

Note: When any ambiguity of interpretation is found in this provisional translation, the Japanese text shall prevail.

## **Chapter 3 Medicinal Inventions**

In this chapter, matters requiring special judgment and handling in examining patent application relating to medicinal inventions are mainly explained.

A medicinal invention here means “an invention of a product” which intends to provide a new medicinal use (Note 2) of a material (Note 1), based on discovering an unknown attribute of the material.

(Note 1) “A material means a component used as an active ingredient, including a compound, a cell, a tissue and a chemical substance (or a group of chemical substances) whose chemical structure is not specified, such as an extract from a natural product, and a combination thereof. Hereinafter, the material concerned is referred to as “compounds etc.”

(Note 2) “A medicinal use” means (i) an application to the specific disease or (ii) an application to the specific disease in which dosage and administration such as dosing time, dosing procedure, dosing amount or administration areas (hereinafter referred to as “dosage and administration”) is specified.

Refer to Part I or Part II for those matters not explained in this Chapter in relation to description requirements of the Description and the Claims, and requirements for patentability.

### **1. Description Requirements of the Description and the Claims**

#### **1.1 Claims**

##### **1.1.1 Patent Act Article 36(6)(i) of the Patent Act**

As Article 36(6)(i) of the Patent Act requires that an invention for which a patent is sought shall be stated in the detailed explanation of the invention, an invention stated in the claim should not extend the scope described in the detailed explanation of the invention. A determination on whether the statement in a claim complies with Patent Act Article 36(6)(i) shall be made based on comparison and review of the claimed invention and an invention described in the detailed explanation (Refer to Examination Guidelines Part I, Chapter 1, 2.2.1.2).

Typical examples of violation of Article 36(6)(i) are as follows.

- (1) While an invention relating to an antiemetic drug having an ingredient A as an active ingredient is claimed, neither a pharmacological test method nor result, which could support the use of ingredient A in an antiemetic drug, is disclosed in the detailed explanation of the invention, and furthermore, as the use of ingredient A in an antiemetic drug cannot be presumed from the common general knowledge as of the filing, the detailed explanation of the invention cannot be regarded as disclosing the invention in such a way that a person skilled in the art could recognize that the problem of providing an antiemetic drug would be solved by the invention; therefore, the claimed invention is not stated in the detailed explanation of the invention. (Refer to Examination Guidelines Part I, Chapter 1, 2.2.1.3 Example 9 and Case 8),
- (2) While an invention relating to a therapeutic agent for a specified purpose, which contains compounds defined by certain properties as active ingredients, is comprehensively claimed, the disclosure in the detailed explanation of the invention supports the use for such specified purpose with regard to only a small portion of the claimed compounds; the content disclosed in

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the detailed explanation of the invention can neither be expanded nor generalized to the scope of the claimed invention even in light of the common general knowledge as of the filing. (Refer to Examination Guidelines Part I, Chapter 1, 2.2.1.3 Example 7 and Case 4).

(Reference: Tokyo High Court Judgment Hei 15.12.26 (Heisei 15 (Gyo Ke) 104), Intellectual Property High Court Judgment Hei 19.3.1 (Heisei 17 (Gyo Ke) 10818))

### 1.1.2 Patent Act Article 36(6)(ii) of the Patent Act

As Article 36(6)(ii) of the Patent Act requires that an invention for which a patent is sought is clear, a claim shall be stated in such a manner that an invention for which a patent is sought can be clearly identified from a single claim.

Considering the purport of Article 36(5) of the Patent Act, various forms of expression can be used in the claim by the applicant to define an invention for which a patent is sought. For example, in the case of “an invention of a product”, various forms of expression such as operation, function, property, characteristics, method, usage and others can be used as matters to define an invention in addition to the forms of expression such as combination of products or the structure of products. As for a medicinal invention, various forms of expression can be used as well (example 3).

On the other hand, since a claim should be stated in such a manner that an invention for which a patent is sought can be clearly identified from a single claim according to the provision of Article 36(6)(ii), it should therefore be noted that such definition of an invention by applicant using the various forms expression is allowed as far as the claimed invention can be clearly identified.

For example, it should be noted that the medicinal invention usually cannot be deemed clear, in case where active ingredient in medicinal invention is defined by a function or characteristics, etc. in a claim, if it is evident, in light of the common general knowledge as of the filing, that the matter defined by a function or characteristics, etc. is not sufficiently specified from a technical perspective, and the invention cannot be clearly identified from the statement of the claim even by taking into account the statements of the description and drawings (refer to Examination Guidelines, Part I; Chapter 1, 2.2.2.4(1)②(ii)).

