IP High Court Decision on Support Requirement in "Formulation of Boronic Acid Compounds" Case

September 14, 2020
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Abstract

The Intellectual Property High Court (IP High Court) handed down a decision on July 2, 2020, i.e., Appeal Case Nos. 2020 (Gyo-ke) 10159 (Case A) and 2020 (Gyo-ke) 10153 (Case B), in which rescission of a JPO decision to invalidate a patent in the name of the United States of America based on lack-of-support (Patent Law, Article 36, paragraph 6, item 1) was sought. In the decision, the IP High Court held that "*the support requirement is satisfied so long as a person skilled in the art who read the specification would reasonably understand that the claimed invention is described in the specification, and with regard to the problem to be solved, would have a reasonable expectation that the problem can be solved by taking common technical knowledge into account*", and overturned the JPO's decision. This ruling is favorable to patentees, since it may ease the current strict practice regarding the support requirement, and may also affect the patent examination process carried out by the JPO. This article summarizes the IP High Court rulings of this case.

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1. Overview of this case

Case Nos.: 2020 (Gyo-ke) 10159 (Case A)
2020 (Gyo-ke) 10153 (Case B)
First instance: JPO, Invalidation Trial, No. 2016-800130
Relevant patent: JP 4162491 B
Counterpart patents in other countries: US 6,713,446, and EP 1355910, etc.
Title of invention: Formulation of Boronic Acid Compounds
Patentee (Appellee of Case A, Appellant of Case B): United States of America
Demandee of invalidation trial (Appellant of Case A, Appellee of Case B): Hospira, Inc.

This case relates to appeals for seeking rescission of JPO decisions in an invalidation trial filed by Hospira, Inc. (hereinafter "the demandee"), against patent JP 4162491 B in the name of the United States of America (hereinafter "the patentee")[1]. In the invalidation trial, the JPO affirmed one of the demandee's requests to invalidate the invention of claims 17 and its dependent claims, based on lack of support (Patent Law, Article 36, paragraph 6, item 1), but dismissed the other requests by the demandee. Thus, the patentee appealed against the former decision (Case A), and the demandee appealed against the latter decision (Case B), respectively, at the IP High Court, and these cases were consolidated. As a result, the IP High Court judged, in the decision handed down on July 2, 2020, that the invention of claims 17, etc., satisfies the support requirement, i.e., it affirmed the patentee's request and overturned the former decision by the JPO.

Although the main issue of this case includes not only the support requirement but also inventive step of the claimed invention, this article summarizes the main issue relating to the support requirement, in which the IP High Court decision differed from that of the JPO.

2. The claimed invention and the descriptions of the specification

(1) The claimed invention

Independent claim 17, which is the claim in question, recites as follows[2]:

> 17. D-mannitol N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate in the form of lyophilized powder.

Incidentally, the dependent claims of claim 17 are also product claims which include all of

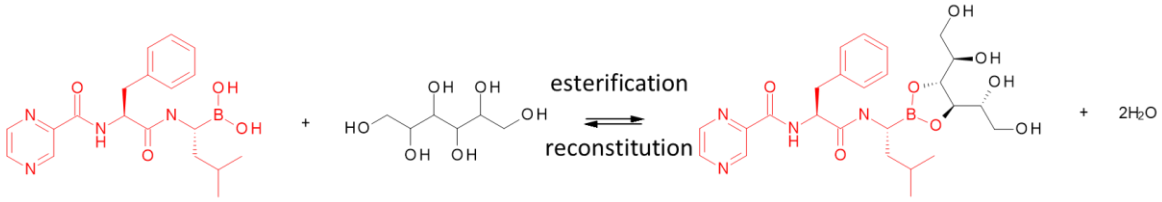
[1] Three other invalidation trials Nos. 2015-800153, 2016-800096 and 2018-800012 were filed against this patent by different generic pharmaceutical manufacturing companies, which shows the high level of interest toward this patented drug. Trial'153 was withdrawn. Trial'096 reached the same conclusion based on substantially the same reasoning as the present invalidation trial, and an appeal was filed at the IP High Court, which also reached the same conclusion based on substantially the same reasoning as the present case. Trial'012 is currently pending at the IP High Court.
[2] Claim 17 was corrected from "D-mannitol N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate" to "D-mannitol N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate in the form of lyophilized powder" in the invalidation trial.

the features of claims 17, and thus if the judgment in relation to claim 17 is incorrect, it follows that the judgment in relation to the dependent claims is also incorrect.

