The Dilemma with Clinical Trials and the Patent Law

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Suppose you are a (patent) attorney in a pharmaceutical company and want to advise your company how to best protect the results of a clinical trial designed to find out the best possible treatment regimen of a certain known and approved drug X. The researchers of your company have devised and been allowed to conduct a clinical study in humans, involving a number of pretty different treatment regimens. The trial will be lengthy and quite costly; its result is not really predictable. In the end, your company's trial will (hopefully) provide mankind with valuable new information how to best administer drug X. Your company's management tells you that they want and need and, in their opinion, deserve patent protection for the new treatment regimen.
Now it's your turn. You know that a compound for a new use can be patented in principle (Art. 54(4) and (5) EPC) and that a new use may consist, inter alia, of a new treatment regimen (established case law since T 1020/03, a decision back from the good old times when important decisions were still published in the OJ EPO). So far, so good. But now comes the BIG question: Should you file the patent application that your company expects you to file before your company starts the trial, possibly including all treatment regimens included in the trial, or only after your company has received and evaluated the results?

I cannot and will not try to answer this question in this generality. Clinical trials and the circumstances under which they are conducted can be quite different; as can be the common general knowledge and the internal information available to the inventor/applicant when filing the application. But I wonder whether there are

certain scenarios where it is truly difficult to get the decision right.

Firstly, filing a patent application directed at a new use of a known compound X without any supporting data may be very risky. The EPO may easily pull out and fire the plausibility gun at you, which may result in problems for your compound-for-use claims either under insufficiency (T 609/02) or under inventive step (T 1329/04) or both. In the end, you are supposed to invent, not to speculate.

Conversely, waiting with your application until the results of the trial have become (internally) known can also be very risky. First and foremost, there is always the risk that somebody else pre-publishes something pertinent. Secondly, there may be certain clinical trials where confidentiality cannot be or is not maintained for one reason or another. The latter scenario is particularly painful: In this case, it is already known that a clinical trial is ongoing and – in the worst case – that certain treatment regimens of drug X are being tested. Naturally, the result of the trials may not yet be known at your priority date. But your generic opponent drily argues (i) that the published information about the trial already anticipates your claim, as it includes the treatment regimen which you have (later) claimed when you knew it worked, and thus all the technical steps necessary and sufficient to anticipate the invention and (ii) even if this information were not to anticipate the invention, it would at least render it obvious.

This brings us to the recent decision T 239/16 brought up by the commendable Just Patent Law Blog, wherein the claimed invention was *„Zoledronic acid or a pharmaceutically acceptable salt thereof or any hydrate thereof for use in a method of treating osteoporosis in which the zoledronic acid or the pharmaceutically acceptable salt therefore or the hydrate thereof is administered intravenously and intermittently and in which the period between administrations is about one year."*

The Board first established that the trial information summarized in a document (55) and describing, inter alia, this treatment regimen, was public and then proceeded to examine novelty and inventive step.

With regard to novelty, the Board stated:

> *In the present case the next step involves analysing whether the effect discussed above would arise with certainty from the treatment as described in document (55), i.e. whether the disclosure of document (55) has to be read as*

an implicit disclosure of the effective treatment of osteoporosis.

Thus, the Board – in my opinion, rightfully – was apparently not satisfied that all the necessary technical steps sufficient to obtain the claimed effect (successful treatment of osteoporosis) were described in document (55). In other words, the effect was not seen to be inherent in the use as described in document (55). The Board additionally wanted to establish that the trial information (which obviously included no prediction as to the outcome) had to be read as an implicit disclosure of the effective treatment of osteoporosis.

The Board then went on to examine this question by looking at various other documents filed by the opponents. You may perhaps find this odd, but we can put the question whether and when secondary references can inform the skilled person about what was implicit in a primary reference to one side. The Board's result was that there is no such implicit disclosure in document (55).

But then… you probably guessed it. Document (55) still killed the invention:

6.2 A possible starting point for the assessment of inventive step is document (55). The content of document (55) is discussed in detail in point 5.2 above. The five study arms are presented in the same manner. Each can be seen as a valid starting point. In the present case, the board considers the last study arm pertaining to once-yearly administration as the most promising starting point for the assessment of inventive step.

6.3 As can be seen from the discussion under point 5.2 above, the difference between the disclosure of document (55) and the subject-matter of claims 1 and 2 of the main request lies in the failure of document (55) to directly and unambiguously disclose the effective treatment of osteoporosis.
Consequently, the technical problem to be solved in view of the once-yearly arm as starting point in document (55) is the provision of an effective treatment of osteoporosis.

6.4 As already stated under point 5.2 with regard to the content of document (55) in the context of novelty, a certain doubt remains as to whether the yearly treatment arm leads to an effective treatment of osteoporosis. The question to be answered is thus whether this doubt would diminish the skilled person's expectation of success for this yearly treatment arm. The board considers that

the mere fact that an active agent selected from the group of bisphosphonates is being tested in a clinical study for the treatment of osteoporosis (as disclosed in document (55)) leads to an expectation of success, due to the fact that clinical studies are based on data obtained by pre-clinical testing both in vitro and in animals and require authority approval which takes ethical considerations into account. This means in the present case that the skilled person would expect all study arms to treat osteoporosis effectively, unless he was dissuaded from this by the prior art.

And, perhaps unsurprisingly, the Board did not find the prior art to dissuade the skilled person from believing that each of the tested treatment arms might be effective.

It cannot be said that the patent proprietor did not try what it could to persuade the Board to come to a different conclusion, including properly citing case law such as T 158/06, T 293/07, T 715/03 and T 2506/12. But the Board rejected each of these attempts. When discussing T 2506/12, the Board argued as follows:

The appellant-proprietors argued that, unlike the situation in case T 2506/12, in the present case there was only pre-clinical evidence that the active agent, zoledronic acid, could be effective in the treatment of osteoporosis.

The board refers to point 5.2 above, in which the fact that zoledronic acid has not yet been shown to be effective in humans is exhaustively discussed. The board holds that there remained a residual doubt that the desired treatment would be obtained, which however did not diminish the prospects of success to such an extent that the reasonable expectation turned into a mere "hope to succeed". Clinical trials in humans are planned scientific investigations. They require authority approval, which is only given after a risk/benefit evaluation. For ethical (but so economic) reasons it has to be ensured that research risks are minimised and are reasonable in relation to any potential benefits. Ethical and economical considerations require that the "benefit" will arise with reasonable certainty and will not only "be hoped for". This has to be taken into consideration as part of the technical circumstances when assessing the level of confidence of the skilled person in making rational predictions about achieving the envisaged treatment. Consequently, even though the circumstances are different from those of case T 2506/12, that does not automatically mean that an

inventive step is to be acknowledged.

So all in all, a sad outcome for the patent proprietor, which is perhaps also a bit unsatisfactory from a more general point of view. Is it possible at all to protect the (valuable) outcome of such (lengthy and costly) clinical trials, particularly if they cannot be conducted under full confidentiality? And if not, what could be done about it?