The Patent Lawyer

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May / June 2021

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Finnegan, Henderson, Farabow, Garrett & Dunner, LLP experts Christopher Howes, Zachery Olah, Forrest Jones, and Karthik Kumar, discuss the developments in the augmented and virtual reality sphere with advice for protecting innovation.

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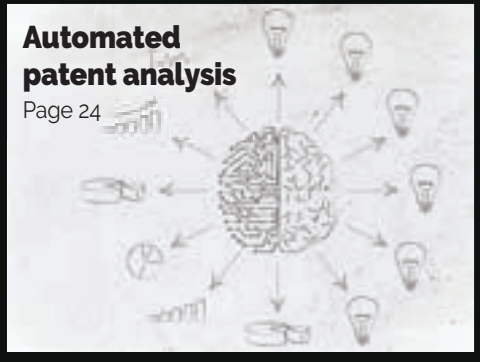

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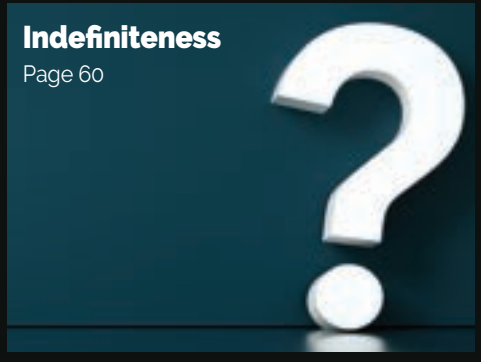

Indefiniteness
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Does a third party infringe a patent right by conducting clinical trials on an original drug?

Osamu Yamamoto explains the impact of the recent Intellectual Property High Court decision, as well as the necessity for reforming the patent system relating to drug marketing approval in Japan.

On February 9, 2021, the Intellectual Property High Court (IPHC) decided that conducting clinical trials by a third party to obtain marketing approval as an original drug does not infringe a patent right (Reiwa 2 (Ne) 10051). According to this IPHC judgment, a third party can freely conduct clinical trials on any original drugs within the scope of a patent right, even during the term of the patent right. In some cases, a third party can obtain marketing approval prior to the patentee.

I explain below impacts of the IPHC decision, as well as the necessity for reforming the patent system relating to drug marketing approval in Japan.

Osamu Yamamoto

Virotherapy Patent

JP No. 4212897 relates to "a method of virotherapy for cancers." Virotherapy, in which cancer cells are infected with viruses that multiply only on cancer cells, to destroy cancer cells, has recently been attracting attention. Several virotherapy drugs are being developed in Japan.

Claim 1 of the patent reads "A herpes simplex virus comprising a deletion within the BstEII - EcoNI fragment of the BamHI x fragment of said virus." An example of the claimed herpes simplex viruses (HSVs) is an HSV having inactivated mutations of ICP47 gene.

The application was filed by two U.S. corporations and Georgetown University. After filing, one of the inventors, a Japanese university professor, succeeded to the right to obtain a patent, became the applicant, and thereafter the patentee. The registration date of the patent is November 7, 2008, and the expiration date is March 27, 2022.

The patentee group has developed virus G47Δ, which includes ICP47 gene deletion as well as modifications of γ34.5 gene and ICP6 gene. From around 2015, the group started a phase II study in Japan for the indication of glioblastoma, a type of malignant brain tumor. The group submitted an application for marketing approval for malignant glioma on December 28, 2020. G47Δ will be the first virotherapy product to be approved in Japan. This can be seen as a successful example of academia-led drug discovery.

Résumé

Osamu Yamamoto, Partner

Mr. Yamamoto is a patent attorney and a partner of Yuasa & Hara. He has extensive experience in pharmaceutical and biotechnology research and development at a chemical company for ten years before specializing in intellectual property. He has represented a variety of companies in the fields of pharmaceuticals, biotechnology, diagnostics, and food and beverages. He is experienced in all aspect of patent issues, including filing patent applications, dealing with Office Actions, providing expert opinions, defending or attacking patent rights in invalidation trials and oppositions, and patent infringement litigations.

Case

In the U.S. and Europe, Amgen conducted T-VEC (herpes simplex virus type-1 (HSV-1) attenuated by functional deletion of ICP34. 5 (γ34.5) and ICP47) clinical trials under license for the corresponding U.S. and European patents. Amgen Inc., received FDA (Food and Drug Administration) approval in October 2015, and EMA (European Medicines Agency) approval in December 2015, for T-VEC.

