Patent Right	Date	December 15, 2020	Court	Intellectual Property High Court, Third Division
	Case number	2019 (Gyo-Ke) 10136		
- A case in which it was determined that it was not erroneous for a trial decision to determine that an invention does not fulfill the support requirement.				

Case type: Rescission of Trial Decision of Invalidation

Result: Dismissed

References: Article 36, paragraph (6), item (i) of the Patent Act

Related rights, etc.: Patent No. 5551658

Decision of JPO: Invalidation Trial No. 2018-800028

Summary of the Judgment

1. The present case is a lawsuit against a trial decision for a trial for invalidation of a patent concerning an invention of "LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSETRON." The trial decision determined that the invention has a reason for invalidation, because the invention does not fulfill the support requirement. For this reason, the trial decision invalidated the patent. In response to this, the Plaintiff (patentee) filed a lawsuit against the trial decision made by the JPO.

2. The statement of the scope of claims in the present patent specifies compositions of drugs such as a concentration of "palonosetron" which is an active ingredient, and includes in the configuration a requirement "with storage stability for at least 24 months" (hereinafter referred to as "24-months requirement").

The description of the present patent states in "Summary of the Invention" that "These formulations are storage-stable for a period exceeding 24 months at room temperature", and further states "storing the containers (containing the formulations) … for ... 24 months or more" in the explanation of the embodiment. However, in the description of the present patent, the statements relating to the 24-months requirement are limited to these brief statements, and no experimental data are disclosed.

3. This judgment held in summary as follows, and dismissed the Plaintiff's (patentee's) claim on the grounds that it was not erroneous for the trial decision to determine that the invention does not fulfill the support requirement.

(1) According to the experimental results, etc. stated in the working examples of the present description, the stability test was not actually conducted. Thus, it cannot be deemed that it is stated that the pharmaceutical formulations stated in the present

description have storage stability for at least 24 months. In addition, in other portions of the present description, factors which contribute to stabilization are listed. However, there are no direct statements that these factors achieve storage stability for 24 months. Further, there is no concrete indication to provide grounds for inferring what factors would make it possible to achieve what level of storage stability. After all, it cannot be deemed that it is stated with concrete supporting evidence that the specific pharmaceutical formulations have storage stability for at least 24 months.

Therefore, it cannot be deemed that the present description states a palonosetron formulation with the 24-months requirement. Furthermore, even in light of the common general technical knowledge at the time of filing the present application, it cannot be deemed that each of the present inventions is within the scope of the invention which a person ordinarily skilled in the art can recognize as being able to solve the problem of each of the present inventions; i.e., the problem of providing a palonosetron formulation which increases pharmaceutical stability and allows storage for 24 months or more and of providing an acceptable range of concentrations which stabilize the palonosetron formulation.

(2) The Plaintiff (patentee) asserts that it is construed that: in order to acknowledge the compliance with the support requirement, it is sufficient that there is a statement to the extent that a person ordinarily skilled in the art can obtain a reasonable expectation that the problem could be solved in view of the common general technical knowledge; and with regard to the solution to the problem, it is sufficient that there is a statement to the extent that a person ordinarily skilled in the art can obtain a reasonable expectation that the problem could be solved in view of the common general technical knowledge; and it is not necessary to state the extent to which the statement reaches a rigorous scientific proof, because [i] the support requirement is derived from the essence of the patent system which grants an exclusive right as a reward for laying an invention open to the public, and thus, the purpose of imposing the support requirement can be achieved to some extent if a person ordinarily skilled in the art who has read the description can contribute to the further development of the art by conducting a retest and an analysis of the invention, and [ii] taking into consideration that the description is prepared within a time constraint under the first-to-file principle, it is not reasonable to require that the content of the description be demonstrated to the same degree of rigor as required in a scientific paper.

However, since the present description lacks any concrete statements in line with the 24-months requirement, it cannot be acknowledged that there is a statement to the

extent that a person ordinarily skilled in the art who has read the present description can obtain a reasonable expectation that the problem (storage stability for 24 months or more) could be solved. In addition, even if there is a time constraint under the first-to-file principle, the compliance with the support requirement cannot be affirmed by statements which do not even reach the extent that "a reasonable expectation" can be obtained as mentioned in the Plaintiff's (patentee's) assertion. With regard to this, in the present description, it cannot be acknowledged that there is a statement to the extent that "a reasonable expectation" can be obtained.