In case that the statement in the claim does not express a specific medicinal use but a general medicinal use, where the claim directed to a medicinal invention (for example, in case where the statement expresses not a “pharmaceutical agent for disease X consisting of...” but a “pharmaceutical agent consisting of...”), it should not be deemed a violation of Article 36(6)(ii) merely because the statement expresses a general use (i.e., merely because the scope of the claim is relatively broad) unless the expression makes unclear the invention for which a patent is sought. (Refer to Examination Guidelines, Part I, Chapter 1, 2.2.2.2(3)).

Medicinal invention can be described in a claim as “an invention of a product” as follows:  
 Example 1: A medicine for disease Z containing an active ingredient A  
 Example 2: A medicinal composition for disease Y containing an active ingredient B  
 Example 3: A medicine for disease W containing active ingredients C and D in combination  
 Example 4: A kit for disease V comprising an injection agent including an active ingredient E and an oral agent including an active ingredient F.

## 1.2 Detailed Explanation of the Invention

### 1.2.1 Enablement Requirement

As a medicinal invention resides in technical field where it is generally difficult to infer how to make and use a material on the basis of its structure and its name, normally one or more representative embodiments or working examples are necessary in order to state the detailed explanation of the invention so as to enable a person skilled in the art to work the invention, except the case where a person skilled in the art can manufacture the compounds etc. and can use the compounds etc. for medicinal use, in the light of common general technical knowledge as of the filing. As for working examples supporting the medicinal use, a description of the result of the pharmacological test is usually required (Refer to Examination Guidelines, Part I, Chapter 1, 3.2.1 (5)). The following examples display concrete practices regarding the description of the result of the pharmacological test sufficient to support a pharmacological effect.

#### (1) Description of the Result of the Pharmacological Test

Since the result of the pharmacological test is to confirm the pharmacological effect of compounds etc. of the claimed medicinal invention, all of the followings should be made sufficiently clear, in principle; (i) which compounds etc. are (ii) applied to what sort of the pharmacological test system, (iii) what sort of result is obtained, and (iv) what sort of relationship the pharmacological test system has with the medicinal use of the claimed medicinal invention. It should be noted that the result of the pharmacological test should be described with numerical data as a general rule, but when the result cannot be described with the numerical data due to the nature of the pharmacological test system, an objective description equivalent to the numerical data for example, a description of the objective observation result by a medical doctor may be accepted. Furthermore, a clinical test, an animal experiment, and in-vitro test are employed as the pharmacological test system.

#### (2) Examples of Cases where Reasons for Refusal are Notified

##### (a) A case in which the result of the pharmacological test is not described

Generally, since it is difficult to predict whether the compounds etc. are actually usable for a specific medicinal use from only the structure and name of the compounds etc., it is still difficult for a person skilled in the art to predict whether the compound etc. are actually usable for the specific medicinal use when an effective dose, a mode of administration, and formulation method are described in the description as filed but the result of the pharmacological test is not described. Accordingly, in such a case, in principle, reasons for refusal are notified. It should be noted that even if the result of the pharmacological test is submitted afterward, the reasons for refusal are not overcome.

(Tokyo High Court Judgment Hei 10.10.30 (Heisei 8 (Gyo Ke) 201) "Judgment on Antiemetic Drug": Refer to Examination Guidelines Part I, Chapter 1 Case 8: Tokyo High Court Judgment Hei 14.10.1 (Heisei 13 (Gyo Ke) 345: Tokyo High Court Judgment Hei 15.12.22 (Heisei 13 (Gyo Ke) 99)

##### (b) A case in which the existence of a pharmacological effect of the compounds etc. of a claimed medicinal invention can not be confirmed, as the compounds etc. used in the pharmacological test are not specified

It should be noted that, in many cases the existence of the pharmacological effect of the compounds etc. of the claimed medicinal invention cannot be confirmed; for example, when the

compounds etc. used in the pharmacological test system described in the description as filed are merely stated as being “any of a plurality of the compounds etc.” and it is not concretely specified which compounds etc. are actually used, this case comes under the case where (i) in “(1) Description of the Result of the Pharmacological Test” is not clear.

