Pharmaceutical polymorph patents are regarded as effective means and important sources for pharmaceutical authorities to enhance the efficiency of pharmaceutical patent protection. However, the current examination criteria for pharmaceutical polymorph patents have become stricter in China while the amount of patent applications is rising.

The clinical research of pharmaceutical polymorphs commenced in 1960s internationally. It was validated that the differences among the polymorphs of the same compound have effects on solubility, bioavailability, crystal form, and physical stability. Pharmaceutical polymorphs are usually distinguished to different groups (e.g., amorphous, crystalline, etc.) according to their microstructural features. Even different polymorphs of a compound might present different effect.

In China, the specific rules on pharmaceutical polymer patents are included in the Patent Examination Guidelines, which are also for authorities to ascertain certain technical aspects of deciding whether an application for pharmaceutical polymer patent is novel or not. The patent examination practice in China is to a large extent based on the authorization of pharmaceutical patents. Since the very beginning, it has been a long-term endeavor of the authorities to decide the stability of chemical compounds. The success of pharmaceutical polymorph patents is generally bound to the similarity and the similarity evaluation should be based on the chemical structure of the core active element rather than the whole compound.

The eight judicial precedents were made between 2010 and 2016, including one decision issued by the Supreme People’s Court. The eight precedents are taken as samples in the following analysis. They identified eight judicial precedents in total (counted in the number of final judgments to avoid repeated calculations). The eight judicial precedents are identified in the databases of IP House, PKU Law, and on the IP Precedent Guiding Service Platform, and they are eventually referred to as the “Three-Step Approach” and the general case in ascending patent examination levels.

In order to review the judicial situation regarding the inventiveness examination of pharmaceutical polymorphs, this article would summarize the current inventiveness examination standards for pharmaceutical polymer patents in China and propose some strategic suggestions for potential patent applicants.

1. Current Examination Standards over Inventiveness of Chinese Pharmaceutical Polymorph Patents

There are two sets of rules for inventiveness assessment under the Patent Examination Guidelines, both of which relies on the core evaluation foundation: whether a polymorph invention can produce an unexpected technical effect in the core examination standards.

1.1 General Standard: the “Three-Step Approach”

1.1.1 Relevant Rules

Section 5 of Article 4 of the Patent Examination Guidelines (2015) clarifies the general procedures and standards for inventiveness assessment, i.e., (1) determining the closest prior art; (2) determining the distinguishing features of the invention and the technical problem actually solved by the invention; and (3) determining whether the distinguishing technical features of the invention are expected or unexpected.

In short, following the “Three-Step Approach”, it is generally recognized as an “obvious” technical solution to prepare a new polymorph based on a known compound or a known polymorph, given that there has been an obvious motivation, the preparation process of polymorph is generally known and the technical effects can be anticipated. The assessment of inventions of pharmaceutical polymorphs was then supposed to conduct a further unexpected technical effect evaluation.

1.2 Special Standard for Chemical Inventions

2.1 Relevant Rules

Since polymorph is a type of chemical products, the inventiveness assessment of polymorph patents can follow the special provisions on prior art examination in Chapter 5 of Article 4 of the Patent Examination Guidelines (2015). That is, if a compound that is similar in structure to a known compound can be anticipated to produce an unexpected technical effect, the invention can be considered novel.

2.1.1 Examination Standard

Section 5, Article 4 of the Patent Examination Guidelines (2015) states that, “An invention process is considered anticipated if it is considered to be the same as or could be derived from the prior art. Anticipated processes include (1) a known process and a known process variant; (2) a new process which differs from the known process and its variant in a nonobvious way; and (3) a new process which is not a nonobvious variation of the known process.”

2.1.2 Examination Standard

There were debates on whether a certain chemical compound is similar in structure to a known compound or a known polymorph in prior arts. A decision made by the Chinese Supreme People’s Court (2015) suggested that the technical effect of the difference between the chemical structure of the core active element and the known compound or polymorph should be regarded to have similar structure with the compound and its amorphous and crystal forms. The difference in the amorphous crystal structure of different polymorphs is only considered if such amorphous-crystalline structural forms are unexpectedly technical effect.

Standard for “Unexpected Technical Effect”

2.2 Relevant Rules

Section 5, Article 4 of the Patent Examination Guidelines (2015) states that, “An unexpected technical effect is a qualitative or quantitative change which is unexpected. Such a change which is unexpected is regarded as a technical effect which is unexpected and unexpected technical effect is required to be anticipated. If the patent examiner in a technical field cannot anticipate the effect claimed in the patent application or cannot anticipate the unexpected technical effect claimed in the patent application, the examiner will not consider the technical effect claimed as unexpected.”

2.2.1 Examination Standard

For pharmaceutical polymorphs, the conventional effects usually include identity, purity, and stability, which are common knowledge or cannot be deduced from the common general knowledge.

