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Hospira clears the way for generic Herceptin

Brian Cordery (Bristows) · Tuesday, April 15th, 2014

The development of Herceptin (trastuzumab) in the late 1980s and 1990s is one of the most remarkable advances in the treatment of breast cancer. The story of the drug and its pioneer, the "velvet jackhammer", Dennis Slamon, is neatly summarised in Siddhartha Mukherjee's award winning novel: "*The Emperor of All Maladies – a Biography of Cancer*" – a fascinating if not necessarily uplifting read.

In short, unlike traditional chemotherapy, trastuzumab is a monoclonal antibody which specifically targets a receptor known as HER-2 which is involved in the development of breast cancer. No-one disputes that the development of Herceptin was a landmark advance in the field of oncology – an area which above all others in medicine is full of uncertainty and false dawns.

Genentech had a compound patent to trastuzumab, the SPC for which will expire in July 2014. This was not challenged. However Hospira were aware of two additional patents held by Genentech in relation to a dosage regimen for trastuzumab and a composition of trastuzumab with less than certain thresholds of certain impurities. Both patents had been held invalid by the EPO Opposition Division but appeals to the TBA were pending. Therefore Hospira sought to invalidate the patents in the English Patents Court.

Following nine days of argument in Court in March, Birss J issued his judgment on 10 April 2014, finding both patents invalid, and also granting Hospira a declaration of non-infringement in respect of certain trastuzumab formulations.

The judgment contains a number of significant legal points, particularly in relation to the dosage regimen patent. This patent was essentially to a dosage regimen whereby the trastuzumab was administered to a breast cancer patient every three weeks, in contrast to the weekly dosage which was in use at the priority date of the patent. Claim 1 was in Swiss-type form which will be familiar to many readers as "*use of X in the manufacture of a medicament for the treatment of Y*". Two of the most interesting legal issues, said to be common ground between the parties, related to claim construction for Swiss-type claims. The first was that it was agreed that "treatment" in the context of a Swiss-type claim means that the treatment is a functional technical feature – i.e. the claim is to something which is indeed an effective treatment – in this case for breast cancer. The second was that in the context of second medical use patents, "for" does not mean "suitable for" but rather "suitable for and intended for". Although noting that these aspects of claim construction were necessary to confer novelty on the claim over a proposal to administer the drug in the manner claimed, Birss J observed that clinical data was not always demanded in such patents. However

plausibility was required by both the EPO (T609/02 **Salk**) and the UK Courts (**Regeneron**). Having construed the dosage regimen claim, the Judge considered the allegation of obviousness and in particular the prior art label for Herceptin from the US FDA which described a once weekly regimen with the chemotherapeutic agent paclitaxel being administered every three weeks. Birss J described a notional exercise involving the clinician consulting with a pharmacokinetics expert about the possibility of a three weekly regimen, and held that "*there was no reason on pharmacokinetic grounds not to conduct the trial*". In the circumstances, the Judge held that the patent was obvious over the FDA label for Herceptin combined with the common general knowledge. Having come to this conclusion, the Judge did not need to consider sufficiency. However, citing the leading Court of Appeal decision in **Regeneron** which held that the scope of the monopoly, as defined in the claims, must correspond to the technical contribution that the patentee has made to the art, the Judge held, *obiter*, that if the patent did involve an inventive step, then the skilled team would not conduct a clinical trial of the claimed three weekly dosage regimen on the basis of the information in the patent. Thus, if it involved an inventive step, the patent would be bad for insufficiency.

Finally on the dosage regimen patent, entitlement to priority was challenged and Genentech accepted that if priority was lost, the patent was invalid. Birss J noted the requirement for the priority document to provide an disclosure of the invention but also that "*in a specification filed without claims, the various features found in the claim of the granted patent are unlikely to be written out in a neat paragraph*". This is an interesting observation and probably of more general application since it is settled law that the content of any claims in the priority document is not crucial – the overall technical disclosure is what matters. The Judge also reluctantly disagreed with the TBA decision in **Gemvax** (T903/05) which had held that plausibility was not a requirement for priority. Rather Birss J held that an "enabling disclosure" was needed as has been the law in the UK since at least the **Biogen** case in 1997. Overall, the Judge held that the priority document satisfied the "pure disclosure" requirement even though the enablement requirement was not met given his earlier findings.

As regards the second patent in issue, this claimed a composition containing trastuzumab and impurities known as "acidic variants" whereby the amount of acidic variant was less than about 25%. In common with recent decisions on numeric limitations, the parties agreed that the amount of impurity must be less than 24.5% in the composition. Birss J noted that during the trial, he had made a declaration in respect of certain formulations of trastuzumab which contained impurity levels of 25% and upwards. As regards validity, most of the claims were held anticipated by an earlier patent application called "Andya" and the remaining claim was held obvious over this citation. The claims were also held obvious by some slides presented at a conference by Reed Harris from the Analytical Chemistry Department of Genentech.

It remains to be seen whether Genentech will appeal and if so, if they will try and prevent Hospira launching their generic trastuzumab medicines pending that appeal.

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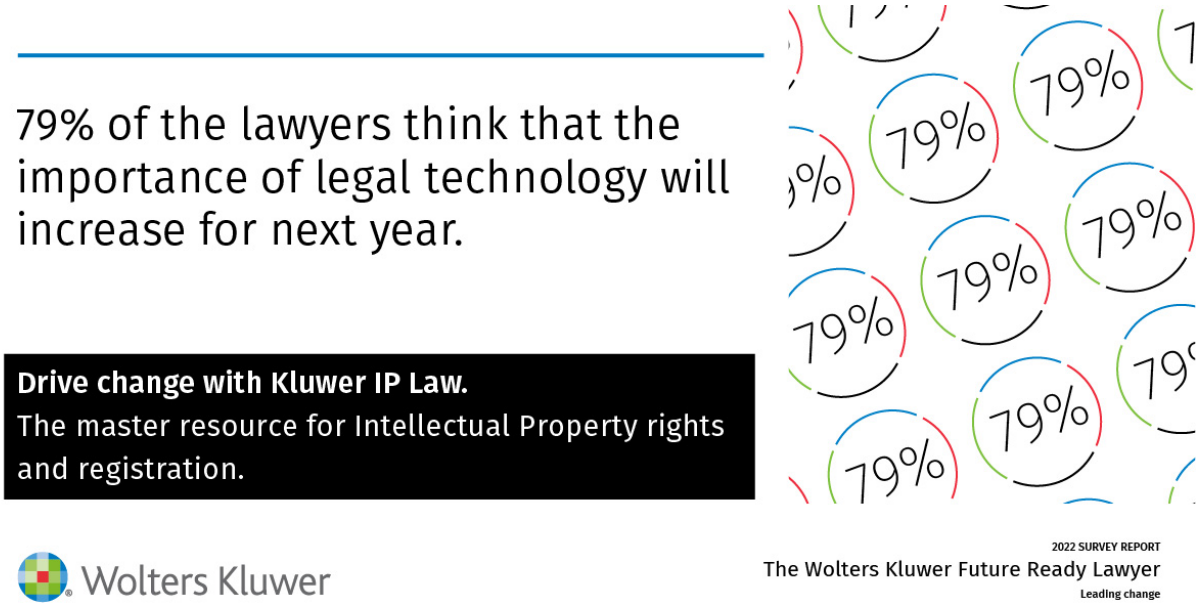

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