## **2. Requirements for Patentability**

### **2.1 Industrial Applicability**

As a medicinal invention means “an invention of a product.”, it does not come under the category of “methods of surgery, therapy or diagnosis of humans” despite the fact that the application possibly involves the administration of a dosage to a human body or the spreading on the human body, and it is considered to be an “industrially applicable invention.” It should be noted that a medicinal invention defined by combination of two or more medicines, or defined by dosage and administration is handled in the same way because it is also “an invention of a product” (Refer to the Examination Guidelines Part II, Chapter 1, 2.1 “Industrial Applicability”).

### **2.2 Novelty**

#### **2.2.1 Principle of Method of Determining whether a Claimed Medicinal Invention is Novel**

A medicinal invention means “an invention of a product” based on discovering an unknown attribute of compounds etc. and finding that compounds etc. are suitable for a new medicinal use due to the presence of such attribute, and its novelty is judged from two points of view; (i) compounds etc. having a specific attribute and (ii) a medicinal use based on the attribute. (Tokyo District Court Judgment Hei 4.10.23 (Heisei 2 (Wa) 12094))

#### **2.2.2 Methods of Judging Novelty**

##### **(1) Finding of a claimed medicinal invention**

The finding of a claimed invention should be made on the basis of the statements in the claim. Matters (terms) stated in the claim defining the claimed invention should be construed in the light of the statements in the description, the drawings and the common general technical knowledge as of the filing. (Refer to Examination Guidelines Part II, Chapter 2, 1.5.1.)

##### **(2) Finding of an invention described in a publication**

Since a medicinal invention consists of compounds etc. having a specific attribute and a medicinal use based on the attribute, it is necessary that both compounds etc. and the medicinal use are described in a publication (or essentially described, though not literary, in the publication) in order to find that the medicinal invention is described in the publication.

Unless it is clear that an invention is described in a publication in such a manner that a person skilled in the art can make or acquire compounds etc. of claimed medicinal invention based on the description of the publication and common general technical knowledge as of the filing, the medicinal invention shall not be deemed to be described in the publication.

Furthermore, if it is unclear that the invention is described in the publication in such a manner that a person skilled in the art can use the compounds etc. for a medicinal use based on

the description of the publication or common general technical knowledge as of the filing, the medicinal invention also shall not be deemed to be described in the publication (refer to Part II, Chapter 2, 1.5.3(3)(ii)).

For example, in the case where a medicinal use is merely listed without any support in the publication, it cannot be considered that the invention is described in the publication in such a manner that it is clear that a person skilled in the art can use the compounds etc. for the medicinal use, and the medicinal invention shall not be deemed to be described in the publication.

### (3) Determining whether a claimed medicinal invention is novel

Guidelines for determining whether a claimed medicinal invention is novel are stated below in sections (3-1) to (3-2), based on “Determining whether a Claimed Invention is Novel” in Examination Guidelines Part II, Chapter 2, 1.5.5 and “Method of Determining whether a Claimed Medicinal Invention is Novel” of this Chapter 2.2.1.

Hereinafter, “a cited invention” means a cited invention as provided in Patent Act Article 29(1)(i)-(iii).

#### (3-1) Regarding the compounds etc. having a specific attribute

When the compounds etc. having a specific attribute of the claimed medicinal invention differs from the compounds etc. of a cited invention, the novelty of the claimed medicinal invention is not denied.

#### (3-2) Regarding the medicinal use based on a specific attribute

##### (3-2-1) Application to a specific disease

Even if the compounds etc. of the claimed medicinal invention do not differ from the compounds etc. of the cited invention, the novelty of the claimed medicinal invention is not denied when the claimed medicinal invention and the cited invention differ in medicinal use of applying to a specific disease based on the attribute of such compounds etc. (Examples 1 to 3)

For example, when a claimed invention is “a medicine for disease Z comprising an active ingredient A,” and a cited invention is “a medicine for disease X comprising an active ingredient A,” the novelty of the claimed medicinal invention is not denied, in the case that it is clear that the disease X and the disease Z are different diseases in the light of the common general technical knowledge as of the filing.

The lines of thoughts regarding the differences in medicinal use are as follows.

(a) Even if the medicinal use of the claimed medicinal invention and the medicinal use of the cited invention are different in expression, the novelty of the claimed medicinal invention is denied when the medicinal uses are judged to come under (i) or (ii) described hereunder taking into consideration the common general technical knowledge as of the filing.

- (i) In the case that the medicinal use is conceived from a working mechanism thereof,
- (ii) In the case that the medicinal use inevitably results from closely related pharmacological effect.

