PATENT COURT
THE THIRD DEPARTMENT
DECISION

Case No. 99Heo9373 Dismissal of Amendment (Patent)

Plaintiff: Pfizer Inc.
Counsel for the Plaintiff: Chang Se KIM,
Eunhwa CHOI, Youngmi NAH, Patent Attorney
Youngmo KWON, Attorney-at-law
Substitutes for the Counsels: Dongin SHIN,
Hyunsil LEE, Patent Attorney

Defendant: Commissioner of the Korean Intellectual Property Office ("KIPO")
KIPO Litigators: Jaecheol NOH, Manho MIN

Closure of Hearing: June 23, 2000

Order

1. The Plaintiff's claim is dismissed.
2. The trial costs shall be borne by the Plaintiff.

Tenor of Claim

The decision of the Intellectual Property Trial and Appeal Board, which was issued on October 30, 1999 in Case No. 99Bo4, shall be cancelled.

Reasoning

1. Background facts

The following facts are recognized after considering the descriptions and arguments based on Exhibit Nos. Kap-1 to 5, Kap-9, Eul-2-1, Eul-2-2 and Eul-3.

A. Details and procedures relating to the subject decision

1) The Plaintiff filed a patent application for an invention entitled "5 -Arylindole derivatives and use thereof for serotonin agonist" in the United States on November 2, 1992 (Application No. 07/970758), filed an international patent application under Patent Cooperation Treaty (PCT) on October 19, 1993 while claiming priority to the above patent application (International Patent Application No. PCT/US 93/09790), submitted a translation of the international patent application to the KIPO on May 2, 1995 (Application No. 95-701729), and filed a divisional application with the claims reproduced below in Section 'B' on June 23, 1998 (Application No 98-704854; hereinafter referred to as the 'Subject Invention'; for the compounds used for the Subject Invention, a separate divisional application was filed and registered as a patent on September 5, 1998).

2) The KIPO issued Grounds of Rejection on August 22, 1998 based on the following grounds: the Subject Invention cannot be patented according to Article 29, Paragraph 1 of the Patent Act since Claims 1 and 2 (which recite use inventions for medicines) are not supported by the descriptions of materials (such as data) for demonstrating pharmacological effect as a requisite for establishing a medicinal invention in the Detailed Description of Invention such that the Subject Invention cannot be deemed to be an invention having been completed as an invention of medicinal use as of the application date;

and the Subject Invention cannot be patented pursuant to Article 42, Paragraph 3 of the Patent Act since the requirement for description as an invention of medicinal use was not fulfilled since there is no data directed to toxicity.

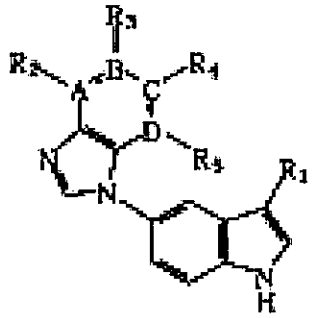
3) The Plaintiff submitted an Amendment on December 22, 1998, wherein the specification was amended as described in Section 'C'. However, the KIPO issued a Dismissal of Amendment on December 28, 1998 based on the ground that the description of pharmacological test results, which was added according to the Amendment, constituted an additional matter that had not been described in the original specification at the time of filing. According to the KIPO, the Amendment changed a significant matter of the specification, and thus, the amendment cannot be admitted according to Article 51, Paragraph 1 of the Old Patent Act (the Patent Act prior to the revision of Law No. 5329 on April 10, 1997).

4) In response to the Dismissal of Amendment, the Plaintiff filed an appeal on February 5, 1999. The Intellectual Property Tribunal decided to dismiss the appeal on October 30, 1999 based on the grounds described in Section 'D' (hereinafter, the decision is referred to as the 'Subject Decision').

B. Claims of the Subject Invention

Claim 1: A pharmaceutical composition for treatment of a disease selected from a group consisting of hypertension, depression, anxiety, dietary disorder, obesity, drug addiction, multi-centric headache, migraine, sharp pain, chronic paroxysmal migraine and headache in connection with vascular disorder, which comprises a compound represented by Chemical Formula (I) [description of the substituents being omitted] in an effective amount for treating such a disease, and a pharmaceutically acceptable carrier.

(Chemical Formula 1)



Claim 2: A pharmaceutical composition for treatment of a disease caused by serotonergic neural transmission deficiency, which comprises a compound represented by Chemical Formula (1) [as shown above] in an effective amount for treating such a disease, and a pharmaceutically acceptable carrier.

