How to Deal with Unusual Prior Art in the Determination of Inventive Step?

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The EPO's Problem-Solution-Approach is, on the face of it, simple and widely applied also in the national jurisprudence of the EPC member states. It starts with the determination of a "closest prior art document" (CPAD) which is to serve as the starting point of the further analysis. It is then evaluated which technical differences exist between this closest prior art document and the claimed invention, and which problem the claimed invention objectively solves over this CPAD. Thereafter it is examined whether it was obvious to solve this objective problem in the way as the claimed invention does. Both the closest prior art document itself, as well as further prior art documents and the skilled person's common general knowledge are scrutinized in regard to this question. A combination of two or more documents usually requires a motivation or pointer for it to be obvious.
So far, so good. But what happens if the closest prior art document is not enabled, or if the results it describes are not reproducibly obtainable, because essential information is missing? And what if the secondary prior art document arguably discloses some of the information missing in the CPAD, but in a quite different context and without essential information that could motivate the skilled person to take it further and use it in the context of the CPAD?

These interesting legal questions formed the backdrop before which multi-national patent litigation and two EP opposition proceedings unfolded [disclosure: this author has been involved in several of these proceedings on behalf of the patentee]. More specifically, the lawsuits revolved around a patent family concerning a formulation for AstraZeneca's successful breast cancer drug fulvestrant (Faslodex®), of which aspects have already been discussed on this blog here (NL) and here (DK). A decision by the Higher Regional Court of Düsseldorf in another patent family relating to a further medical use of fulvestrant has also been reported lately on this blog.

Two members of the formulation patent family stand out: EP 1 250 138 and its divisional EP 2 266 573. Both patents refer to a specific formulation of the antiestrogen drug fulvestrant and its use in the treatment of breast cancer via intramuscular injection. The '138 patent was granted based on claims directed to the formulation as such. A subsequently filed opposition was rejected and the patent maintained as granted. On appeal, however, a third party introduced a new reference ("McLeskey") that was said to disclose a formulation falling under the claims of EP'138 and thus appeared to be highly relevant in regard to these claims. However, this formulation was only used in the quite different context of an exploratory mechanistic study looking at a different (estrogen-independent) type of breast cancer, against which this formulation showed no efficacy even at extremely high doses, when given to transfected mice via weekly subcutaneous injections. McLeskey also contained no data about the physical properties of the formulation, its pharmacokinetics and, in particular, its safety, its efficacy against estrogen-dependent breast cancer and the duration of its effect.

Following the introduction of "McLeskey", the Board of Appeal remitted the case back to the first instance where AstraZeneca amended the claims of EP'138 into "formulation for use" claims, arguing that the use of McLeskey's formulation for the treatment of breast cancer was neither disclosed in McLeskey nor obvious therefrom. The Opposition Division agreed and maintained EP'138 in the thus-amended form. As the sole opposition had been withdrawn before the OD's decision and no appeal was filed, this decision became final.

In the meantime, the divisional EP'573 was also granted with "formulation for use" claims and opposed by five generic manufacturers. The opposition grounds raised were added subject-matter (Art 76 / Art 123(2) EPC), lack of novelty (Art 54 EPC), lack of inventive step (Art 56 EPC) and insufficient disclosure (Art 83 EPC). The inventive step argument used by the opponents was mainly based on the assertion that the patent is not inventive over a combination of CPAD "Howell" (used as starting point) with "McLeskey".

Howell was used as CPAD by the Opponents, since it described a Phase II clinical trial, in which a formulation containing 50 mg/ml fulvestrant in a castor oil-based vehicle was intramuscularly administered to patients having a tamoxifen-resistant breast cancer. However, undisputedly, the reference did not disclose the complete formulation that had been used in this clinical study. In particular, Howell was missing a disclosure of the co-solvents needed to provide the desirable physical and biological properties of the formulation tested. Yet it was precisely the composition of these co-solvents which formed the core of AstraZeneca's patented invention. AstraZeneca therefore argued that Howell was not enabled, or that at least the therapeutic success shown in Howell should not be assigned to the state of the art (because Howell's results were not made available to the public in a reproducible way). In fact, according to AstraZeneca it was the opposed patent that disclosed for the first time a formulation that was safe, efficacious and provided the necessary even release of therapeutic levels of fulvestrant, so that it enabled its use as a long-acting depot preparation in the treatment of breast cancer by intramuscular administration. These effects should therefore go into the objective technical problem solved by the EP'573 patent, rather than be assigned to Howell. AstraZeneca further argued that there was no pointer in McLeskey for the solution of this problem.

While these arguments proved to be successful when defending EP'138 in opposition proceedings before the EPO, a different EPO Opposition Division revoked the EP'573 for lack of inventive step in view of Howell in combination with McLeskey. This led to a bit of a "rollercoaster ride" (as Presiding Judge Kircher of the Regional Court of Mannheim quipped) for both parties in the numerous national infringement and revocation litigations between AstraZeneca and its generic competitors who used exactly the formulation claimed and exemplified in both patents. Due to the two diverging decisions of the EPO, i.e. the maintenance of EP'138 on the one hand and the revocation of EP'573 on the other hand, the results of the national infringement and nullity courts were likewise inconsistent: In some countries (e.g. Denmark, Italy) the generics were initially successful, in other countries (e.g. Finland, Greece, Scotland) AstraZeneca prevailed, and in others (e.g. Germany, the Netherlands, Spain, Switzerland) the outcome varied from instance to instance.

But the story continues. AstraZeneca appealed the first instance EPO decision relating to EP'573, and oral proceedings took place before the Technical Board of Appeal 3.3.01 on 23.1. and 24.1.2019. These proceedings ended with a significant success for AstraZeneca: The Board of Appeal ruled that the decision by the opposition division is set aside and that the oppositions are rejected. That is, the EP'573 patent was maintained as granted.

In addition, also the Court of Appeal of the Netherlands and the Swiss Bundesgericht recently issued important decisions in favour of the patentee. By now, AstraZeneca has won 9 recent decisions (CH appeal, 2 * GR, 2 * PL, FI, SE, NL appeal and EPO appeal) and obtained one favourable technical opinion in the ongoing Swiss proceedings. Thus, although several proceedings are still ongoing and each and every court is (and should of course be) autonomous in its decision-making, it seems that the rollercoaster ride is levelling out and that the national courts and the EPO are converging in finding that a combination of the unreproducible CPAD Howell with McLeskey does not render the invention underlying AstraZeneca's patents obvious.