[Example of (i) above]

(Cited invention) Bronchodilator

→ (Claimed medicinal invention) Therapeutic agent for Asthma

(Cited invention) Vasodilator → (Claimed medicinal invention) Hypotensive agent

(Cited invention) Coronary vessel dilator

→ (Claimed medicinal invention) Therapeutic agent for Angina

- (Cited invention) Histamine release inhibitor  
→ (Claimed medicinal invention) Anti-allergy drug
- (Cited invention) Histamine H-2 receptor inhibitor  
→ (Claimed medicinal invention) Therapeutic agent for Gastric ulcer

[Example of (ii) above]

- (Cited invention) Cardiotonic agent → (Claimed medicinal invention) Diuretic agent
- (Cited invention) Anti-inflammatory agent  
→ (Claimed medicinal invention) Painkiller

(Note) It is known in the field of medical treatment that there are certain compounds etc. having two or more medicinal uses inevitably. However, in the examples listed under (ii) above, it is also well known that all the compounds etc. having a first medicinal use coming under (ii) above do not have necessarily a second medicinal use. Accordingly, when the novelty of the claimed medicinal invention in such a case is considered, it is necessary to consider the common general technical knowledge as of the filing regarding the structure-activity correlation or the like of the compounds etc.

(b) When the medicinal use of the cited invention is expressed in a more specific concept of the medicinal use of the claimed medicinal invention, the novelty of the claimed medicinal invention is denied.

[Example]

- (Cited invention) Antipsychotic agent  
→ (Claimed medicinal invention) Agent acting on central nervous system
- (Cited invention) Therapeutic agent for Lung cancer  
→ (Claimed medicinal invention) Anticancer agent

(c) When the medicinal use of the cited invention is expressed as a generic concept of the medicinal use of the claimed medicinal invention and the medicinal use of the claimed medicinal invention is expressed as a more specific concept which can be conceived from the medicinal use of the cited invention based on the common general technical knowledge as of the filing, the novelty of the claimed medicinal invention is denied.

(Note) It should be noted that a medicinal use expressed as a more specific concept can not be conceived only because the medicinal use expressed as a more specific concept is conceptually included in the medicinal use expressed in a generic concept or the medicinal use expressed in a more specific concept can be listed from the medicinal use expressed in a generic concept.

(d) When the medicinal use of the claimed medicinal invention is only expressed as a newly found working mechanism in place of the medicinal use of the cited invention and both uses cannot be substantially distinguished from each other, the novelty of the claimed medicinal invention is denied.

[Example]

- (Cited invention) Antibacterial agent  
→ (Claimed medicinal invention) Bacterial cell membrane formation inhibitor

- (e) When there is no difference in the component compositions and the medicinal uses of the claimed medicinal invention and the cited invention, and the component contained in the claimed medicinal invention is merely expressed in a manner that the working mechanism of a part of the component of the cited invention is defined as if it is a use, the novelty of the claimed medicinal invention is denied.

[Example]

(Cited invention) Skin anti-inflammatory agent containing indomethacin and capsicum extract

→ (Claimed medicinal invention) Skin anti-inflammatory agent containing indomethacin and long-term stability improving agent for indomethacin composed of capsicum extract

(Note) As the component constitutions of the composition are the same, it is obvious that the components contained in the skin anti-inflammatory agent of both inventions perform the same working effect despite the subjective object for adding. Accordingly, even if the capsicum extract is defined as a stabilizer for improving long-term stability of the indomethacin, this cannot make the invention different from the invention described in the publication. (Tokyo High Court Judgment Hei 13.12.18 (Heisei 13(Gyo Ke) 107)

(3-2-2) Application to a specific disease in which dosage and administration is specified

Even if compounds etc. of a claimed medicinal invention do not differ from those of a cited invention and there is no difference in the applied disease, the novelty of the claimed invention is not denied when there is a difference between the claimed medicinal invention and the cited invention in medicinal use of applying to a specific disease with a specific dosage and administration based on the attribute of compounds etc. thereof (Example 4 to 6).

## 2.3 Inventive Step

### 2.3.1 Inventive Step regarding Medicinal Invention

(1) Finding of a claimed medicinal invention

The finding of a claimed invention is handled as described in “2.2.2(1).”

(2) Finding of an invention described in a publication

The finding of a invention described in a publication is handled as described in “2.2.2(2).”

(3) The judgment of the inventive step

The judgment of the inventive step regarding medicinal invention is handled as described in Examination Guidelines Part II, Chapter 2, 2. Inventive Step.

