S.A. (“Ratiopharma”), filed a lawsuit against F. Hoffmann La Roche AG (“Roche”) claiming the invalidity of patent ES 348 due to lack novelty and inventive step, based on the following prior art documents: EP 0.375.329 A2 (EP 329), GB 8829571 (GB 571) and the “*Druckexemplar”* of the patent application EP 329.

Initially, Roche defended the validity of the patent as granted and, *ad cautelam,* in case the Court understood that the current wording of the claims lacked novelty and/or inventive step, Roche requested one main amendment of claim 1 and two subsidiary amendments in order to limit the scope of protection of patent ES 348. Later on, Roche asked the Court to agree to the limitation of patent ES 348 according to the terms of the “most subsidiary” amendment request, and in the absence of opposition by the plaintiffs, Commercial Court No. 5 accepted the limitation during the pre-trial hearing.

Finally, after the amendment, claim 1 no longer protected the use of valganciclovir as such, but instead protected the use of valganciclovir hydrochloride in the form of mixtures of its (R)- and (S)- diastereomers, as a therapeutically-active agent.

After said amendment, the plaintiffs dropped the novelty attack but maintained the lack of inventive step attack. Barcelona Commercial Court No. 5 rendered its decision on September 14, 2015, declaring the nullity of ES 348 due to lack of inventive step.

Roche appealed said decision, alleging lack of reasoning and wrongful assessment of the evidence. It argued, among other reasons, that the Commercial Court had not correctly applied the problem-solution approach and that it had taken into account the *Druckexemplar* of the patent application EP 329 which, according to Roche, was not prior art with regard to EP 547.

Teva and Ratiopharma opposed the appeal, requesting the confirmation of the First Instance decision. The opposition to the appeal highlights an essential fact: voluntary modification of the patent at stake. Thus, Roche declined to defend the patentability of valganciclovir as protected by the granted patent, and added three features:

1. It must be presented in the form of hydrochloride salt
2. It must be in the form of mixtures of its diastereomers.
3. It must be used as a therapeutically active agent.

The plaintiffs also considered that none of the features added to the patent by means of the limitation conferred inventiveness to the patent’s subject-matter.

Both parties filed new exhibits before the Court of Appeals. The defendant filed an expert report drafted by an Italian expert appointed by the Court in the proceedings followed before the Courts of Milan that had heard the validity of the Italian part of EP 547. On the other hand, Teva and Ratiopharma filed the decision of the German Federal Supreme Court, issued on December 6, 2016, which concluded that the patent at stake was void. The Court of Appeals accepted the filing of the German decision but expressed its doubts regarding the filing of the expert report. The plaintiffs further contended that the submission of the opinion at that procedural stage prevented the parties from requesting clarification from the expert or submitting new evidence to contradict the expert’s conclusions.

However, the Court of Appeals understood that said report had been prepared based on the grounds alleged in the Italian procedure, which may not have coincided with those invoked in Spain, and that it has less evidentiary value than a foreign judgment. Finally, the expert report was admitted as another exhibit, not as an expert report per se.

Regarding the incorrect application of the problem-solution approach, it is important to establish the different positions of the parties with regard to the technical problem the patent sought to solve.

On the one hand, Teva and Ratiopharma, as well as the First Instance decision, considered that the technical problem to be solved was the low oral bioavailability of ganciclovir. This conclusion is drawn from the description of the patent where it is claimed that it would be highly desirable to provide ganciclovir with an improved oral absorption profile. Therefore, both the Commercial Court and the plaintiffs considered the *Druckexemplar* to be the closest prior art document since it expressly mentions valganciclovir and teaches that it makes it possible to increase the oral bioavailability of ganciclovir.

On the other hand, Roche believed that the technical problem in question was how to improve the oral bioavailability and toxicity of bis L-valinate ester of ganciclovir.