Judgment rendered on December 15, 2020
2019 (Gyo-Ke) 10136 A case of seeking rescission of the JPO decision
Date of conclusion of oral argument: October 22, 2020

Judgment

Plaintiff: Helsinn Healthcare Société Anonyme

Defendant: Nipro Corporation

Main Text

1. The Plaintiff's claim shall be dismissed.

2. Of the court costs, those caused by the intervention of the Plaintiff's supporting intervener shall be borne by the supporting intervener, and the remainder shall be borne by the Plaintiff.

3. The additional period for the Plaintiff to file a final appeal and a petition for acceptance of final appeal against this judgment shall be 30 days.

Facts and reasons

No. 1 Claim

The court shall rescind the decision made by the Japan Patent Office (JPO) on June 11, 2019 with regard to the case of Invalidation Trial No. 2018-800028.

No. 2 Outline of the case

1. History, etc. of procedures at the JPO

(1) With regard to an invention titled "LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSETRON", the Plaintiff filed a new application on July 28, 2011 (Patent Application No. 2011-165212, hereinafter referred to as "the present application") by dividing a part of a patent application (Patent Application No. 2006-501686, hereinafter referred to as "the original application") having an international filing date of January 30, 2004 (Priority date: January 30, 2003

(hereinafter referred to as "the present priority date", Priority country: United States of America)), and obtained a registration of establishment of a patent right (Exhibit Ko 48, Patent No. 5551658, Number of claims: 18, hereinafter, this patent will be referred to as "the Present Patent") on May 30, 2014.

(2) The Defendant filed a request for a trial for invalidation of the Present Patent with regard to Claims 1 to 17 on October 27, 2016 (the case of Invalidation Trial No. 2016-800125). The Plaintiff filed a request for correction on November 22, 2017 (hereinafter referred to as "the Present Correction"), and Claims 10 and 17 were canceled.

On January 5, 2018, the JPO made a trial decision to accept the Present Correction and to dismiss the request for the trial for invalidation of the Present Patent with regard to Claims 1 to 9 and 11 to 16 after the Present Correction. Thereafter, the trial decision became final and binding.

(3) The Defendant filed a request for a trial for invalidation of the Present Patent with regard to Claims 1 to 9, 11 to 16, and 18 on March 6, 2018 (Exhibit Ko 50, the case of Invalidation Trial No. 2018-800028).

On June 11, 2019, the JPO made a trial decision to invalidate the Present Patent with regard to Claims 1 to 9, 11 to 16, and 18 (hereinafter referred to as "the Present Trial Decision"). A certified copy of the Present Trial Decision was served on the Plaintiff on June 20, 2019. A period of 90 days was added as a time limit for the Plaintiff to file a lawsuit against the Present Trial Decision.

(4) The Plaintiff filed the present lawsuit on October 16, 2019.

The Plaintiff's supporting intervener is a licensee of the Present Patent and made a supporting intervention on November 29, 2019.

2. Statement of the scope of claims

(1) Among the claims of the Present Patent after the Present Correction (hereinafter referred to as "Present Invention 1", etc.), independent claims are as follows.

[Claim 1]

A solution for preventing or reducing emesis having storage stability for at least 24 months, comprising:

a) 0.01 to 0.2 mg/ml palonosetron or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically acceptable carrier,

wherein the pharmaceutically acceptable carrier comprises mannitol.

[Claim 3]

A solution for treating cancer chemotherapy-induced nausea and vomiting (CINV) for preventing or reducing emesis having storage stability for at least 24 months, which is filled in a vial with a volume of 5 ml, comprising:

a) 0.03 to 0.2 mg/ml palonosetron or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically acceptable carrier.

[Claim 9]

A solution for intravenous administration for treating cancer chemotherapy-induced nausea and vomiting (CINV) for preventing or reducing emesis having storage stability for at least 24 months, comprising:

a) 0.01 to 0.02 mg/ml palonosetron or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically acceptable carrier.

[Claim 15]

A solution for preventing or reducing emesis at pH of 4.0 to 6.0 having storage stability for at least 24 months, comprising:

a) 0.01 to 0.2 mg/ml palonosetron or a pharmaceutically acceptable salt thereof; and

b) a pharmaceutically acceptable carrier.