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8. Relevant Judicial Practice

8.1 The Reckitt Benckiser (Hungary) Ltd. v. PEM and Jiangsu Chao-chun Trading Pharmaceutical Co. Ltd.

On 28 May 2013, the Reckitt Benckiser (Hungary) Ltd. v. PEM and Jiangsu Chao-chun Trading Pharmaceutical Co. Ltd. case was heard by the Supreme People’s Court, which is the highest people’s court in China. The case involved international pharmaceutical patents and the inventiveness examination of pharmaceutical polymorphs.

The Supreme People’s Court issued the invalidation decision, explaining in its ruling that, there is no evidence of inventiveness of the composition and the composition may harm different kinds of polymorphs based on the same chemical structure and common knowledge. The decision was made on the basis of the unobvious technical effect of the inescapable combination of the chemical structure and other features of the pharmaceutical polymorph.

Since the very beginning, it has been a long-term endeavor of the authorities to decide the stability of chemical compounds. The success of pharmaceutical polymorph patents is generally bound to the similarity and the similarity evaluation should be based on the chemical structure of the core active element rather than the whole compound.
2.2 Observations and Speculations

2.2.1 The determinations on the inventiveness of pharmaceutical polymorph patents are fully consistent. In the eight judicial precedents, Chinese courts at all levels denied the inventiveness of pharmaceutical polymorph patents.

2.2.2 The legal grounds for denying the inventiveness of pharmaceutical polymorph patents are highly unified. Among the eight decisions, four of them were against the generic standard of “Three-Step Approach” plus the “Unexpected Technical Effect” examination, and the rest four were against the special inventiveness standard for chemical compounds. In both circumstances, “unexpected technical effect” was examined and denied. The decisions show that the examination standards for inventiveness of pharmaceutical polymorph patents are broadly consistent between PRB and courts and among Chinese courts at all levels.

2.2.3 The examination standards for inventiveness of pharmaceutical polymorph patents have significantly changed. We note that the six invalidated patents involved were granted between 2000 and 2009, and the final judgments denying their inventiveness were made between 2010 and 2016. The results reflect the substantial change of the examination standards for inventiveness of pharmaceutical polymorph patents in recent years.

In the past time when the patents were granted, it was at the initial stage of polymorph studies in China. A generally accepted understanding at that time was that, even though a person skilled in the art could expect the improvement in certain properties of a compound by producing a crystalline form, whether a polymorph could be obtained and what polymorph would be obtained were unpredictable for a known compound disclosed in the prior art, which might bring non-obviousness to the polymorphic invention. Therefore, the patent examination office generally recognized the inventiveness of pharmaceutical polymorph patents at that time.

In the recent years, the progress of polymorph research and development brought changes to minds of examiners and judges, who have gradually reached consensus, as reflected by the eight decisions. That is, a deeper understanding of the importance of pharmaceutical polymorphs provides stronger motivation to a person skilled in the art to study polymorphs, so that it becomes a routine for a person skilled in the art to prepare polymorphs based on a known compound. Moreover, the richer experience in polymorph preparation makes it much easier to obtain a new polymorph. Therefore, the standards for inventiveness review of polymorph inventions are significantly raised.

2.2.4 Retroactivity in inventiveness evaluation is improper. It is a natural process that technology development causes changes of patent examination practice. However, whether a stricter examination standard can apply to invalidate a patent that was granted following a less strict examination standard is an issue worthy of attention.

It is a universal practice that whether a patent has inventiveness shall be evaluated from the technical level and the cognitive level of a person skilled in the art before the filing date or the priority date. The approach of using the present stricter examination standard to invalidate granted patents appears inconsistent to the said examination norm.

III. Suggestions

As mentioned above, “unexpected technical effect” is an essential factor for inventiveness assessment of pharmaceutical polymorph patents. Accordingly, this article intends to make some suggestions from the perspective of technical effect.

1. “Qualitative change” of technical effect should be exploited more to qualify polymorph patent applications. Since stability, purity and bioavailability of a polymorph are considered to be conventional, “new performances” of a new polymorph are preferred to be introduced in the application. Taking an example of bioactivity, if a new polymorph improves bioavailability, which is a “new performance” and accordingly shows a “qualitative change” of the technical effect.

2. “Quantitative changes” of technical effects achieved by a new polymorph has to have unpredictability. For example, based on the common knowledge in the art, between stability and solubility there exists a relation of mutual restriction; however, if it is proven with experimental data in the original application that a new polymorph can simultaneously improve the stability and solubility of a drug, it will be recognized that such “quantitative change” is a “unexpected technical effect” of the new polymorph.

3. Finally, it is worth noting that “unexpected technical effect” can only be the technical effects specified in or can be directly determined from the original disclosure of application documents. According to the examination practice, any experimental data submitted after the filing date to prove the technical effect will hardly be taken into consideration for inventiveness evaluation.