The claimed invention relates to formulation of a pharmaceutical compound "Bortezomib" (product name "Vercade®"), the compound name of which is "N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid". Bortezomib is known as a therapeutic drug of multiple myeloma, i.e., an anticancer agent, based on a new mechanism called proteasomal inhibition. However, Bortezomib, which is a boronic acid compound, is readily oxidized when it comes into contact with the atmosphere, and thus there has been demand for a new formulation that can improve the stability and extend the expiration date thereof.

In this regard, the claimed invention can improve the stability of Bortezomib, by esterifying it with "D-mannitol" (one of the sugar alcohols) to form "D-mannitol N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate" (hereinafter "BME"), and making it into "lyophilized powder" form, as recited in claim 17. BME in the form of lyophilized powder can be hydrolyzed by dissolving it in water to reproduce the original pharmaceutical compound, i.e., Bortezomib. Such a characteristic is called the "reconstitution" property.

The relationship between Bortezomib, D-mannitol and BME can be shown as in the following formula (prepared by the author).



Bortezomib　　D-mannitol　　BME

(2) The descriptions of the specification

The specification describes, in the Example, that a lyophilized powder formulation of Example 1 (hereinafter "Formulation 1FD") was produced by stirring and heating an aqueous solution comprising Bortezomib, tert-butanol and an excess amount of D-mannitol, and then lyophilizing it in a freeze dryer. It also describes that Formulation 1FD showed a strong peak indicating formation of BME analyzed by Fast Atom Bombardment (FAB) mass spectrometry, and had improved preservation stability, dissolubility and reconstitution property, etc., in comparison with a solid/liquid Bortezomib.

In view of the manufacturing process of Formulation 1FD, it must contain not only BME, but also Bortezomib and D-mannitol which remain without esterifying in the formulation. However, BME was not isolated or quantified in the Examples, and the specification does not include any descriptions regarding the specific concentration of BME contained in Formulation 1FD.

3. The JPO decisions

The JPO judged that the invention of claim 17 does not satisfy the support requirement and invalidated it for the reason that "... since the concentration of BME contained in Formulation 1FD is unclear, it is deemed that the result of the Examples merely show that 'lyophilized powder of Bortezomib' had the improved stability and reconstitution property, etc. In other words, it is deemed that these descriptions do not explicitly show that BME in the form of lyophilized powder can provide a stable formulation of the medicine, and readily reproduce the original boronic acid compound, i.e., good reconstitution property, by dissolving it into water." (emphasis added).

4. The parties' arguments at the IP High Court

In this appeal for cancellation of the JPO decisions, the demandee of the invalidation trial, i.e., Hospira (hereinafter "demandee"), further argued that the claimed invention in question is not supported, since it is unclear as to whether or not the effects of Formulation 1FD were derived from "lyophilized powder BME", and thus a person skilled in the art would not understand that the claimed invention can solve the problem to be solved thereby. In other words, the effect may be merely a well-known effect of lyophilizing Bortezomib with D-mannitol.

On the other hand, the patentee argued that there is no scientifically unreasonable descriptions which would give rise to doubt regarding the formation of "lyophilized powder BME" in the manufacturing conditions of Formulation 1FD, and the FAB showed a strong peak indicating formation of BME. Thus, a person skilled in the art would understand that Formulation 1FD contained a substantial amount of BME.

5. The IP High Court decisions

With regard to interpretation of the support requirement (Patent Law, Article 36, paragraph 6, item 1), the IP High Court held that "Whether or not the claimed invention satisfies the support requirement of the specification should be judged by comparing the claimed invention with the detailed description of the invention, and considering if the claimed invention is an invention described in the detailed description of the invention, and if a person skilled in the art would understand, based on descriptions and suggestions of the detailed description of the invention, that the claimed invention can solve the problem to be solved by the present invention, or if a person skilled in the art would understand, even without such descriptions and suggestions, that the claimed invention can solve the problem to be solved by the present invention based on common technical knowledge at the time of the filing date." (emphasis added)

The IP High Court further held that "The support requirement is satisfied so long as a person skilled in the art who read the specification would reasonably understand that the claimed invention is described in the specification, and with regard to the problem to be solved, would have a reasonable expectation that the problem can be solved by taking common technical knowledge into account. Thus, no descriptions at a level of thorough scientific evidence is necessary." They added that "... This is because the support requirement is derived from the essence of the patent system, i.e., granting an exclusive right in compensation for publication of the invention, and thus the aim of support requirement can be achieved at any rate, if the claimed invention, with supplemental examination or analysis by a person skilled in the art who read the specification, can contribute to further development of technology. Moreover, considering that patent specifications are prepared under time pressure of the first-to-file rule, it is inappropriate to require them to include thorough descriptions at a level of scientific evidence that is supposed to be required if they were scientific articles." (emphasis added)

In this particular case, the IP High Court deemed that the problem to be solved by the claimed invention is "to provide 'lyophilized powder BME' which can be a stable medicine when it is formulated, and can readily provide isolated boronic acid when it is dissolved in an aqueous medium, i.e., superior in reconstitution property". Incidentally, there were no conflicts between the parties on the interpretation of the problem to be solved, which is the same as the interpretation by the JPO.