[Claim 16]

A solution for preventing or reducing emesis having storage stability for at least 24 months, comprising:

a) 0.01 to 0.2 mg/ml palonosetron or a pharmaceutically acceptable salt thereof;

b) 10 to 100 millimoles of a citrate buffer; and

c) 0.005 to 1.0 mg/ml EDTA.

[Claim 18]

A method of filling a container in which a solution of palonosetron or a pharmaceutically acceptable salt thereof is contained, comprising:

a) providing one or more sterile open containers;

b) filling the containers with a solution of palonosetron in a non-aseptic environment;

c) sealing the filled containers; and

d) sterilizing the sealed, filled containers,

wherein: (i) the palonosetron or a pharmaceutical salt thereof is present in a

concentration of 0.01 mg/ml to 0.2 mg/ml in an injectable formulation; (ii) pH of the solution is 4.0 to 6.0; (iii) the solution comprises 0.005 to 1.0 mg/ml EDTA; (iv) the solution comprises mannitol; and (v) the solution comprises 10 to 100 millimoles of a citrate buffer, and wherein the solution of palonosetron or a pharmaceutically acceptable salt thereof has storage stability for at least 24 months.

(2) As mentioned above, each of the present inventions includes "storage stability for at least 24 months" (hereinafter referred to as "24-months requirement") as a matter for defining the invention. However, this requirement did not exist in the claims at the time of filing the present application and was added by the written amendment of November 14, 2013 (Exhibit Ko 8).

No. 3 Summary of the Present Trial Decision

1. The Present Trial Decision determined that Reason 2 for Invalidation (Failure to fulfill the clarity requirement) is unfounded, but Reason 1 for Invalidation (Failure to fulfill the support requirement) and Reason 3 for Invalidation (Failure to fulfill the enablement requirement) are well founded. Based on this determination, the Present Trial Decision invalidated the Present Patent with regard to all of the claims after the Present Correction. With regard to Reasons 1 and 3 for Invalidation, the Present Trial Decision explained that Reasons 1 and 3 for Invalidation are well founded on the 24-months requirement which is a common matter for defining the invention in each of the claims after the Present Correction. No determination was made with regard to other matters for defining the invention (a concentration of palonosetron, etc.).

Therefore, hereinafter, a summary of the reasons of the Present Trial Decision on the grounds that the 24-months requirement fails to fulfill the support requirement and the enablement requirement will be presented below.

2. Reason 1 for invalidation (failure to fulfill the support requirement)

(1) In the description of the Present Patent (hereinafter referred to as "the Present Description"), there are the following statements which are directly related to the 24-months requirement. (Judgment Note: Underlines are added by this judgment. In this judgment, the "detailed description of the invention" in the description may be referred to simply as "the description." Among the claims after the Present Correction, the Present Trial Decision separately explains Claims 1 to 9 and 11 to 16 which are inventions of products, and Claim 18 which is an invention of a process. However, the explanations are substantially the same. Thus, both categories of the inventions are hereinafter collectively referred to as "each of the present inventions.")

"[0017]

Summary of the Invention

The inventors have made a series of discoveries which support a surprisingly effective and versatile formulation for the treatment and prevention of emesis using palonosetron. These formulations are storage-stable for a period exceeding 24 months at room temperature, and thus can be stored without refrigeration, and manufactured using non-aseptic, terminal sterilization processes."

"[0037]

Still further embodiments relate to improved methods with which the palonosetron formulation can be easily stored or manufactured. In particular, the present inventors have discovered that the formulation of the present invention allows storage of the product for a prolonged period at room temperature. Thus, in yet another embodiment, the present invention provides a method of storing one or more containers in which a solution of palonosetron or a pharmaceutically acceptable salt thereof is contained, comprising: a) providing a room comprising the one or more containers; b) maintaining the temperature of the room at higher than about 10, 15, or 20°C; and c) storing the containers in the room for 1 month, 3 months, 6 months, 1 year, 18 months, 24 months or more (but preferably not exceeding 36 months), in which: (i) the palonosetron or a pharmaceutical salt thereof is present in a concentration of about 0.01 mg/mL to about 5.0 mg/mL; (ii) the pH of the solution is about 4.0 to about 6.0; (iii) the solution comprises about 0.01 to about 5.0 mg/ml palonosetron or a pharmaceutically acceptable salt thereof, about 10 to about 100 millimoles of a citrate buffer, and about 0.005 to about 1.0 mg/ml EDTA; (iv) the solution comprises a chelating agent; or (v) the solution comprises about 10 to about 100 millimoles of a citrate buffer."

