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The EPO raises the bar on plausibility when assessing inventive step: T688/16 - Dasatinib

On 1 February 2017 the Board of Appeal of the EPO upheld the revocation of Bristol-Myers Squibb's (BMS) patent for anti-cancer drug dasatinib due to a lack of inventive step. It is common for post-published data to be taken into account by the EPO when such data supports a technical effect rendered plausible by the application. In this case the Board decided that the original application did not make it plausible that the dasatinib had any useful properties, i.e. any technical effect. As a consequence, the post-filing data could not be taken into account when assessing inventive step and the patent was revoked for merely claiming an obvious further organic compound.

This finding raises the bar on whether a patent specification makes it plausible that a technical problem has been solved and could have far-reaching effects for the patentability of pharmaceutical and other inventions.

Matthew Fletcher
Partner, Bath
matthew.fletcher@abelimray.com

The "plausibility" requirement

In recent years, European Patent Office (EPO) practice has evolved a requirement that an application renders "plausible" or "credible" that a claimed invention has a technical effect. Only when an effect is rendered plausible can later data verifying that the effect exists be taken into account when assessing inventive step. This practice prevents applicants from speculatively reciting a boilerplate list of possible uses for the subject matter of a claim without any clear understanding of which of those uses will turn out to be realised. This is to some extent a reaction to biotech inventions of the early 1990s relating to newly discovered gene sequences and only later identifying their utility.

Background to the case

The original patent application filed by BMS in this case identified a range of compounds by means of a general formula and included dasatinib in a list of 580 example compounds. Assays known to enable the identification of protein kinase (PTK) inhibitors were described and it was stated in the specification that:

"Compounds described in the following Examples have been tested in one or more of these assays, and have shown activity."

No data or other evidence that any of the example compounds had PTK inhibitory activity was present in the application as filed. The patent was opposed by generics companies and revoked by the EPO's Opposition Division. By the time the case reached the Board of Appeal, the patent only contained a single claim directed to dasatinib as a new chemical entity.

This case has caused considerable interest from the pharmaceutical industry, with representatives of various innovator companies and generics companies attending the hearing and the European Federation of Pharmaceutical Industries and Associations (EFPIA) submitting observations on the case. The view of many was that surely a patent narrowly directed to a single novel chemical entity that has been a commercially successful and life-saving drug must be patentable.

The issues to be decided in T688/16

The novelty of dasatinib as a single compound was never in doubt. Nor did any of the cited prior art documents disclose a compound that was structurally similar to dasatinib.

The key issue was whether the application as filed made it plausible that there is any technical effect associated with dasatinib. If it was credible that dasatinib had PTK inhibitory activity, then additional data filed by BMS during examination that

confirmed the activity of dasatinib could be taken into account. That data clearly demonstrated that dasatinib solved the technical problem of finding new PTK inhibitors which, given the structural differences between dasatinib and previously known PTK inhibitors, was not obvious and so inventive.

In the event that the effect was not considered plausible and data was not admitted, then under established EPO practice applying the "problem-solution" approach, the claim would lack an inventive step. In the absence of a technical effect, new chemical entities are considered a merely arbitrary enlargement of the pool of available compounds (see for example T 939/92 - Agrevo). No matter how different a compound is from those previously known, its mere synthesis is not an invention. Thus, if it is not plausible that dasatinib is a PTK inhibitor, the claim to the compound would fail.

The Appeal hearing

At the Appeal hearing held on 1 February, the Opponents' position was that in the absence of any verifiable evidence, the statements made in the application were not enough to render it plausible that dasatinib is a PTK inhibitor.

The Patentee argued that (1) the application provided positive technical information as to the activity of all example compounds; (2) there is no legal requirement to file raw data and no reason to doubt the accuracy of the information provided in the application; and (3) it is now incumbent on the Opponents to establish that there is a reason to doubt the statements made in the application.