The defendant, a Japanese subsidiary of Amgen Inc., conducted a bridging study in Japan based on these foreign clinical data. The patentee filed a lawsuit before the Tokyo District Court against the defendant claiming that clinical trials conducted in Japan using a virus within the scope of the patent violated the patent right, and requested the defendant to suspend use of the virus etc.

Tokyo DC and IPHC Decisions

In this lawsuit, there was no dispute between the parties on the issue of whether "T-VEC belongs to the scope of the patent right," since the defendant admitted it. The Tokyo DC judged that the clinical trials for T-VEC as innovator drug conducted by the defendant do not infringe the patent right, stating that the clinical trials fall under the exemption of a patent right in the category of "experimental or research purposes" stipulated in Article 69, par. 1 of the Patent Act (Heisei 31 (Wa) 1409, judged on July 22, 2020). The IPHC, in a subsequent appeal trial, supported the Tokyo DC decision (Reiwa 2 (Ne) 10051; judged on February 9, 2021).

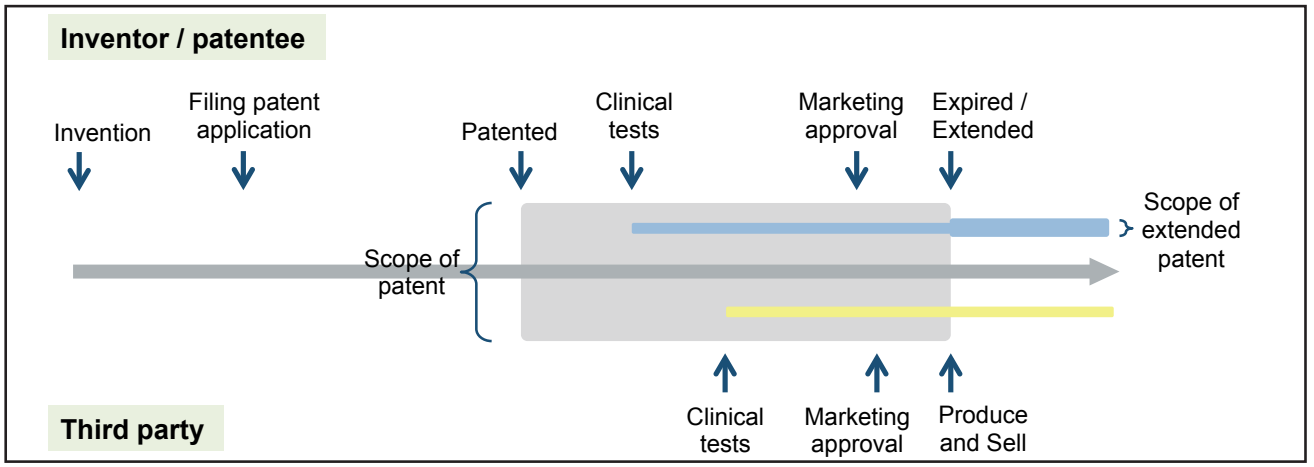
Experimental or research purposes

Article 69, par. 1 of the Patent Act stipulates that "a patent right shall not be effective against the working of the patented invention for experimental or research purposes." The aim of the article is to realize harmonization between a patent right and public interest, in order to accomplish the fundamental purpose of the Patent Act ("encouraging inventions, thereby to contribute to the development of industry" (Article 1 of the Patent Act). However, a scope of "experimental or research purposes" is not stipulated in the Patent Act. In this regard, a commonly accepted theory is that a scope of "experimental or research purposes" should be limited to acts aimed at "advancement of technology."

> **According to this IPHC judgment, a third party can freely conduct clinical trials on any original drugs within the scope of a patent right, even during the term of the patent right.**

In case of generic drugs

In the case of generic drugs, a "simplified application" that merely includes data showing biological equivalence, etc. with reference to the data that have been submitted by an originator is sufficient. The Supreme Court ruled in 1999 that tests for generic marketing approval fall under the category of "working of the patented invention for experimental or research purposes" set forth in Article 69, par.1 of the Patent Act, and therefore such tests for generic drug approval do not constitute a patent right infringement (1998 (Ju) No. 153; Judged on April 16, 1999). However, this Supreme Court judgment did not make clear what acts falls under "experimental or research purposes" in Article 69, par.1 of the Patent Act, but rather made a decision mainly from the viewpoint of duration of the patent right. Specifically, the Supreme Court held that "if it is prohibited to produce chemical substances or drugs that fall within a patent right, it will result in a third party being unable to



use the invention even after expiration of a patent right for a certain time period. This would be contrary to the fundamental premise of the patent system, which enables any person to freely use a patented invention after expiration of a patent right."