However, all of these statements only literally state the period during which the palonosetron formulation can be stably stored, and do not concretely indicate the period during which the palonosetron formulation can be stably stored with supporting evidence which can be understood by a person ordinarily skilled in the art. Therefore, it cannot be deemed that, based on these statements, each of the present inventions in which the 24-months requirement is a matter for defining the invention is substantially stated in the description.

(2) The Present Description states in [0019], [0020], [0032], and [0034] to [0037] that it has been discovered that the stability of the palonosetron formulation can be increased by adjusting the pH and/or excipient concentrations and by adding mannitol and a chelating agent. However, the Present Description does not state that

the period during which the palonosetron formulation can be stably stored has been concretely confirmed. Thus, none of these statements concretely indicates the period during which the palonosetron formulation can be stably stored with supporting evidence, etc. which can be understood by a person ordinarily skilled in the art. Therefore, it cannot be deemed that, based on these statements, each of the present inventions in which the 24-months requirement is a matter for defining the invention is substantially stated in the description.

(3) The Present Description states Examples 1 to 5 in [0039] to [0045]. However, none of these statements concretely indicates the period during which the palonosetron formulation can be stably stored with supporting evidence, etc. which can be understood by a person ordinarily skilled in the art. Therefore, it cannot be deemed that based on these statements, each of the present inventions in which the 24-months requirement is a matter for defining the invention is substantially stated in the description.

(4) In [0046] to [0051] of the Present Description, test results on the storage stability of the palonosetron formulation are disclosed as Examples 6 and 7. All of the test results were obtained by first storing test samples in the dark at 4°C for 14 days and then exposing them to standard laboratory fluorescent light at 23°C for 48 hours, and thus a total period is 16 days (14 days plus 48 hours).

In this regard, according to Exhibit Ko 3 (Notification No. 43 of Examination Division, Pharmaceutical Affairs Bureau of February 15, 1991, "Iyakuhin no Seizo (Yunyu) Syonin Shinsei ni saishite Tenpu Subeki Anteisei Shiken Seiseki no Toriatsukai ni tsuite (Tsuchi) (Handling of Stability Test Results to be Attached to Applications for Manufacturing (Import) Approval of Pharmaceuticals (Notification))" (in Japanese)) and Exhibit Ko 4 (Notification No. 0603004 of Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau of June 3, 2003, "Anteisei Deta no Hyoka ni kansuru Gaidorain ni tsuite (Guidelines on the Evaluation of Stability Data)" (in Japanese)) both of which were distributed prior to the time of filing the original application, it can be acknowledged that it was common general technical knowledge at the time of filing the original application that in order to confirm a period during which a pharmaceutical composition can be stably stored, results for a period exceeding the above period to be confirmed are, in principle, required, and that if long-term data show little change or variation over time, extrapolation may be made, but the presented period should be up to twice the period covered by the long-term data, and should not exceed the period covered by the long-term data by 12 months or more.

Thus, the above statements on Examples 6 and 7 also do not concretely indicate that the solution comprising palonosetron or a pharmaceutically acceptable salt thereof "has storage stability for at least 24 months," with supporting evidence, etc. which can be understood by a person ordinarily skilled in the art. Therefore, it cannot be deemed that, based on these statements, each of the present inventions in which the 24-months requirement is a matter for defining the invention is substantially stated in the description.

(5) Even after considering other statements in the Present Description, there are no statements which concretely indicate that the solution comprising palonosetron or a pharmaceutically acceptable salt thereof "has storage stability for at least 24 months."

(6) In addition, even after considering the statements in each of the evidences of the present case, it is not possible to find any common general technical knowledge at the time of filing the original application to provide grounds for concluding that each of the present inventions in which the 24-months requirement is a matter for defining the invention is substantially stated in the description.

(7) According to the above, each of the present inventions in which the 24-months requirement is a matter for defining the invention is not substantially stated in the description, regardless of whether or not the pH, mannitol, and a chelating agent are specified.

3. Reason 3 for invalidation (failure to fulfill the enablement requirement)

Since each of the present inventions has the 24-months requirement as a matter for defining the invention, in order to fulfill the enablement requirement, the statement of the Present Description must be sufficient to enable a person ordinarily skilled in the art to produce and use the palonosetron formulation which satisfies the 24-months requirement according to each of the present inventions.