The Board focused on the question as to whether statements in the application was enough to establish plausibility or whether verifiable evidence is needed. The Board also made it clear that plausibility must be assessed solely on the basis of what was disclosed in the application as filed; and later documents either showing that not all the compounds disclosed in the application were active, or evidencing that the activity of dasatinib was known to BMS when the application was filed, were not relevant.

The Opponents argued that if the disclosure of verifiable evidence was not required on filing, then the filing of speculative patent applications before an invention was made would be encouraged. The Patentee argued that the statements in the specification went beyond more speculation and provided technical information in summary form that made it credible that the invention had been made and that the technical effect had been found. The Patentee also contended that there is no legal requirement to provide absolute proof of a technical effect on filing.

The Board questioned whether the statement in the specification shows that all compounds were found to be active. The Patentee argued that on the basis of the information provided in the application, the skilled person would expect all the compounds to have been made, tested and found active and pointed to declarations of experts confirming that they believed the statements in the application.

The Board raised a question as to whether plausibility was a matter of fact and so could be informed by expert opinion, or a matter of law. The Opponents argued that experts were not competent to provide an opinion on whether the statement made a technical effect plausible, which was a matter of law; whereas the Patentees considered it a question of fact that could be corroborated by expert testimony.

The Board decided that the specification did not make it plausible that dasatinib was a PTK inhibitor and as such post-filing data confirming the activity could not be taken into account.

The Patentee argued in vain that a life-saving drug like dasatinib could never be considered a mere "arbitrary compound" and its low HPLC retention time showed it had the technical effect of improved solubility. However, in the absence of a comparison with the solubility of PTK inhibitor compounds of the prior art, that argument also failed.

An attempt to have a question referred to the Enlarged Board of Appeal (the highest level of appeal in the EPO) to clarify the plausibility threshold was rejected, and the Board of Appeal dismissed on the grounds of a lack of an inventive step.

Implications

While the Board of Appeal issued their decision on the day of the hearing, in accordance with normal EPO practice the reasons for the decision will be published in a few months' time. The decision appears to have raised the bar with respect to the plausibility threshold. However, the full implications of this case and where the bar now sits will become clearer once the reasoned decision of the Board of Appeal is published. However, it appears that the admissibility of additional supporting data may in future be restricted to cases where statements made in the application are verifiable by the reader.

In this case, BMS appears to have had relevant data at the filing date but elected not to include it in their patent application, a practice that was

common at the time the application was filed in 2000.

Increasingly over recent years, patent offices around the world have been requiring applications to include data on filing to support inventive step, at least in the life sciences sector. The decision of the EPO Board of Appeal in the dasatanib case is reflective of a general trend towards imposing higher requirements on patent specifications. This case serves as a warning that not including verifiable evidence, such as raw data, at the time of filing and only submitting it later is a dangerous tactic that could be fatal to the prospects of a patent filing.

Action in the light of T488/16

It is apparent that to have the best chance of having a patent granted and maintained by the EPO, the safest approach is to include as much verifiable evidence as possible at the time of filing. In an ideal situation, data should be included that both demonstrates that the principle aim is met and also renders plausible as many additional advantages as possible, in case these need to be relied upon later.

Filing strategies should also be reconsidered in the light of this decision. BMS were at pains to point out that this application was no speculative filing. The application embodied many years of research, contained hundreds of worked example, summarized real data and met all the legal requirements at the time. However, the sand has shifted beneath BMS's feet in the intervening years and a patent that would have been considered unshakable a few years ago has now been revoked. Given the unpredictability of the EPO, consideration should be given as to whether putting all your eggs in the EPO basket is the wisest tactic. Filing parallel national applications e.g. in Germany and the UK, a sensible precaution for cases of key commercial importance to insure against the unpredictability of the EPO.

London
20 Red Lion Street
WC1R 4PQ, UK
T +44(0)20 7242 9984
F +44(0)20 7242 9989

Cardiff
3 Assembly Square
Britannia Quay
CF10 4PL, UK
T +44(0)29 2089 4200
F +44(0)29 2089 4201

Bath
Westpoint Building
James Street West
BA1 2DA, UK
T +44(0)1225 469 914
F +44(0)1225 338 098