C. Amendment

The values of IC_{50} (inhibitory concentration of a drug that causes 50% of the maximum inhibition) for twenty (20) compounds of Chemical Formula I, which were described in the Examples of the Subject Invention, i.e., measured values of activities of the compound of Chemical Formula I on serotonin (5-HT1A and 5-HT1D) receptor, were added to the specification (Exhibit No. Kap-3, page 30). Further, the toxicity data were supplemented (page 98).

D. Gist of the Decision Grounds

1) Since an invention of medicinal use is established on the basis of pharmacological activity of a certain substance or composition that was confirmed, the pharmacological activity must be described in the specification at the time of filing a patent application (hereinafter referred to as the 'original specification') such that the activity can be specifically identified. Further, the pharmacological activity cannot be

simply presumed for an invention of medicinal use since there are numerous cases wherein compounds having similar molecular structures show completely different chemical properties. Thus, the pharmacological activity should be described with specific experimental data or concrete substance that can replace the same.

2) The Subject Invention is directed to an invention of a medicine that employs a pharmaceutical composition (hereinafter referred to as the "compound of the Subject Invention"), which comprises a compound represented by Chemical Formula (I) and a pharmaceutically acceptable carrier, for treating a disease selected from a group consisting of hypertension, depression, anxiety, dietary disorder, obesity, drug addiction, multi-centric headache, migraine, sharp pain, chronic paroxysmal migraine and headache in connection with vascular disorder, as well as for treating a disease caused by serotonergic neural transmission deficiency. Since the Subject Invention states that its compound demonstrates a therapeutic effect to treat said diseases due to an activity as a serotonin agonist, the pharmacological effect of the compound of the Subject Invention with respect to said diseases such as activity as a serotonin agonist must be specifically identified in the original specification. However, the original specification of the Subject Invention has no specific description, which state that the compound of the Subject Invention is useful for treating a disease caused by serotonergic neural transmission deficiency or has an activity as a serotonin ($5\text{-}HT_1$) agonist. The table added on page 30 of the amended specification of the Subject Invention describes the specific values of binding affinity (IC_{50}) as the test results of pharmacological effect of twenty (20) compounds among the compounds of the Subject Invention (which were synthesized in Examples) on serotonin ($5\text{-}HT_1$) receptor. Thus, the pharmacological effect of the compound of the Subject Invention was specifically identified after the additional amendment was filed.

3) Accordingly, such an Amendment changed a significant matter of an invention described in the original specification.

2. Arguments of parties concerned

A. Summary of Plaintiff's arguments

1) The original specification of the Subject Invention describes the constitution of the invention including the object of the invention, chemical structures of the compounds, and a process of preparing the same. It also discloses the pharmacological activity of the Subject Invention, which the compounds of the Subject Invention are useful for treating a disease caused by serotonergic neural transmission deficiency such as depression, anxiety, dietary disorder, obesity, migraine and hypertension, as well as conventional methods to determine the activity of compounds as serotonin agonists. Further, total substances to carry out the Subject Invention as an invention of medicine, including methods for formulation and administration and doses, are described so that a person having ordinary skill in the art ("PHOSITA") can easily confirm the activity as a serotonin agonist demonstrated by the compound of the Subject Invention after reviewing the descriptions in the original specification, and easily carry out the Subject Invention as an invention of a medicinal use.

Further, Article 42, Paragraph 3 of the Patent Act (which prescribes the requisites for a specification) only prescribes that a specification should be described so that PHOSITA can easily carry out the invention. The Patent Act does not prescribe anywhere that specific experimental data for the activity must be described in order to demonstrate the pharmacological effect.

Accordingly, the original specification of the Subject Invention simply includes somewhat less experimental data to identify the pharmacological effect. However, all the requisites for PHOSITA to understand that the Subject Invention is effective on hypertension,

headache and the like (and to easily carry out the Subject Invention) are described therein. Thus, the Subject Invention has sufficient descriptions and is not an incomplete invention.

2) The gist of the Subject Invention, as disclosed by the original specification, is that the pharmaceutical composition according to the Subject Invention acts as a serotonin agonist, thereby being effective on diseases caused by serotonergic neural transmission deficiency such as depression. Even though the experimental data added through the Amendment could not be directly anticipated from the disclosure in the original specification, PHOSITA can reproducibly contrive them by easily carrying out the experiments according to the known procedure disclosed in the specification with the compounds of Examples, the chemical structures of which are disclosed in the original specification.