However, for the same reasons as discussed in 2(1) to (5) above, in the Present Description, there are no statements which concretely indicate that the solution according to each of the present inventions "has storage stability for at least 24 months," with supporting evidence, etc. which can be understood by a person ordinarily skilled in the art. Thus, it is not possible to find any statements to provide grounds for concluding that a person ordinarily skilled in the art can produce and use the "solution having storage stability for at least 24 months" according to each of the present inventions. In addition, even after considering the statements in each of the evidences of the present case, it is also not possible to find any common general technical knowledge at the time of filing the original application to provide grounds

for concluding that a person ordinarily skilled in the art can produce and use the "solution having storage stability for at least 24 months" according to each of the present inventions in light of the common general technical knowledge at the time of filing the original application.

Therefore, the statement of the Present Description is not stated in a manner clear and sufficient for a person ordinarily skilled in the art to work each of the present inventions.

(omitted)

No. 6 Judgment of the court

1. Reasons 1 for rescission (erroneous determination on fulfillment of the support requirement)

(1) Statement of the Present Description

A. Statement on the problem of each of the Present Inventions

The Present Description states in [0001] to [0007] and [0012] to [0015], concerning the background art and the problem of the invention, that the problem of each of the present inventions is to provide a palonosetron formulation which has increased pharmaceutical stability and allows storage for a prolonged period, and to provide an acceptable range of concentrations which will stabilize the palonosetron formulation. In these paragraphs, there is no mention of the specific length of the "prolonged period". However, since the 24-months requirement was added to each claim by the written amendment on November 14, 2013 (Exhibit Ko 8) during the examination of the present application, it can be deemed that the "prolonged period" had been defined to mean 24 months or more.

B. Statement on the 24-months requirement

(a) The Present Description states in [0017] that an effective and versatile formulation using palonosetron is storage-stable for a period exceeding 24 months at room temperature, and thus can be stored without refrigeration. Further, the Present Description states in [0037] that by a method of storing a container containing a solution of palonosetron or a salt thereof in which a product can be stored for a prolonged period at room temperature, the container can be stored for 24 months or more.

However, none of the paragraphs includes any concrete statements as to how it was confirmed that the formulation or the container could be stored for 24 months or more.

(b) Taking into overall consideration [0032] to [0034] of the Present Description, it is stated that in a stable solution containing: a) about 0.01 mg/ml to about 5.0 mg/ml palonosetron or a salt thereof; and b) a carrier, the stability of the palonosetron formulation can be increased by adjusting the pH and/or the excipient concentrations of the formulation. In addition, it is stated that the pH is about 4.0 to about 6.0, and about 10 to about 100 millimoles of a citrate buffer and about 0.005 to about 1.0 mg/ml EDTA are mixed. Further, it is stated that the addition of mannitol and a chelating agent can increase the stability of the palonosetron formulation, and that the chelating agent is added at about 0.005 to about 1.0 mg/ml and mannitol is added at about 10.0 mg/ml to about 80.0 mg/ml.

However, none of the paragraphs includes any statements directly related to the 24-months requirement.

(c) In [0039] to [0041] of the Present Description, concerning Examples 1 to 3 of the invention, there are statements on the results of tests on the pH value at which the formulation containing palonosetron hydrochloride is most stable [0039], the results of investigations on the preferred concentration range of palonosetron hydrochloride, a citrate buffer, and EDTA [0040], and the results of investigations on the optimum level of mannitol contained for the stability of the formulation [0041], respectively.

Further, in [0042] to [0044] of the Present Description, concerning Examples 4 and 5 of the invention, there are statements on the ratios of ingredients of "representative pharmaceutical formulations containing palonosetron which are useful for intravenous formulations or other liquid formulations of drugs." The ratios of the ingredients are included in the ranges specified by Present Invention 2 for Example 4 and by Present Invention 1 for Example 5.

However, with regard to Examples 1 to 3, there are no statements as to what kinds of tests or investigations were conducted and what kinds of test or investigation results were used to evaluate the stability of the formulation. In addition, with regard to Examples 4 and 5, there are no statements that a stability test was conducted to provide supporting evidence in the first place. Moreover, there are no statements directly related to the 24-months requirement.

