

Sandoz Limited and Anor v Bristol-Myers Squibb Holdings Ireland Unlimited Company [2023] EWCA Civ 472

The Court of Appeal has dismissed BMS' appeal against the Patents Court's finding that EP (UK) 1 427 415 (the "**Patent**") is invalid. This case is notable as it is the first in the UK to consider the recent Enlarged Board of Appeal decision in G2/21. In dismissing BMS' appeal, the Court held that due to a lack of plausibility, the Patent made no technical contribution to the art and therefore lacked inventive step and was insufficient.

The Patent

The title of the Patent is "*Lactam-containing compounds and derivatives thereof as factor Xa inhibitors*"; it is a compound patent covering the anticoagulant apixaban. Apixaban is a factor Xa inhibitor, sold by BMS under the trade mark Eliquis and is one of the world's biggest-selling medicines. Accordingly, the utility of apixaban as a potent factor Xa inhibitor and its use as a treatment for thromboembolic disorders was not in dispute.

Sandoz and Teva argued that the Patent was invalid because the specification did not make it plausible that apixaban would have any useful factor Xa inhibitory activity. The parties agreed that to the extent that plausibility is required for validity, it should be tested by reference to the application for the Patent, ("**the Application**"), because if plausibility arose from something that was only in the Patent and not in the Application, the Patent would be invalid for added matter. The Application disclosed a very large number of compounds by way of Markush formulae, lists of individual compounds, and synthesised examples. Apixaban was one of the synthesised examples and was claimed as part of a list with seventy three other compounds. However, there was no specific disclosure of the activity of apixaban (or any other compound) as a factor Xa inhibitor and no rationale provided as to why it, or any other of the disclosed compounds, would be useful as a factor Xa inhibitor. Instead there was merely a generic statement that some compounds had been tested and found to have an inhibitory constant (Ki) of less than or equal to 10 μ M, but which compounds these were was not identified in the Application.

Issues on appeal

Arnold LJ, giving the leading judgment, summarised BMS' grounds of appeal on why the first instance judge had erred as follows:

- (1) The judge erred in law because, in the case of a claim to a single chemical compound, there is no requirement that the specification makes it plausible that the compound is useful. It is sufficient that the specification discloses the structure of the compound and a method of synthesis and contains an assertion of potential utility, provided that that assertion is not manifestly speculative or wrong.
- (2) The judge erred in law because he applied the standard of plausibility laid down by the majority in *Warner-Lambert Co LLC v Generics (UK) Ltd* [2018] UKSC 56 when he should either have applied the standard advocated by the minority, or applied the standard laid down by the majority in that case less strictly.
- (3) The judge erred in law because he wrongly held that it was not enough for the specification to encourage the skilled person to test the efficacy of the claimed compound and to identify simple tests which the skilled person could carry out for that purpose and which, if carried out, would confirm that the compound was likely to have the efficacy claimed.
- (4) The judge erred in law or principle because he failed to stand back and consider whether the claimed invention fulfilled the "patent bargain".
- (5) The judge erred in principle because he should have held that the Application contained an implicit disclosure that apixaban had a nanomolar Ki against factor Xa or had a Ki which made it suitable for therapeutic use.
- (6) The judge was wrong to hold that the disclosure of the Application did not make it plausible that apixaban was an effective factor Xa inhibitor.

In relation to point 1, the judgement notes that BMS did not contend that the inventive concept merely lay in the identification of a new compound but that the claimed invention involves an inventive step and is sufficiently disclosed because apixaban is an effective factor Xa inhibitor, as was subsequently confirmed.

In relation to Grounds 1 to 4, the key issue for the Court was whether the case was legally distinguishable from *Warner-Lambert* on the basis that the claim was to a single compound. BMS had not argued that G2/21 itself justified diverging from the approach in *Warner-Lambert* and whilst Arnold LJ acknowledged that the concept of plausibility originated as a response to overly-broad claims, he noted that the concept had also found utility in relation to second medical use claims (as noted by Lord Sumption in *Warner Lambert*) and had been applied in such cases as T 488/16 *Bristol-Myers Squibb/Dasatinib and Generics (UK) Ltd v Yeda Research & Development Co Ltd* [2013] EWCA Civ 925. The fundamental principle is that the scope of the patent monopoly must be justified by the patentee's technical contribution to the art. This remains so whether the claim scope is broad or narrow. If it is not plausible that the invention solves any technical problem, then the patentee has made no technical contribution and the invention does not involve an inventive step. It follows that, in order for a claim to a single chemical compound to be patentable, the application must make it plausible, when read in the light of the skilled person's common general knowledge, that the compound has the asserted utility. It would make no difference whether the claim incorporates the use of the compound as a technical feature or whether the claim is simply to the compound per se and the assertion of utility is only to be found in the specification – there is no invention in merely identifying a new chemical compound; invention can only lie in identifying its utility. Accordingly, Grounds 1 to 4 were dismissed.

Arnold LJ agreed with the first instance judge that Ground 5 amounted to a new case put forward by BMS. BMS' statement of case on plausibility did not aver that the skilled team reading the Application with the benefit of their common general knowledge would interpret the Application as disclosing (whether explicitly or implicitly) that apixaban had been tested and found to have a particular K_i , nor did BMS adduce any evidence to that effect, put that proposition to any of the Sandoz and Teva witnesses or advance such a case in submissions. Instead, the case which BMS advanced at trial was that the Application impliedly disclosed that apixaban had been tested and found to have a K_i of less than 10 μM . This ground also failed.

Finally, Arnold LJ found that Ground 6 amounted to a bald assertion that the first instance judge was wrong in his evaluation of plausibility. BMS sought to argue that the skilled team would infer from the Application that apixaban was an effective factor Xa inhibitor, relying on the general statement that “a number of the compounds of the present invention were found to exhibit $K_i \leq 10 \mu\text{M}$, thereby confirming the utility of the compounds of the present invention as effective Xa inhibitors”; and the fact that in Example 18 apixaban had been synthesised in a much larger quantity than any of the other examples, which BMS asserted was because early results had been favourable and the patentee wanted to take work on the compound forwards. Arnold LJ dismissed this submission on the basis that the general statement could not be specifically attributable to apixaban and, although a possible explanation for the large quantity synthesised was that early results were promising, there were other possible reasons and therefore nothing could be inferred from this.

Obiter commentary on G2/21

In his summary of the case law, Arnold LJ observed that it was clear from G2/21, as well as the Enlarged Board's earlier reasoning, that the fundamental consideration when a court or tribunal is considering whether a claimed invention involves an inventive step is whether the technical effect asserted by the patent applicant or proprietor is derivable by the skilled person from the application as filed read with the common general knowledge. Arnold LJ also noted that while the Enlarged Board has taken the view in G 2/21 that the two approaches of ab initio plausibility and ab initio implausibility can be reconciled, his own view was that the divergence of opinion in the Supreme Court in *Warner-Lambert* shows that the two approaches do not necessarily produce the same outcome. He commented that the harmonised approach adopted by the Enlarged Board, while eschewing the language of ab initio plausibility and ab initio implausibility, is as a matter of substance much closer to the former than to the latter. However, this was of no consequence to the present decision since it was not suggested by BMS that G 2/21 justified departing from *Warner-Lambert*.