Accordingly, the Amendment does not change a significant matter since the pharmacological effect of the Subject Invention was achieved as of the filing date of the patent application. Further, the effect described in the original specification was identified via the Amendment without departing from the substance of the original specification.

B. Summary of the Defendant's arguments

Since the essential of an invention of a chemical material resides on the material, it is enough to describe (concerning use of the material) for which the material can be used, i.e., utility of the material in the specification. However, in case of an invention of medicinal use to treat a disease (like the Subject Invention), the essential of the invention is use for treating the disease. Thus, the technical substance directed to the pharmacological effect that demonstrated the therapeutic usefulness of the material, i.e., objective and specific test materials to support a medicinal effect that was elucidated by tests in practice, should be described in the specification. Accordingly, in the specification of the Subject Invention, test materials that objectively support the

therapeutic effect for treating a disease related to serotonergic deficiency should be described regarding the medicinal use, or at least specific test result should be described to confirm the mechanism related to activity of the compound of the Subject Invention as a serotonin agonist. However, the original specification of the Subject Invention simply lists the diseases (including hypertension, depression, anxiety, dietary accentuation, obesity and migraine), which can be treated according to the Subject Invention, without any description of test materials that can objectively support the therapeutic effect for treating a disease related to serotonergic deficiency, nor any specific test result to confirm the mechanism related to activity of the compound of the Subject Invention as a serotonin agonist. As such, the original specification of the Subject Invention fails to meet the requisite for description of an invention.

2) The Subject Invention adds IC_{50} values through the Amendment, which are concentrations of test material when binding of a reactant having radio-active label to a receptor is inhibited by 50%. Determination of IC_{50} values is to carry out practical tests to find out how much the binding affinity of the test material to the receptor is, and the determined IC_{50} values are objective and specific experimental data that may confirm the level of activity or mechanism of the test material. Thus, an amendment of adding IC_{50} values corresponds to adding a new technical matter to support the use of a medicine, which is beyond the scope of the originally described specification, and substantially changes the constitution of an invention of medicinal use. Accordingly, such an amendment corresponds to altering a significant matter of an invention.

3) If an amendment of adding a pharmacological effect (which is a core requisite for describing an invention of medicinal use) is permitted for an invention of medicinal use, then this would result in substantial retroaction of the application date. This would be contrary to the

Korean patent system, which follows the first-to-file rule.

3. Decision

A. Level of description of pharmacological effect in the specification for an invention of medicinal use

Article 42, Paragraph 3 of the Patent Act prescribes that the object, constitution and effect of an invention should be described in the Detailed Description of Invention so that PHOSITA can easily carry out the invention. Further, Article 42, Paragraph 4 prescribes that the claims of a patent application must be supported by the Detailed Description of Invention. This is so that those skilled in the art can: clearly understand the substances of the invention and easily carry out the invention by specific description of the subject to be solved by the invention, means selected to solve the subject or technical constitution of the invention, and inherent effect achieved by the invention in the Detailed Description of Invention; clarify the substance of the invention to facilitate examination of the requisites as a patent; and elucidate the technical scope of the invention.

In case of inventions directed to chemical materials in general, the invention is characterized by the material itself. Accordingly, if the use of the material should be described in the Detailed Description of Invention, then it is enough to describe the usefulness of the material to an extent that the material can be utilized in a certain technical field or the like. However, in case of an invention of medicinal use, the invention is characterized by discovering use of a certain material as a medicine, i.e., the effect of treating or preventing a certain disease, not being an invention of the material itself used for a medicine, so that the use or effect should be an essential constituent of the invention. The effect cannot be anticipated simply on the basis of chemical structure since there are a number of compounds having quite different chemical properties between the compounds having

similar chemical structures. Further, since a medicine is used on human bodies, which have complicated structures and functions, even though an effective dose, route of administration and particulars for formulation are described to some extent in the specification, PHOSITA cannot recognize whether the medicine is actually active for such a use. Thus, in the specification of a patent application for an invention of medicinal use, the pharmacological effect of a certain substance should be objectively and concretely described so that PHOSITA can clearly understand, recognize and reproduce the pharmaceutical activity of the certain substance without adding any particular knowledge at the technical level as of the application date. If the pharmacological mechanism of a certain substance, which demonstrates a certain pharmacological effect, had been already clarified before filing of the patent application, then it is enough to simply describe such a pharmacological effect. However, if it is not, then experimental results from specific experiments to confirm such a pharmacological effect of the certain substance should be quantitatively described or at least specifically described to replace such quantitative data.