(d) In [0046] to [0051] of the Present Description, concerning Examples 6 and 7 of the invention, test results on the stability of palonosetron in the absence and presence of dexamethasone are stated, respectively.

With regard to the compositions of the samples used in the tests, there are statements which suggest that the concentrations of palonosetron hydrochloride are

approximately included in the range specified in each of the present inventions. However, there are no statements on the presence or absence and concentrations of other ingredients (excipients, isotonic agents, etc.), and no statements on the pH value. Further, the period during which the stability was evaluated was 16 days for the longest sample (sample collected after storage at 4°C for 14 days and at 23°C for 48 hours), which was far from 24 months.

(2) Common general technical knowledge at the time of filing the original application

According to each of the evidences below, it can be found that there was the following common general technical knowledge at the time of filing the original application.

A. Stability tests in an application for approval of a pharmaceutical product are tests which are conducted to evaluate the stability of the quality of the pharmaceutical product necessary to maintain its efficacy and stability, and to obtain the information necessary to establish the storage method and the shelf life of the pharmaceutical product. Among these tests, a long-term storage test is conducted for a test period of 3 years or more (if a shelf life is set in a written application for approval, the test period should be the above shelf life or more), and an accelerated test is conducted to estimate the stability of quality in a short period, and the test period should be 6 months or more. (Exhibit Ko 3)

B. If long-term data and accelerated data for an item show little change and variation over time, the extrapolation of a retest period or shelf life beyond the period covered by the long-term data may be presented, and up to twice the retest period or shelf life covered by the long-term data may be presented, but it should not exceed the period covered by the long-term data by 12 months or more. (Exhibit Ko 4, Exhibit Ko 5 (Notification No. 196 of Osaka Pharmaceutical Manufacturers Association of June 7, 2002, "Anteisei Deta no Hyouka ni kansuru Gaidorain (An) ni tsuite (Guidelines on the Evaluation of Stability Data (Draft))" (in Japanese)))

C. Factors for finding reasonable conditions for stabilization of drugs include temperature, pH, solubility, solvents, and additives. The transformation of injectable formulations is often affected by pH. Thus, it is important to select a buffer solution system to maintain the most stable pH. (Exhibit Ko 21 (Naoki Wakiyama "Iyakuhin no Anteisei to Yuko Kikan (Stability and Shelf Life of Pharmaceuticals)", Materials Life, Vol. 3, No. 2, pages 104 to 109, 1991 (in Japanese))

D. Preformulation (preliminary formulation design) is positioned at an initial stage of pharmaceutical formulation research in pharmaceutical development and

refers to a process of clarifying physicochemical, mechanical, chemical, and biopharmaceutical properties of a drug substance necessary for subsequent formulation research (formulation design) and reflecting them in the formulation research. (Exhibit Ko 59 ("Saishin Seizai Gaku (The Latest Formulation Science)", Hirokawa Shoten, page 135, lines 3 to page 136, lines 2, September 25, 2001 (in Japanese)), Exhibit Ko 60 ("Iyakuhin no Kaihatsu, Dai 16 Kan, Purefomyureshon to Yakubutsu Bussei Shiken (Development of Pharmaceuticals, Volume 16, Preformulation and Drug Property Testing)", Hirokawa Shoten, page 1, lines 2 to 20, published on January 15, 1990 (in Japanese)), Exhibit Ko 61 ("Seizai Gaku Tekisuto (Textbook of Formulation Science)", Hirokawa Shoten, page 122, lines 2 to page 123, lines 4, May 15, 1992 (in Japanese))

(3) Discussion

As mentioned in (1)B(b) and (c) above, the Present Description states that the stability of a solution containing palonosetron or a salt thereof is increased by adjusting the pH and/or excipient concentrations and by adding mannitol and a chelating agent at appropriate concentrations. In addition, in Examples 1 to 3 of the Present Description, the pH value at which the formulation is most stable, the preferred concentration range of a citrate buffer and EDTA, and the optimum level of mannitol are presented. Further, in Examples 4 and 5 of the Present Description, the representative pharmaceutical formulations are presented, but the stability tests were not actually conducted in Examples 4 and 5. Thus, it cannot be deemed that it is stated that the pharmaceutical formulations stated in the Present Description have storage stability for at least 24 months. In addition, in other portions of the Present Description, factors which contribute to stabilization are listed. However, there are no direct statements that these factors achieve storage stability for 24 months. Furthermore, there is no concrete indication to provide grounds for inferring what factors would make it possible to achieve what level of storage stability. After all, it cannot be deemed that it is stated with concrete supporting evidence that the specific pharmaceutical formulations have storage stability for at least 24 months.