With regard to the amount of BME contained in Formulation 1FD, the IP High Court deemed that a person skilled in the art would reasonably understand that a substantial amount (an amount that can solve the problem to be solved by the present invention as a medicine) of BME was generated in Formulation 1FD, by taking into consideration, for example, the following matters: According to Example 1, the esterification reaction which forms BME may progress under the conditions of mixing and heating the solution containing a relatively higher ratio of tert-butanol, i.e., a relatively lower ratio of water, and an excess amount of D-mannitol, i.e., equilibrium between Bortezomib and BME; and a strong peak indicating formation of BME was detected by the FAB mass spectrometry.

With regard to the problem to be solved, the IP High Court deemed that a person skilled in the art could have a reasonable expectation that the claimed invention can solve the problem, since improved preservation stability and dissolubility of Formulation 1FD in comparison with solid or liquid Bortezomib are described in the Examples.

In conclusion, the IP High Court judged that the claimed invention satisfies the support requirement, and overturned the JPO decisions regarding this matter.

6. Our comments

(1) Interpretation of the support requirement

Patent Law, Article 36, paragraph 6, item 1 (support requirement) prescribes that "the claimed invention must be an invention described in the detailed descriptions of the invention".

With regard to the interpretation of this law, the IP High Court held that the support requirement is judged by considering:
(a) "if the claimed invention is an invention described in the detailed description of the invention", and
(b) "if a person skilled in the art would understand, based on descriptions and suggestions of the detailed description of the invention, that the claimed invention can solve the problem to be solved by the present invention, or if a person skilled in the art would understand, even without such descriptions and suggestions, that the claimed invention can solve the problem to be solved by the present invention based on common technical knowledge at the time of the filing date."

This interpretation is based on and substantially the same[3] as the ruling of the 2nd IP High Court Grand Panel decision handed down on November 11, 2005 (Case No. 2005 (Gyo-ke) 10042), i.e., "Production Method of Polarizing Film" case, which clarified that it is necessary to consider not only (a) formality correspondence between the claimed invention and the descriptions in the specification, but also (b) substantial correspondence therebetween from the viewpoint of the problem to be solved.

In many prosecutions of patent applications, invalidation trials as well as lawsuits, the support requirement has been examined/judged based on these criteria since then.

(2) New rulings in this IP High Court case

However, it has been an important issue at a level of practice as to what degree of thoroughness of descriptions is required in order to satisfy the support requirement. In particular for bio and chemistry inventions, it is critical that the claimed invention be supported by concrete examples included in the scope thereof, since the technical effect of the invention is, in general, unpredictable based merely on the claimed features without carrying out an experiment. Thus, it has often been the case that the claimed invention is restricted too narrowly or even invalidated due to lack of support in which a high level of scientific evidence supporting technical effects of the claimed invention is required, even though the claimed invention has novelty and inventive step.

[3] The ruling of this case differs from the IP High Court case in that the ruling of this case added "and suggestions". However, it may be a mere clarification of the current patent practice, i.e., it has been common to take not only descriptions, but also suggestions thereof into account, in examination/judgement of the support requirement.

In this regard, the IP High Court ruled that the support requirement is satisfied so long as a person skilled in the art who read the specification
(a') "would reasonably understand that the claimed invention is described in the specification"; and
(b') "with regard to the problem to be solved, would have a reasonable expectation that the problem can be solved by taking common technical knowledge into account. Thus, no descriptions at a level of thorough scientific evidence is necessary."

Rulings (a') and (b') have clarified the degree of thoroughness of descriptions in relation to above (a) formality correspondence and (b) substantial correspondence, respectively. With regard to ruling (b'), there have been several other court decisions in which the support requirement was satisfied without thorough scientific evidence under specific circumstances, by taking common technical knowledge into consideration[4]. However, this IP High Court case is the first one in which the court explicitly held, as a general ruling along with the reasons, that thorough scientific evidence is not necessarily required in order to satisfy the support requirement.