Case of original drugs

The plaintiff argued that "the clinical trials of this case are for an innovator bio-pharmaceutical, and are different from those for a generic drug in the case of 1999 Supreme Court judgment." However, the Tokyo DC and the IPHC rejected the plaintiff's arguments stating that contents of experiments for market approval should not be affected with regard to judgment of "experimental or research purposes," and judged that the clinical trials to obtain market approval for an innovator drug are within the range of the 1999 Supreme Court judgment. In other words, the Tokyo DC and the IPHC followed the 1999 Supreme Court judgment stating that the clinical trials necessary for obtaining marketing approval of an original drug also fall under the category of "experimental or research purposes" under Article 69, par.1 of the Patent Act.

Problems

Experimental or research purposes?

It appears incomprehensible that clinical trials necessary for obtaining marketing approval of original drugs fall under the category of "experimental or research purposes" under Article 69, par.1 of the Patent Act. However, given the precedent of the 1999 Supreme Court judgement concerning a generic drug, it is difficult to find a reason that clinical trials for original drugs do not fall under the category of "experimental or research purposes." In that sense, the decisions of the Tokyo DC and the IPHC are reasonable. Rather, the 1999 Supreme Court judgment "tests for application of a generic drug fall under the category of working of the patented invention for experimental or research purposes set forth in Article 69, par.1 of the Patent Act" is questionable, in particular as to why the issue "experimental or research purposes or not" was judged mainly from the viewpoint of duration of the patent right.

> **The patentee filed a lawsuit before the Tokyo District Court against the defendant claiming that clinical trials conducted in Japan using a virus within the scope of the patent violated the patent right.**

Enormous disadvantage to patentees

Compared with the case of a generic drug, namely the 1999 Supreme Court case, disadvantages to patentees resulting from the decisions are enormous.

In spite of duration of a patent right, any third party can conduct clinical trials. This means that there is a possibility that a third party potentially could obtain marketing approval prior to a patentee. Particularly, in case of innovative bio-pharmaceuticals having efficacy for many indications, it is unrealistic for patentee to be able obtain marketing approval for all possible indications during the term of a patent right. Therefore, in such a case, there is a real probability that a third party will conduct clinical trials for different indication(s) from a patentee's interests, and obtain marketing approval in advance of a patentee.

In addition, in a case of orphan drugs and in a case where a third party precedes a patentee in clinical trials, it may become extremely difficult for a patentee to secure sufficient subjects for establishing a clinical trial.

Patent term extension

In Japan, a patent term extension system that allows extension of a patent term for up to five years was introduced in 1987.

The plaintiff argued that even if a patent term is extended, the extended patent right would likely not cover T-VEC, and that would allow the defendant to manufacture and sell T-VEC immediately after expiration of the original term of the patent. This argument is based on the IPHC Ground Panel judgement issued on January 20, 2017 (Heisei 28 (NE) 10046)) that the extended patent right covers only the "product" (medicine) specified by the "ingredient, quantity,

administration, dosage, indication and effect" on which the registration of the patent term extension was based, as well as substantially the same "products." This means that the scope of the extended patent right is limited to the specific product and substantially the same products. From this aspect, if the patent term is extended, it is highly unlikely that the extended patent right will cover the implementation of T-VEC in which gene modifications and indications are different from those of virus G47Δ. This is quite different from the case of a generic drug in the 1999 Supreme Court decision, in which if the patent term is extended, it is not possible to manufacture and sell a generic drug during the extended term.

Necessity of reform

As mentioned above, the Tokyo DC and the IPHC judgments themselves might be reasonable in light of the 1999 Supreme Court decision. If so, my opinion is that the patent system in Japan relating to pharmaceuticals needs to be reformed.

In this case, G47Δ is the first virotherapy product to be put into markets in Japan. For such unprecedented innovative biopharmaceuticals, regulatory hurdles for marketing approval are even higher than those of biopharmaceuticals such as antibody pharmaceuticals. Therefore, it is inevitable that the timing of commercialization of such biopharmaceuticals with marketing approval will be close to the expiration of the patent term. This means that even if innovative new drugs, especially biopharmaceuticals, are developed, protection under a patent right is not sufficient.

> **A third party potentially could obtain marketing approval prior to a patentee.**

Those who have been developing innovative new drugs make large up-front investments while bearing extremely high risks. It is important to secure opportunities for these drug developers to recoup their investment. In order to properly ensure incentives to develop innovative drugs, the patent system relating to pharmaceuticals should be drastically overhauled.

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