Moreover, as mentioned in (1)B(b) above, the series of Examples in the Present Description is to explore the factors to find a reasonable condition for stabilization of drugs. In particular, it can be deemed that Examples 1 to 3 correspond to preformulation (preliminary formulation design) to explore individual factors, and the representative pharmaceutical formulations of Examples 4 and 5 correspond to formulation research (formulation design). However, as mentioned above, the Present Description does not state what action and mechanism are involved in the

improvement of stability and to what extent the improvement of stability and the contribution to stability can be expected by adjusting the pH and the concentrations of excipients, mannitol, and chelating agents. Thus, it cannot be deemed that it is stated that the pharmaceutical formulations of Examples 4 and 5 have storage stability for at least 24 months. In addition, even taking into consideration other portions of the Present Description, it cannot be deemed that it is stated with reasonable explanation that the specific pharmaceutical formulations have storage stability for at least 24 months.

Therefore, it cannot be deemed that the Present Description states a palonosetron formulation with the 24-months requirement. In addition, even in light of the common general technical knowledge at the time of filing the present application, it cannot be deemed that each of the present inventions is within the scope of the invention which a person ordinarily skilled in the art can recognize as being able to solve the problem of each of the present inventions ((1)A above); i.e., the problem of providing a palonosetron formulation which increases pharmaceutical stability and allows storage for 24 months or more and of providing an acceptable range of concentrations which stabilize the palonosetron formulation.

Furthermore, as mentioned in (1)B(d), since Examples 6 and 7 lack statements on the presence or absence and the concentrations of ingredients (excipients, isotonic agents, etc.) other than palonosetron hydrochloride as well as the pH values, it cannot be deemed that these are working examples on the formulations corresponding to each of the present inventions. In Examples 6 and 7, the stability was confirmed for only 16 days at the longest. Therefore, even in light of the common general technical knowledge in (2)B above, Examples 6 and 7 cannot be grounds for solving the problem of each of the present inventions ((1)A above) such as providing a palonosetron formulation with the 24-months requirement.

(4) The Plaintiff's assertion

A. Assertion in No. 4, 1(1) and (2) above

As mentioned in (3) above, the Present Description does not state what action and mechanism are involved in the improvement of stability and to what extent the improvement of stability and the contribution to stability can be expected by adjusting the pH and the concentrations of excipients, mannitol, and chelating agents. Thus, even based on the common general technical knowledge at the time of filing the present application, it cannot be deemed that it is stated that the pharmaceutical formulations of Examples 4 and 5 have the 24-months requirement. In addition, even taking into consideration other portions of the Present Description, it cannot be

deemed that it is reasonably explained, based on concrete grounds, that the specific pharmaceutical formulations have storage stability for at least 24 months. Further, the statements [0017] and [0037], which directly mention the period of 24 months, also lack any concrete mention as to how it was confirmed that the formulation or the container can be stored for 24 months or more, as mentioned in (1)B(a) above. Thus, it cannot also be deemed that the statements of these paragraphs indicate that the 24-months requirement is substantially stated in the Present Description.

Therefore, the Plaintiff's assertion in No. 4, 1(1) and (2) above is not acceptable.

B. Assertion in No. 4, 1(3) above

(a) Compliance with the support requirement should be acknowledged on the basis of the matters stated in the description and the common general technical knowledge at the time of filing the application. Thus, as mentioned in (3) above, even though the Present Description and the common general technical knowledge do not enable us to recognize that a formulation with the 24-months requirement is stated, it should be deemed that it is not permissible to compensate for the above deficiency in the description by submitting experimental data (Exhibits Ko 36 and Ko 33) after filing of the present application.

(b) In addition, the Plaintiff asserts to the effect that Exhibits Ko 36 and Ko 33 are not new experimental results, because Exhibits Ko 36 and Ko 33 merely compensate for paragraphs [0017] and [0037] of the Present Description. However, the Present Description does not state at all by what method and under what condition the tests were conducted to confirm the storage stability for 24 months as stated in [0017] and [0037]. Thus, it is unclear whether or not the tests in Exhibits Ko 36 and Ko 33 were conducted using the same method and conditions as those in the Present Description. Therefore, the Plaintiff's assertion is improper.

