Weighing ‘reasonable expectation of success’ in drug patent inventiveness assessments in China

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Wu Xiaoping of Wanhuida Intellectual Property says the methodology often applied in assessing inventiveness in pharmaceutical patent litigation cases is set to be used in re-examination and invalidation proceedings after the CNIPA makes an invalidation decision a quasi-precedent

On August 13 2024, the Re-examination and Invalidation Department (previously known as the Patent Re-examination Board) of the CNIPA published the Compilation of Synopses of Exemplary Patent Re-examination and Invalidation Cases in 2023.

The compilation is a collection of 58 synopses abstracted from 53 exemplary cases, which were selected from a pool of 7,700 invalidation cases and 65,400 re-examination cases the agency concluded in 2023. The compilation is expected to serve as a frame of reference in the application of law in patent re-examination and invalidation cases.

Case No. 27 pertains to the finding of "reasonable expectation of success" in the inventiveness assessment of an invention for pharmaceutical use.

Facts of the case

The patent at issue is the Chinese invention patent No. 200780004302.4 owned by Novartis AG, which is entitled ‘Use of 40-O-(2-hydroxyethyl)-rapamycin for the preparation of drugs’ (the Patent). The petitioner, Chia Tai Tianqing Pharmaceutical Group Co., Ltd, challenged the validity of the Patent before the CNIPA, which rendered invalidation decision No. 54747 (the Invalidation Decision), declaring the Patent invalid in its entirety.

Claim 1 of the Patent reads: “Use of 40-O-(2-hydroxyethyl)-rapamycin in the preparation of drugs for the treatment of renal angiomyolipoma (AML) and lymphangioleiomyomatosis (LAM).”

40-O-(2-hydroxyethyl)-rapamycin is available under the name everolimus.

In the procedure of invalidation, the petitioner submitted 27 pieces of evidence, launching an all-out attack against the clarity, sufficient disclosure, deficient support of the description, novelty, and inventiveness of the Patent. The patentee tried to thwart the attack by submitting an equal number of pieces of counterevidence but failed. The CNIPA invalidated the Patent on the ground that the claims lack inventiveness over the combination of Evidence 6, Evidence 8, and Evidence 2, wherein:

- Evidence 6, as the closest prior art, discloses that mammalian target of rapamycin (mTOR) kinase inhibition may be a useful targeted therapy for tuberous sclerosis complex (TSC), and CCI-779, an mTOR kinase inhibitor, when used in animal models of AML and LAM, can reduce the severity of TSC-related diseases without significant toxicity, indicating the necessity to continue well-designed clinical trials;

- Evidence 8 reveals that rapamycin, everolimus, and CCI-779 are effective specific mTOR inhibitors, and everolimus and CCI-779 are more suitable for clinical use because they improve drug properties (water solubility and solution stability) without altering cellular effects; and

- Evidence 2 discloses the phase I clinical use of everolimus for the treatment of TSC syndrome.

However, the adduced evidence also corroborates the following facts:

- In view of the complexity of the mTOR pathway mechanism and TSC's upstream position over mTOR, how TSC regulation is related to the mTOR pathway remains unclear;

- There were no observed associations between mTOR inhibition and tumour response; and

- Everolimus and rapamycin vary in structure and pharmacological activity.

CNIPA reasoning

In the Invalidation Decision, the CNIPA observed that the distinguishing feature of claim 1 as compared with the technical solution disclosed by Evidence 6 is the use of a different drug in treating LAM and AML.

The decision found that the available evidence in the case fails to prove that claim 1 has achieved a more beneficial technical effect than Evidence 6, and thus the technical problem actually solved by claim 1 is the selection of an alternative derivative of rapamycin to replace CCI-779 for the preparation of drugs for the treatment of LAM and AML.

As for "whether the complexity of the mTOR pathway and the differences in the structure and performance of rapamycin analogues hinder the replacement of CCI-779 with everolimus in the treatment of the said indication", the CNIPA held that despite the complexity of the mTOR pathway, there is no evidence showing that everolimus and CCI-779 function in different routes and manners in the mTOR pathway. Although there is evidence attesting to the differences in structure and pharmacological activity among rapamycin analogues, specifically, more evidence tends to juxtapose the application of CCI-779 with that of everolimus, suggesting the close correlation there-between, and the motivation afforded to a person skilled in the art to choose therefrom.

Therefore, based on the disclosure of CCI-779 for treating AML and LAM in Evidence 6, in combination with the disclosure of the phase I clinical use of everolimus for treating TSC syndrome in Evidence 2, it would be obvious for a person skilled in the art to envisage using everolimus to replace CCI-779 for the treatment of AML and LAM.

The CNIPA therefore found that the Patent is devoid of inventiveness and thus invalidated it in its entirety.

Implications of the CNIPA's decision

This case is quite intriguing.

"Reasonable expectation of success" refers to the likelihood of success in combining prior arts to meet the limitations of the claimed invention. A technical solution of a patent would be rendered obvious (devoid of inventiveness) provided that it is sufficient to establish that a skilled person would have followed the teaching of the prior art with a reasonable expectation of success.

Although the finding of "reasonable expectation of success" is closely associated with inventiveness assessment, China's Guidelines for Patent Examination does not refer to the matter in outlining the three-step methodology in assessing patent inventiveness.

The Invalidation Decision articulates the parameters to be taken into account in establishing "reasonable expectation of success" in the context of assessing inventiveness of an invention for pharmaceutical use: "If the prior art has disclosed that two drugs are interchangeable drugs of the same class, and the mechanism of action of such drugs is closely related to the mechanism of treatment of an indication, the complexity of the mechanism of action of the drugs and the structural differences among the drugs are not sufficient to constitute a technical obstacle so as to hinder the substitution of the two drugs, and the person skilled in the art could determine that one drug may be interchangeably used with another for the treatment of the indication with a reasonable expectation of success."

China's Supreme People's Court (SPC) first elaborated on the correlation between the establishing of "reasonable expectation of success" and the finding of obviousness in an administrative decision, Novartis AG v CNIPA (2019 Zui Gao Fa Zhi Xing Zhong No. 235). The apex court found that "'reasonable expectation of success' may be taken into consideration in assessing the obviousness of an invention. If factoring into the status quo of the prior art at the date of patent application the characteristics of technological evolution, the mode and conditions of innovation, the average cost of innovation and the overall success rate of innovation, a person skilled in the art has the motivation to start from the closest prior art and has a reasonable expectation to obtain the patented technical solution, the said patented technical solution could be deemed obvious. A 'reasonable expectation of success' only requires that there is necessity for those skilled in the art 'to try', without the 'certainty of success' or 'high probability of success.'"

The SPC has been applying the aforesaid methodology in assessing inventiveness in a slew of pharmaceutical patent litigation cases. The inclusion of the subject case in the CNIPA's annual exemplary cases seems to herald the application of the

methodology in patent examination proceedings, which is expected to further align the agency's practice with that of the nation's judiciary in terms of inventiveness assessment.