### 2.3.2 Examples of Concrete Practices Regarding Judgment of Inventive Step

(1) Relationship between the medicinal use and the working mechanism

Even if the medicinal use of the claimed medicinal invention differs from the medicinal use of the cited invention, when the relevance of the working mechanism between both has been derived from the state of the art as of the filing, the inventive step of the claimed medicinal invention is usually denied, unless there is another ground for inferring inventive step such as advantageous

effect or the like.

(2) Conversion of a medicine for animals other than human beings to a medicine for human beings

A claimed medicinal invention, derived by merely converting compounds etc. of a cited invention used for the same or a similar kind of diseases of animals other than human beings into a medicine for human beings, usually does not involve an inventive step even if there is no suggestion in the contents of the cited invention about the pertinent conversion, unless there is another ground for inferring inventive step such as advantageous effect or the like.

The situation is the same with the conversion of a medicine for human beings to into a medicine for animals other than human beings.

(3) Medicine formulated by combining two or more medicinal components

In order to solve a problem well known to a person skilled in the art such as the increase in a medicinal effect, or the reduction of a side effect, optimization of the combination of two or more medicinal components is among exercise of ordinary creativity of a person skilled in the art. When the difference between the claimed medicinal invention and the cited invention falls only on these points, ordinarily, the inventive step of the claimed medicinal invention is denied.

For example, if the pertinent combination corresponds to the followings, in most cases, it is reasoned that a person skilled in the art would have easily arrived at the claimed medicinal invention and the inventive step is usually denied (Example 8 to 11):

- (a) combination of publicly known components of which major effects are the same,
- (b) combination of a major component having a publicly known problems related to the efficacy thereof with a subordinate component having publicly known ability to eliminate the problem (for example, in case of the combination of the major component having a publicly known side effect and a subordinate component having a publicly known ability of reducing the side effect), and
- (c) combination of publicly known components having respective curative effects for a variety of symptoms arising from a major disease, and the like.

However, in the case where there is another ground for inferring the inventive step such that an advantageous effect compared with the cited invention cannot be foreseen by a person skilled in the art from the state of the art, the claimed medicinal invention is considered to involve an inventive step (Example 7).

Although the medicine formulated by combining two or more medicinal components can be assumed to be claimed in such a manner as “combination drug for the treatment of...,” “composition for the treatment of...,” “...medicine characterized in that ... and ...are combined,” there is no fundamental difference in any of the cases as the method of judgment.

(4) Medicine characterized in the medicinal use of an application to a specific disease with a specific dosage and administration

As for a specific disease, in order to solve a problem well known to a person skilled in the art such as the increase of a medicinal effect, the reduction of an adverse effect or the improvement in drug compliance, the optimization of dosage and administration of a medicine is among exercise of ordinary creativity of a person skilled in the art. Accordingly, in the case where the advantageous effect compared with the cited invention can be foreseen by a person skilled in the art, the inventive step is usually denied, even if the claimed medicinal invention is novel compared with the cited invention in that applied disease does not differ but dosage and administration differ from each other (Example 6).



However, in the case where there is another ground for inferring the inventive step such that an advantageous effect compared with the cited invention cannot be foreseen by a person skilled in the art from the state of the art, the claimed medicinal invention is considered to involve an inventive step (Example 4 and 5).

## **2.4 Patent Act Article 29-2**

### **2.4.1 Application of Patent Act Article 29-2**

(1) Finding of a claimed medicinal invention

The finding of a claimed invention is handled as described in “2.2.2(1).”

(2) Finding of a invention described in a initial description etc. of another application.

The finding of a invention described in a initial description etc. of another application is handled as described in “2.2.2(2).”

(3) The judgment of the requirement of “Patent Act Article 29-2”

The judgment of the requirement of “Patent Act Article 29-2” is handled as described in Examination Guidelines Part II, Chapter 3, Patent Act Article 29-2.

### **2.4.2 Examples of Concrete Practices Regarding Judgment of Patent Act Article 29-2**

A claimed medicinal invention and an invention described in a prior application are deemed to be substantively identical if the difference between them is considered to be a very minor difference (e.g. addition, deletion, or replacing of well-known or commonly used art, generating no new effects) in an embodied means to solve a problem.

## **2.5 Patent Act Article 39**

### **2.5.1 Application of Patent Act Article 39**

(1) Finding of a claimed medicinal invention

The finding of a claimed invention is handled as described in “2.2.2(1).”

(2) The judgment of the requirement of “Patent Act Article 39”

The judgment of the requirement of “Patent Act Article 39” is handled as described in Examination Guidelines Part II, Chapter 4, Patent Act Article 39.