As such, when the specification of an invention of medicinal use lacks such description, the predetermined requisites for describing the specification according to Article 42, Paragraphs 3, 4 are not satisfied. Further, a specification lacking such description cannot be deemed to recite a complete invention since the technical completion or incompletion of an invention is decided on the basis of descriptions provided in the specification.

B. Whether pharmacological effect is sufficiently described in the original specification of the Subject Invention

1) The Subject Invention relates to a pharmaceutical composition for treating hypertension, depression, anxiety, dietary disorder, obesity, drug addiction, multi-centric headache, migraine, sharp pain, chronic

paroxysmal migraine and headache in connection with vascular disorder, or a disease caused by serotonergic neural transmission deficiency. Although being novel substances, the compounds of the Subject Invention have been already registered as a material patent. As noted above, the Subject Invention corresponds to a medicinal use invention. As disussed below, the original specification of the Subject Invention describes that indole derivatives (compounds of same type as the compounds of the Subject Invention) are useful for treating hypertension, Raymond's disease and migraine. For chemical compounds, there are many cases of demonstrating remarkably different chemical properties between compounds having similar structural formulas, and the pharmacological mechanism of the compounds of the Subject Invention (as different types of indole derivatives) cannot be definitely stated to be elucidated simply because some examples of indole derivatives having such therapeutic effect are described in the original specification. There is no evidence to regard the pharmacological mechanism being already elucidated otherwise. As such, the specification of the Subject Invention must involve quantitative description of experimental results from specific experiments, or any detailed description that may replace the experimental results, to confirm the pharmacological effect described in Claims 1 and 2 of the Subject Invention.

2) Now, the section concerning the pharmacological effect in the original specification of the Subject Invention will be discussed.

Page 1 of the specification describes the background art as follows: "USP 4,839,377 and 4,855,314, and European Patent Application Publication No. 313,397 mentions 5-substituted 3-aminoalkylindoles. These compounds are clearly expressed to be useful for treating migraine. GB Patent Application No. 40,279 mentions 3-aminoalkyl-1H -indole-5-thioamide and carboxamide. These compounds are clearly expressed to be useful for hypertension, Raymond disease and migraine." On pages 11 and 12, the specification describes: "The

present invention relates to a pharmaceutical composition which is useful for treating diseases caused by serotonergic neural transmission deficiency such as hypertension, depression, anxiety, dietary disorder, obesity, drug addiction, multi-centric headache, migraine, sharp pain, chronic paroxysmal migraine and headache in connection with vascular disorder." On page 28, the specification describes the following: "Compounds of Chemical Formula I and pharmaceutically acceptable salts thereof are used in mental therapeutics, being usable for treating depression, anxiety, dietary disorder, obesity, drug addiction, multi-centric headache, migraine, chronic paroxysmal migraine and headache in connection with vascular disorder, sharp pain and other diseases caused by serotonergic neural transmission deficiency, as a useful serotonin ($5-HT_1$) agonist and benzodiazepine agonist and antagonist. Alternatively, these compounds can be primarily used as an anti-hypertensive agent and a vasodilator." However, the descriptions simply mention the utility of compounds of the Subject Invention by listing the types of diseases that can be treated with the compounds. They cannot be deemed to be specific descriptions of the pharmacological effect.

Pages 28 and 29 of the specification describe: "The active compounds according to the present invention are evaluated as anti-migraine modifiers by examining the degree of imitating sumatriptan upon shrinkage of isolated hiatus saphenous of a dog [P.P.A. Humphrey et al., Br. J. pharmacol., 94, 1128 (1988)]. The efficacy may be blocked by metiodepin which has been known as a serotonin antagonist. Sumatriptan is known to be useful for treating migraine, and to selectively increase vascular resistance of carotid in an anesthetized dog. The basis of efficacy was suggested in W. Fenwick et al., Br. J. Pharmacol., 96, 83 (1989). The active compounds according to the present invention can be evaluated by plasma protein ejecting response in dura mater of guinea pig after one-way electric triple irritation of ganglion, as is described in Markowitz et al., J. Neurosci., 7(12) 4129-4136 (1987). From the aspect of potency, efficacy, or both, the degree

