How does pharmacological action affect the defence of a pharmaceutical compound patent in China?

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In April 2023, the China National Intellectual Property Administration (CNIPA) released the Top Ten Patent Reexamination and Invalidation Cases of 2022. Three of them relate to the pharmaceutical field.

One involves the inventiveness assessment of small interfering RNA inventions, another discusses the authenticity determination of experimental data recorded in a traditional Chinese medicine patent, and the third elaborates on the correlation between a pharmacological mechanism and a drug indication, between in vitro and in vivo experiments and the technical effect as required under the patent law.

The third case will be discussed in detail in this article.

Background

The case relates to the Chinese invention patent ZL02819025.4, entitled ‘Phenyl-piperazine derivatives as serotonin reuptake inhibitors’, which is owned by Lundbeck. The patent is a compound patent covering an antidepressant marketed as Brintellix®.

The patent has survived four successive invalidation proceedings. The case discussed herein is the fourth invalidation decision, No. 54793, made by the CNIPA, which affirmed the validity of the patent at issue.

The patent claims a compound with a general formula, covering vortioxetine, the active ingredient of Brintellix®.

In the invalidation proceeding, the petitioner raised several grounds for invalidation, including sufficient disclosure and inventiveness, both challenging the technical effect achieved by the patent. In fact, the patent description has recorded an

IC50 (the half maximal inhibitory concentration) value of the claimed compound for inhibiting serotonin reuptake in an in vitro experimental model. However, the petitioner asserted that the technical effect achieved by a pharmaceutical compound patent shall be ascertained based on the data showing the efficacy for an indication, rather than the in vitro data.

The main reasoning behind the assertion is that depression involves very complex mechanisms and the serotonin reuptake recorded by the patent at issue is just one of them. Therefore, the inhibition of serotonin reuptake is not sufficient to show the potential of the claimed compound as an antidepressant. On top of that, the petitioner also asserted that the inhibition effect claimed by the patent is an in vitro test result, which cannot be equated to effectiveness in treating depression.

The CNIPA's decision

The panel dismissed the petitioner's assertions and clarified in the decision the interplay of pharmacological mechanisms, indications for treatment and the technical effect required by the law.

The panel elucidated that there is no legal provision mandating that the technical effect achieved by a pharmaceutical patent be established based on verification of the efficacy of the claimed compound in treating an indication. In other words, under the framework of patent law, it is not necessary for a patent to prove the medical use of a compound patent all the way up to the level of indication.

As the legislative purpose of the patent law is to encourage inventions and advance technologies, the parameters on which the law relies in deciding whether to grant a patent are markedly different from those in drug market approval.

Where a person skilled in the art could anticipate the medical use of a compound from the patent description and the prior art, the medical use would be recognised under the patent law. The patentee would be under no obligation to verify the efficacy of the compound in the patent by way of administering the compound to a human subject for treating an indication.

Moreover, if there is a general consensus over the correlation between the pharmacological mechanism and an indication in the art, and if the person skilled in the art could reasonably expect that the pharmaceutical compound has the potential for treating an indication based on the verified pharmacological mechanism, the patent claiming the compound shall be deemed as meeting the requirement for disclosure of the medical use and/or technical effect of a pharmaceutical compound.

The panel also affirmed the significance of in vitro data for proving the technical effect of a patented invention. The panel opined that different experiments or tests are needed at different stages of a drug R&D process. In vitro tests are used at an early stage to screen and narrow down compounds, which could also lay the groundwork for subsequent studies.

In vitro tests or animal experiments cannot be replaced by clinical trials, for cost and ethics reasons. The fact that some compounds with in vitro activity may not be considered as promising in the context of in vivo tests does not negate the significance of in vitro testing.

In this case, since the prior art has clearly established the correlation between serotonin reuptake inhibitory activity and alleviating depression, it would be understandable to a person skilled in the art that the patent used the in vitro tests to verify the compound's activity, so as to show its potential for treating depression.

The panel therefore recognised the technical effect of the invention, based on the activity of inhibiting serotonin reuptake verified in the patent at issue. Given the technical effect verified, the patent fulfilled the requirement of sufficient disclosure.

Accordingly, in assessing the inventiveness of the claimed compound, the panel ascertained that the technical problem actually solved is to provide a serotonin reuptake inhibitor, rather than to treat depression.

The panel thus concluded that the prior art evidence concerning the treatment of depression presented by the petitioner did not have merits, as it was silent on the serotonin reuptake inhibition, even though the prior art discloses a compound with a very similar structure to the claimed compound.

Comments

Ascertaining the technical effect achieved by an invention patent is crucial to defend its validity. That is particularly true when the sufficient disclosure and inventiveness of a pharmaceutical patent is challenged.

The technical effect or experimental data of a pharmaceutical patent is an easy target of the petitioner in the invalidation proceeding. In that sense, the petitioner could launch attacks on various fronts, including:

The pharmacological mechanisms;
The correlation with an indication; and
More specifically, the pharmacological action on a target.

In certain cases, with regard to inventiveness assessment, the petitioner overlooking the role of the action mechanism, such as the action on a target, would erroneously simplify the technical effect achieved by a patent as the treatment of the indication. This would inappropriately generalise the technical problem actually solved by the patent and lead to the conclusion that the patent is obvious and unpatentable.

This case, which elucidates the correlation between a pharmacological mechanism and an indication, could serve as a point of reference in assessing the patentability of a pharmaceutical compound.