Insight into recent PRB decisions on pharmaceutical /biotech inventions

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The Patent Reexamination Board (hereinafter referred to as the PRB) is an organization under the SIPO (State Intellectual Property Office) of China. Its main functions are to examine appeals against a rejection decision made by the examining departments and to examine requests for invalidation of a granted patent. Although its decisions can be further appealed to Chinese court, the court is only empowered to decide on legality of the decisions. The final decision on the patentability of a patent application or on validity of a patent has to be made by the PRB itself. Especially, the invalidation proceedings very often parallel the civil proceedings on patent infringement as China adopts the so-called "dual track" system for patent validity and patent infringement. Such being the case, the PRB is recognized as a very important organ in the Chinese patent system and its decisions are intensively researched by both local and foreign patent practitioners. This article is a study of some of its recent decisions which concern pharmaceutical and biotech inventions.

Concerning the manner of claim amendment during invalidation

procedure

In Chinese Patent No. 03139760.3 relating to new pharmaceutical compounds, the claimed compounds are presented as a general formula drafted in a typical Markush format. In the specification of the patent, there are two specific inventive compounds exemplified, namely Examples 2 and 4. However, they are not specifically claimed in the patent as granted. During the invalidation procedure of this patent, the patentee submitted an amendment of claims which narrowed down the claims to the compound of Example 2.

A question arose before the PRB whether the amendment should be accepted. According to the routine practice of the PRB and also as stipulated in the Guidelines for Patent Examination of the SIPO, a general formula compound claimed in Markush style and containing multiple variables is taken as an "integral" solution which cannot be split into specific compounds covered by the general formula (unless the variables are relatively few, say no more than four). Hence, an amendment taking one (or more) specific compound out of the general formula would usually be considered as going beyond the scope of the claims as granted. In this case, however, peculiarities were found by the PRB. It was duly

noted by the PRB that Example 2 was one of the only two specific compounds exemplified in the patent specification and moreover was the only compound on which biological test data were given. In view of this, the PRB concluded that Example 2 was in fact the "core" of the claimed invention, as could be appreciated by a person skilled in the art upon reading the patent specification as a whole. Eventually, the PRB accepted the amendment as an "exceptional" case and made a decision upholding the patent on the basis of the amendment.

To justify its decision, the PRB further commented that allowing the amendment other than not would better embody the legislative intent of the patent system encouraging inventive activities. Moreover, it would facilitate focusing on the substance of the invention in patent invalidation proceedings.

This decision is generally welcomed by both the patent proprietors and professionals. On the issue of amendment of a patent during invalidation proceedings, there have been complaints about apparently over-rigid standards applied by the PRB, which seldom goes beyond the limited manners set forth in the Guidelines for Patent Examination. It has also

been seen that some PRB decisions concerning this issue were considered by the court as overreaching the legal requirement for post-grant amendment. In its decision in this case, the PRB seems to be echoing the court's view as well as the complaints of the public. However, it still carefully emphasized the peculiarities of the case and apparently tried to make it an "exceptional" case but not a precedent.

Notwithstanding this decision, it is still advisable, when prosecuting a Chinese patent with a Markush general formula, to include specific compounds (especially those of commercial importance) as sub-claim(s) of the general formula claim. They could well serve as back-up claims in case the general formula claim is challenged.

Concerning ethic issue of inventions resulting from stem cell research

In China, just as in many other countries, inventions made out of stem cell (especially human embryo stem cell) research often encounter patentability problem and are always a subject of controversy. Since human embryo stem cells are necessarily prepared by obtaining and

disrupting human embryo, which is considered as violating public morality, many of the inventions in this area cannot get patent protection.

In Chinese Patent No. 200680048227.7, the granted claims are directed to a nuclear reprogramming factor useful in inducing nuclear reprogramming of somatic cells and a process for preparing induced pluripotent stem cells by nuclear reprogramming of somatic cells. According to Example 12 of the description of the patent, iPS cells (induced pluripotent stem cells) were prepared from human skin fibroblast cells originated from a fetus. During an invalidation action against the patent, the dispute was focused on whether the patent violates public morality by exploiting human embryo for business purpose.