Based on the opinion issued by the European Patent Office (hereinafter, “EPO”) Examining Division on June 5, 1997, during the prosecution of the patent at stake, as well as its description, the Court of Appeals agreed with the First Instance decision and the plaintiffs concerning the technical problem that patent EP 547 sought to solve, that being the low oral absorption of ganciclovir. On the basis of the technical problem established, the Appeals Court decided that the prior art to consider when applying the problem-solution approach was both patent application EP 329 and the *Druckexemplar* of said patent application EP 329.

In the present case, the discussion about the possibility of considering the *Druckexemplar* as a prior art document is particularly interesting. By way of background, the *Druckexemplar* is the final text of the patent application proposed for granting by the EPO. The *Druckexemplar* of patent application EP 329 was made publicly accessible on May 9, 1994, almost three months before the priority date of patent ES 348.

Roche rejected the argument that the *Druckexemplar* had been made accessible to the public and, consequently, considered that it was not prior art according to Article 54 EPC. Roche stated that this document was sent by mail on May 9, 1994, to the applicant of patent EP 329 (The Welcome Foundation LTD); therefore, only the patent holder had access to it before the priority date of ES 348 (July 28, 1994). At that time, the European Patent Register was not accessible via the internet; therefore, the sending of the *Druckexemplar* was not recorded. According to Roche, given the short time period elapsed between May 9 and July 28, 1994, it was impossible for third parties to potentially find said document.

The Court of Appeals agreed with the conclusions reached in the First Instance decision, which accepts the *Druckexemplar* as the closest prior art document. The Court refers to articles 54.2 and 128.4 EPC, which stipulate that European patent application files can be inspected and are, therefore, publicly accessible from the date of publication.

As the Commercial Court stated in the appealed decision, it is not necessary to demonstrate that certain information has been accessed for accessibility to exist. The mere possibility of a third party accessing a document implies that it is part of the state of the art.

In this case, the communication from the Examination Division to the holder of patent EP 329 was carried out in accordance with the provisions of Article 51.4 of the Implementing Regulation of the EPC, which is a formality in the proceedings before the European Patent Office covered by article 128.4 EPC. Considering that the “*Druckexemplar”* is part of the dossier for the prosecution of a previously published European patent application, all the documents that the dossier comprises are subject to public inspection and, consequently, are part of the state of the art. Therefore, it is not mandatory to prove the effective knowledge of the document; the mere fact of its availability is enough to consider that said document is part of the state of the art.

The Court of Appeals agreed with the conclusion reached by the First Instance Court regarding the lack of inventive step of patent ES 348 concerning claim 1 in its limited version. Starting from the closest prior art document, the “*Druckexemplar”*, the solution provided by patent ES 348 would be obvious for the expert in the field since said document mentions the two suitable solutions to increasing the oral bioavailability of ganciclovir, mono and bis L-valine ester of ganciclovir, without any preference for one over another. The “*Druckexemplar”* refers to both the mono (valganciclovir) and the bis-ester valine of ganciclovir, and according to said document every amino acid ester of valine (mono and bis) “*surprisingly”* presents *“an advantageous bioavailability when orally administered”*.

On the other hand, the Court of Appeals also considered that none of the three features added to claim 1 of patent ES 348 by means of its limitation supported the presence of inventive step since it is not possible to sustain the inventive step of the amended patent by arguing the specific properties of valganciclovir.

In this regard, the Court of Appeals highlighted that the same decision was reached by the German Federal Supreme Court on December 6, 2016, which upheld the judgement of the Federal Patent Court, dated July 8, 2014. The validity of the same patent was analyzed before the German Courts based on the same reasons, and the same prior art was invoked (EP 0.375.329 A2 (EP 329), GB 8829571 (GB 571) and the “*Druckexemplar”* of the patent application EP 329).

The German Federal Supreme Court accepted that the *Druckexemplar* had been made available to the public before the priority date of the patent at stake, since the official EPO dossier was available for public consultation.