of these compounds for imitating sumatriptan is determined via analysis described below. Activity of serotonin 5-HT1 agonist is determined in vitro by employing an analysis of receptor binding by the use of cortex of rats as a receptor source and [^{3}H]-8-OH-DPAT as a radioactive ligand, as was explained for 5-HT1A receptor [D. Hoyer et al., Eur. J. Pharm., Vol. 118, 13 (1985)]; and an analysis of receptor binding by the use of a tail of cow as a receptor source and [^{3}H]serotonin as a radioactive ligand, as was explained for 5-HT1D receptor [R. E. Heuring and S. J. Peroutka, J. Neuroscience, Vol. 7, 894 (1987)]. Affinity to benzothiazepine receptor is determined in vitro by employing an analysis of receptor binding by the use of cerebellum of a guinea pig as a receptor source and [^{3}H] flunitrazepam as a radioactive ligand." However, it merely describes indirectly a method to determine the pharmacological effect such as IC_{50} of the compounds of the Subject Invention. Such description cannot be deemed to be a specific description of the pharmacological effect.

As such, the Subject Invention possesses insufficient descriptions or is an incomplete invention according to Article 42, Paragraphs 3 and 4 since the original specification of the Subject Invention fails to objectively and specifically describe the pharmacological effect such that PHOSITA can clearly understand the pharmacological effect of compounds of the Subject Invention and reproduce it without adding any particular knowledge on the basis of technical level as of the patent application.

C. Whether the Amendment of the specification of the Subject Invention changed a significant matter

1) Criteria

Article 47, Paragraph 1 of the Old Patent Act prescribes: "An applicant of a patent application may amend the specification or drawing(s) attached to the patent application ··· within the scope of not

for changing significant matter of the specification or drawing(s) which were originally attached to the patent application". Here, the amendment refers to clearly correcting any deficiency or insufficient matter in documents such as the specification. Further, the change of significant matter means to increase, decrease or alter the scope of claims recited in the specification, which brought substantial change so that the identity of substance cannot be recognized between the original claims and the amendment, e.g., the addition of a novel significant matter to the original claims or alteration thereof. Accordingly, an alteration, which does not reach such an extent, is not considered as changing a significant matter (*see* Supreme Court Decision No. 93Hu800 rendered on September 27, 1994).

Further, Article 48 of the Old Patent Act prescribes: "An amendment of increasing, decreasing or altering the scope of a claim within a range of what is described in the specification or drawing(s) originally attached to the patent application before the delivery of a copy of Decision of Patent Publication is regarded not to be a change of significant matter". In this respect, 『a range of what is described in the specification or drawing(s)』 includes not only what is described through direct expression, but also what is regarded to be described by PHOSITA through an objective consideration of the technical substance at the time of the patent application (i.e., what is obvious).

2) As discussed above, the pharmacological effect of the compounds of the Subject Invention is not specifically described in the original specification of the Subject Invention. However, the measured values of agonist activity of compounds of Chemical Formula I on serotonin ($5\text{-}HT_{1A}$ and $5\text{-}HT_{1D}$) were added through the Amendment of the specification for twenty (20) compounds from the Examples of the Subject Invention. This means that specific experimental results were expressed as quantitative values to confirm the pharmacological effect of the Subject Invention.

Thus, the description of pharmacological effect in the original specification is vague (not being based on specific experimental results), while actual experimental results were expressed as quantitative values in the amended specification of the Subject Invention. Even if a known experimental procedure to confirm the pharmacological effect of the compounds of the Subject Invention is described in the original specification, and if it is described that compounds similar to the compounds of the Subject Invention have the same effect as that of the Subject Invention, the result cannot be anticipated since the experimental result cannot be known until the experiment is practically carried out with respect to a chemical substance. Consequently, such experimental results do not correspond to an obvious subject matter that can be derived from the descriptions of the original specification. Accordingly, the pharmacological effect of the Subject Invention was specifically confirmed by the Amendment for the first time. As such, the Amendment completed an incomplete invention since the Amendment corresponds to an addition of new technical matters and departs from the scope described in the original specification.

D. Sub-conclusion

Since the Amendment of the subject case changed a significant subject matter in the specification, the Amendment must be dismissed according to Article 51, Paragraph 1 of the Old Patent Act. Thus, the lower decision, which concluded as such, is proper.

4. Conclusion

As such, the Plaintiff's claim is groundless, and the Court issues a decision as set forth in the Order.

Dated this August 25, 2000

Presiding	Judge	Hyosook JEON
	Judge	Gimoon SEONG
	Judge	Myunggyu LEE