After a study of the patent description, the PRB found that the human skin fibroblast cells used in preparing the iPS cells of the invention could be obtained either directly from the fetus or were commercially available and no manipulation on the fetus was involved in the invention according to the description. Specifically, the reference to fetus in Example 12 should be understood as referring to the original source of the human skin fibroblast cells so as to distinguish them from those of some other working examples which were originated from adult skin fibroblast cells. It should not be understood as an indication that they were obtained

directly from the fetus. Moreover, one of the purposes of the invention is to avoid ethic issues of any manipulation on fetuses. With these findings, the PRB concluded that the patent as a whole had excluded any content of obtaining relevant cells directly from human embryos and that the opponent's assertion was invalid.

It seems that the PRB takes a rather technical approach in the analysis of the ethic issue involved in this case. They put emphasis on the inquiry of whether there is any direct manipulation of human embryos, which apparently indicates their understanding of the subtlety of the issue. Overreaching of the legal requirement for abide of public morality could be seen occasionally with the examining practice of the SIPO. However, the PRB's rationale expounded in this case is considered as a good example of correct application of the relevant legal provisions.

It is speculated that this decision represents a liberal position taken by the PRB towards stem cell research in response to the government's recent efforts to promote stem cell research, an area in which the government has been cautious. If this is true, it could be an encouragement for patent filers in this particular technical area.

Concerning inventive step assessment

In China, an invention on second medical use of a known drug can be patented with the so-called Swiss-type claim format. That is to say, the claim can be drafted as "use of compound X in manufacture of a medicament for treating disease Y", with disease Y being a new indication. However, an inventive step issue may arise when the new indication intended in the invention is seemingly close to the existing indication of the drug that is known from the prior art. The PRB's recent decision on a request for reexamination of Patent Application No. 200880011264.X represents its thinking on inventive step of inventions of this kind.

The claimed invention in this case is a new indication, which is estrogen receptor negative breast cancer, of ActRIIa-Fc fusion protein (an activin-binding polypeptide) with identified peptide sequence. The application was initially rejected by the examining department and was brought to the PRB for its review. As prior art, the main reference relied upon by the examining department was D3, which discloses use of

ActRIIa peptides for the treatment of cancers including activin dependent cancers such as ovarian cancer. Another reference, D2, discloses use of an activin antagonist in the treatment of androgen independent tumor such as breast cancer as well as a solution of screening for types of carcinoma suitable for treatment with the activin antagonist. It was concluded by the examining department that, based on D3 in view of D2, it would have been obvious for a person skilled in the art to arrive at the claimed invention, as D2 provides an incentive to use an activin-binding protein to alleviate or inhibit the growth or survival of breast cancer cells.

It was found by the PRB that the indication intended by the claimed invention, which is estrogen receptor negative breast cancer, was not mentioned in D2. In other words, it does not disclose use of activin antagonist in the treatment of estrogen receptor negative breast cancer. Moreover, it also does not disclose ActRIIa-Fc fusion protein as an activin antagonist. It was specifically noted by the PRB that D2 only disclosed inhibition of growth of androgen independent breast cancer cell line SC-4 in the presence of an activin antagonist. However, androgens and estrogens have different receptors and different effects on various types of cancer cells, as is well known in the art. Therefore, D2 would have not made it obvious for a person skilled in the art to think of the

effect of activin on estrogen independent cancer cells, let alone the use of ActRIIa-Fc fusion protein in the treatment of estrogen receptor negative breast cancer, which is the claimed invention. The rejection was overturned based on the above analysis.

As is typical in the Chinese patent practice, the PRB followed the problem-solution approach (as in the European Patent Office) in the assessment of inventive step in this case. It can be seen that its decision was largely based on careful analysis of the technical facts identified in the prior art references. Particularly in this case, androgen independent breast cancer, which was mentioned in D2, was noted as distinctive over estrogen receptor negative breast cancer. In fact, there was no evidence in the prior art showing that use of activin could achieve the same effect on estrogen independent cancer cells.

Interestingly, the PRB referred to additional references submitted by the applicant as proof of the knowledge in the prior art, apart from the analysis of the content of prior art references relied upon by the examining department. These additional references teach that activin has no effect on estrogen receptor negative breast cancer cell lines, meaning that estrogen receptor negative breast cancer is not an activin dependent

cancer. Apparently, these teachings contribute to the finding that there would have been no motivation to use ActRIIa-Fc fusion protein in the treatment of estrogen receptor negative breast cancer.

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