JAPAN

Court addresses foreign clinical trial periods and patent term extension

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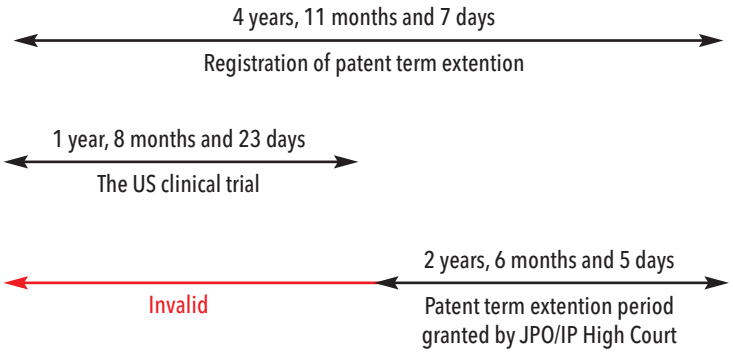

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) which commenced in 1990 made it possible to use common scientific and technical methods in drug development in Japan, the United States and EU. As a result, in approval reviews of medicinal drugs in Japan, results from foreign clinical trials are utilised based on bridging development strategy as stipulated by ICH Guideline E5.

Clinical trial periods in foreign countries can be counted as patent term extension periods if they were necessary for obtaining an approval. In which cases are they considered necessary for obtaining an approval?

Summary of the case

Daiichi Sankyo owns a patent for an invention entitled Pyridobenzoxazine Derivative. Daiichi Sankyo obtained an approval of partial changes in manufacturing approval for a medical drug whose brand name is CRAVIT TABLETS because Legionella genus was added as an applicable microorganism in relation to Levofloxacin, included in the patent. Daiichi Sankyo filed an application for the registration of patent term extension based on this disposition and was granted registration of patent term extension of "4 years, 11 months and 7 days", which includes the period of "1 year, 8 months and 23 days" of the clinical trial in the United States (the US clinical trial).

In relation to the registration of patent term extension, 13 generic drug companies including Mylan filed a request for a trial for invalidation, and a JPO decision was rendered stating that the registration of patent term extension for the period exceeding 2 years, 6 months and 5 days should be invalidated. The US clinical trial period was included in the invalidated period. Daiichi Sankyo appealed to the IP High Court seeking to revoke the JPO's decision, alleging that it was a mistake not to include the period during which the US clinical trial was conducted in the patent term extension period.

Judgment of October 28 2009, IP High Court

The IP High Court (Presiding Judge Iimura) maintained the JPO's decision, holding as follows.

The Court judged whether the US clinical trial was necessary for obtaining an approval under the Pharmaceutical Affairs Act as follows, citing the court decision of the Supreme Court which held that the commencement date of "a period during which the patented invention is unable to be worked" stipulated in Patent Act Article 67 (2) should be the date on which the trial required for obtaining "the disposition designated by Cabinet Order" commenced.

(i) The report of the Pharmaceutical and Medical Devices Agency (PMDA) acknowledged that in the examination before the approval in Japan, the usage of CRAVIT TABLETS for Legionella pneumonia was medically and pharmaceutically publicly known, based on the application example of CRAVIT TABLETS for Legionella pneumonia in foreign countries and the description of Harrison's Principles of Internal Medicine etc. Then it acknowledged that an application with public knowledge was reasonable, and judged that it was appropriate to add Legionella pneumonia to the previously approved effectiveness and efficacy of CRAVIT TABLETS (adding "Legionella genus" to "applicable microorganism") without requiring new clinical trials to support the experience of the usage of CRAVIT TABLETS and Levofloxacin and their efficacy.

(ii) In the United States, in 1996, about 10 years ago from the date on which the approval of this case was learned, the addition of effectiveness and efficacy of CRAVIT TABLETS for Legionella pneumonia was approved. The clinical trial data submitted for the approval application only had the results of the initial US clinical trial targeting 10 cases of Legionella pneumonia in which nine cases were judged to be valid. The US clinical trial at issue was started in case the shortage of cases was pointed out by the US authorities. However, the addition of effectiveness and efficacy for Legionella pneumonia was approved just two months after the beginning of the US clinical trial, and the submission of the US clinical trial data was no longer required.

(iii) The PMDA also judged that in light of pazufloxacin mesilate (PZFX) which is a fluoroquinolones drugs like CRAVIT TABLETS, its usage for Legionella pneumonia should be medically and pharmaceutically publicly known. It pointed to the usage in six cases and the description of Harrison's Principles of Internal Medicine etc. as the basis for this.

Considering the above facts, the following can be found:

(i) In the approval in the United States, the addition of effectiveness and efficacy for Legionella pneumonia was approved based on only the results of 10 cases in the initial US clinical trial, and the result of the US clinical trial was not required. Therefore, it can be reasonably presumed that also in the approval for addition of effectiveness and efficacy for Legionella

pneumonia filed thereafter in Japan, which is similar to the US case, the initial US clinical trial data was sufficient for the approval, and the US clinical trial data was not required.

(ii) In the above examination regarding the addition of effectiveness and efficacy for Legionella pneumonia in relation to pazufloxacin mesilate (PZFX) which is a fluoroquinolones drugs like CRAVIT TABLETS, the addition of effectiveness and efficacy was approved under a condition which is quite similar to the approval application in this case. Considering this, it can be reasonably presumed that if in the initial US clinical trial data containing the clinical trial data of 10 cases, more than six cases of pazufloxacin mesilate are provided, even without the US clinical trial data, the addition of effectiveness and efficacy of CRAVIT TABLETS would have been approved in Japan.

Therefore, the period of "1 year, 8 months and 23 days", the US clinical trial period, out of "4 years, 11 months and 7 days", the granted patent term extension period of this case, does not fall under "a period during which the patented invention is unable to be worked because it is necessary to obtain the disposition designated by Cabinet Order" stipulated in Patent Act Article 67 (2).

Practical tips

According to the JPO Examination Guidelines, periods of clinical trials conducted in foreign countries can be counted as patent term extension periods if they were necessary for obtaining an approval. It is necessary to prove the date on which the clinical trial commenced in foreign countries. Also, it is necessary to prove that all of the following requirements are satisfied: (i) the clinical trial in a foreign country which commenced on that date is indispensable for obtaining a disposition; (ii) enterprises have little discretion in conducting the testing because the testing needs to be conducted in line with the standards for testing methods, description, etc. of testing set forth by administrative agencies; and (iii) the clinical trial is closely related to obtaining a disposition.

In this case, Daiichi Sankyo argued that the US clinical trial was conducted with the purpose of obtaining an additional approval for Legionella genus in Japan. However, it was judged that the US clinical trial period did not correspond to the patent term extension period because the US clinical trial was not necessary for the approval of partial changes to CRAVIT TABLETS. In order to be allowed to count the additional trial periods conducted after the initial clinical trial as patent term extension periods, it should be noted that sometimes it is necessary to positively demonstrate that the additional trial data was necessary (the initial trial data was insufficient) for obtaining an approval.

This judgment provides a reference for constructing development strategy and IP strategy for pharmaceutical companies conducting bridging trials which go through 20 years after introduction and are now usual practice.