Interestingly, the IP High Court added in the reasoning that "the aim of support requirement can be achieved at any rate, if the claimed invention, with supplemental examination or analysis by a person skilled in the art who read the specification, can contribute to further development of technology. Moreover, ... it is inappropriate to require [patent specifications] to include thorough descriptions at a level of scientific evidence that is supposed to be required if they were scientific articles." This reasoning can be interpreted as meaning that scientific facts, even if they are necessary information in the case of scientific articles, are not necessarily required in patent specifications, so long as it can be confirmed by supplemental examination or analysis by a person skilled in the art. However, a problem still remains as to whether or not such supplemental examination or analysis could be considered to be an "excessive burden" for a person skilled in the art[5]. Further, this reasoning can also be interpreted as meaning that late-submission of supplemental examination or analysis confirming such a scientific fact may be accepted, as long as the scientific fact is within a scope which a person skilled in the art would reasonably expect, as held in ruling (b'). However, it should also be kept in mind that, in general, supplemental examination or analysis cannot remedy deficiency of the specification which in nature lacks support, under Japanese patent practice[6].

One of the causes of the main issue in this particular case would be that the stability, i.e., preservation stability, and reconstitution properties, i.e., dissolubility and hydrolyzability, of

[4] For example, in "Precaution and Therapeutic Drug" case (No. 2011 (Gyo-ke) 10146, 10147, IP High Court, handed down on April 11, 2012), the claimed invention is directed to a combination of two different drugs, while the Examples do not include the combination. The court judged that the claimed invention is supported, since these drugs are based on different pharmaceutical mechanisms, and thus can achieve their effects, respectively.
[5] If an excessive burden of experiment is required in order to carry out an invention, it is highly likely that such an invention is deemed as not satisfying enablement requirement (Art. 36, Para.4), under Japanese patent practice.
[6] The 2nd IP High Court Grand Panel decision handed down in November 11, 2005 (Case No. 2005 (Gyo-ke) 10042), i.e., "Production Method of Polarizing Film" case.

BME were not explicitly shown in the Examples by using isolated, lyophilized powder BME. Thus, the essence of the demandee's arguments may reside in that it is still unclear as to what the effects of the claimed invention are derived from, unless stability and reconstitution properties were tested by using isolated, lyophilized powder BME. In this regard, it is strongly doubtful as to the effects derived from, based merely on the descriptions in the Examples, since adding mannitol as an excipient for higher stability and dissolubility, etc., is very common practice in the field of lyophilization of pharmaceuticals, and thus it would be very natural for a person skilled in the art to anticipate that such high stability and dissolubility may not be derived from BME itself, but from the excess amount of mannitol. Although the IP High Court dismissed this issue by merely stating that a person skilled in the art would reasonably understand that a substantial amount of BME was generated in Formulation 1FD, etc., the question may still remain as to whether or not the high stability and dissolubility were derived from the excess amount of mannitol, even if such a substantial amount of BME was generated.

The judgment by the IP High Court in this case can also be understood as meaning that the support requirements should be satisfied, so long as a person skilled in the art would have a reasonable expectation of achieving the effects of the claimed invention, even if there still remains some doubt.

(3) Counterpart foreign patents and international harmonization

The Japanese patent in question is a patent derived from PCT International Patent Application No. PCT/US2002/001907, claiming a priority based on US Patent Application No. 60/264,160 filed in 2001. The PCT application was entered and granted in many countries and regions, not only in Japan, but also the US (US Patent No. 6,713,446) and Europe (EP Patent No. 1355910), etc. Regarding the US Patent, the Delaware District Court judged in a patent infringement lawsuit that the invention of counterpart claims is obvious based on prior arts (35 U.S.C. §103), but the CAFC overturned the district court's judgment[7]. Regarding the EP patent, the opposition division of the EPO judged in an opposition that the counterpart claims lacks inventive step (EPC Article 56), and the Board of Appeal also affirmed the opposition division's judgement and revoked the patent based on lack of inventive step[8].

It is apparent that no description requirement issues based on 35 U.S.C. § 112(a) or EPC Article 84, which may correspond to the support requirement in Japan, were alleged, and no arguments in relation to insufficiency of the Examples were included in the obviousness (inventive step) issue, in both the US and Europe. In this regard, this IP High Court case may have shifted the criteria relating to the Japanese support requirement toward an international, relatively easier criteria.

[7] Millennium Pharmaceuticals, Inc. v. Sandoz, Inc., Nos. 2015-2066, 2016-1008, 2016-1009, 2016-1010, 2016-1109, 2016-1110, 2016-1283, 2016-1762 (Fed. Cir., July 17, 2017)
[8] T1348/14 (Board of Appeal, September 29, 2016)

(4) Summary

Although the magnitude of influence of this IP High Court case has not been apparent yet, the rulings are favorable to patentees, since ruling (b'), in particular, will ease the current strict practice relating to the support requirement, which has often been the case, and may also affect the patent examination process as conducted by the JPO. However, it is still important especially for bio and chemistry inventions to be supported by concrete examples, and thus descriptions of the Examples should be as thorough as possible, as at present.

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