In this regard, the Plaintiff asserts that: A) the experimental method and conditions are substantially the same as those stated in the Present Description; B) the obtained results are substantially the same as those stated in the Present Description; C) the experimental method is within the scope of the common general technical knowledge at the time of filing the original application; and D) the experimental method for measuring storage stability is quite simple. However, as mentioned above, the Present Description does not state at all by what method and under what conditions the tests were conducted to confirm the storage stability for 24 months. Thus, it cannot be deemed that the experimental method and conditions and the obtained results in Exhibits Ko 36 and Ko 33 are substantially the same as those

stated in the Present Description. In addition, the fact that the results are the same does not necessarily mean that the experimental method and conditions are the same. Further, if the experimental method for measuring storage stability is fixed, the Plaintiff's assertion might be acceptable. However, in fact, this is not true (there is no sufficient evidence to admit such circumstances). Thus, even if the experimental method is within the scope of the common general technical knowledge and even if the experimental method is simple, this does not guarantee that the experimental method and condition stated in the Present Description are the same as those in Exhibits Ko 36 and Ko 33.

(c) Therefore, the Plaintiff's assertion in No. 4, 1(3) above is not acceptable.

C. Assertion in No.4, 1(4) above

(a) The Plaintiff asserts that in order to acknowledge the compliance with the support requirement, it is sufficient that there is a statement to the extent that a person ordinarily skilled in the art can obtain a reasonable expectation that the problem could be solved in view of the common general technical knowledge. However, as explained in (1) to (3) above, since the Present Description lacks any concrete statements in line with the 24-months requirement, it cannot be acknowledged that there is a statement to the extent that a person ordinarily skilled in the art who has read the Present Description can obtain a reasonable expectation that the problem (storage stability for 24 months or more) could be solved.

(b) In light of the content of the prosecution history documents (Exhibits Ko 7 and Ko 8) and the Present Description, it can be acknowledged that the circumstances in which the amendment was made to add the 24-months requirement as a matter for defining the invention in the course of the prosecution history of the Present Patent, and the reasons why the experimental results supporting the 24-months requirement were not stated in the Present Description at the time of filing the original application are generally as asserted by the Plaintiff.

However, even if there is a time constraint under the first-to-file principle, the compliance with the support requirement cannot be affirmed by statements which do not even reach the extent that "a reasonable expectation" can be obtained as mentioned in the Plaintiff's assertion in (a) above. With regard to this, it has already been explained that it cannot be acknowledged that there is a statement to the extent that a reasonable expectation can be obtained.

In addition, the Plaintiff asserts to the effect that it was unforeseeable that the amendment to add the 24-months requirement would be necessary in the present case, and that the addition of the experimental results in Exhibits Ko 36 and Ko 33 should

be allowed because there are unavoidable circumstances in which the statement to support this point was insufficient.

However, it is questionable whether such circumstances would allow the later submission of the experimental results in the first place. Further, it is a common situation that various amendments will be necessary in the prosecution of an application. In this regard, from the time of filing the present application, the Plaintiff stated in the Present Description that the problem of each of the present inventions is to provide a palonosetron formulation which has increased pharmaceutical stability and allows storage for a prolonged period, and to provide an acceptable range of concentrations which will stabilize the palonosetron formulation ([0013] to [0015]), and that an effective and versatile formulation using palonosetron is storage-stable for a period exceeding 24 months at room temperature ([0017]). Thus, there is also a question as to whether the amendment to add the 24-months requirement can be deemed to have been unexpected, and the Plaintiff's assertion is questionable even in its premise.

(c) Therefore, the Plaintiff's assertion in No. 4, 1(4) above is not acceptable.

2. According to the above, it is not erroneous for the Present Trial Decision to determine that each of the present inventions fails to fulfill the support requirement. Therefore, without going so far as to determine Reasons 2 for Rescission (Erroneous determination on fulfillment of the enablement requirement), it is not erroneous for the Present Trial Decision to conclude that the patent concerning each of the present inventions shall be invalidated.

For the foregoing reasons, the judgment is rendered as mentioned in the main text.

Intellectual Property High Court, Third Division

Presiding Judge TSURUOKA Toshihiko

Judge UEDA Takuya

Judge TSUNO Michinori