### **2.5.2 Examples of Concrete Practices Regarding Judgment of Patent Act Article 39**

In a case in which the invention of a prior application having a generic concept has a relationship with the invention of subsequent application having a more specific concept, and in a case in which the matters necessary for defining the subsequent application are disclosed in the prior application and the invention of the prior application having the generic concept is deemed to have de facto choices in the range of the disclosed matters, the invention of the subsequent application is the same as the invention of the prior application.

The same method is practiced in judging an identity between each claimed invention of two applications filed on the same day.

### **3. Examples**

#### Explanation of Examples

These examples are prepared for the purpose of explaining examination practices regarding medicinal inventions. Therefore, it is to be noted that the descriptions of claims etc. in these examples are not necessarily exemplary cases because they are modified, e.g., simplified to make the explanation easier to understand. Additionally, it is to be noted that it does not mean that there is no reason for refusal except for reasons discussed in each example (for instance, description requirements for description and claims and the like).

### **3.1 Medicine characterized in a medicinal use applied to a specific disease**

#### **[Example 1] An active ingredient is publicly known, a medicinal use is novel**

##### **Claim**

[Claim 1] A pharmaceutical composition for treatment of Alzheimer's disease comprising a compound A as an active ingredient.

##### **Outline of Detailed Explanation of the Invention**

It is found that a compound A, which is known as an active ingredient for an antimicrobial agent, can inhibit the function of acetylcholine-esterase, and suppress a degradation of acetylcholine.

It is shown in the example with the result of the pharmacological test that a compound A has an excellent inhibitory activity of acetylcholine-esterase, and decreases the symptom of Alzheimer's disease.

##### **Result of Prior Art Search**

Although it is already known that a compound A is an active ingredient for an antimicrobial agent, the prior art documents do not describe a pharmaceutical composition for treatment of Alzheimer's disease comprising a compound A as an active ingredient. Moreover, the documents do not describe or suggest the existence of the structural similarity between a compound A and compounds having an acetylcholine-esterase activity and the relationship between a mechanism of a compound A for affecting as an antimicrobial agent and the treatment of Alzheimer's disease.

##### **Outline of Reasons for Refusal**

No reason for refusal.

##### **[Explanation]**

As a medicinal use of a compound A for a treatment of Alzheimer's disease is clearly distinguished from a known medicinal use for antimicrobial agent, the medicinal invention of claim 1 is novel.

And because there are no prior art documents showing a motivation for applying a compound A to the treatment of Alzheimer's disease, such as the existence of structural similarity between a compound A and a compound having an acetylcholine-esterase activity, or the relationship between a mechanism of a compound A for affecting as antimicrobial agent and a treatment of Alzheimer's disease, the medicinal invention of claim 1 involves an inventive step.

**[Example 2] Medical materials (cells etc.) derived from the living organism which are publicly known, but a medicinal use is novel**

**Claim**

[Claim 1] An implant material for treatment of cardiac infarction, which contains cell sheets consisting of A-cells.

**Outline of Detailed Explanation of the Invention**

It was found that cardiac function was recovered by transplantation of cell sheets consisting of A-cells to a site of cardiac infarction.

It is described in the example with the result of the pharmacological test that cardiac function is recovered and the symptom of cardiac infarction is reduced by transplantation of the said cell sheets to the site of cardiac infarction in a model rat of cardiac infarction.

**Result of Prior Art Search**

It is publicly known that cell sheets are obtained from A-cells and that they are used as implant materials. However, it is not described in any prior art documents that the said cell sheets are transplanted to the site of cardiac infarction and that the symptom of cardiac infarction is reduced by the transplantation.

Furthermore, from the state of the art as of the filing, it is not possible to predict that cardiac function is recovered and the symptom of cardiac infarction is reduced by transplantation of A-cells.

**Outline of Reasons for Refusal**

No reason for refusal.

**[Explanation]**

The medicinal invention of the claim 1 is considered to be novel because the medicinal use (treating cardiac infarction) of cell sheets consisting of A-cells is different from the conventionally-known medicinal use of the sheets.

The medicinal invention of the claim 1 is considered to involve the inventive step because the prior art documents have not been publicly known which describe the relationship between the A-cell and recovery of cardiac function etc., and then motivate the use of cell sheets consisting of A-cells for treatment of cardiac infarction.

**[Remark]**

It should be noted that, if the claimed invention is related to the cell with the limitation of use such as “A-cell for the treatment of cardiac infarction”, such limitation of use usually only indicates the utility of the cell itself and the claim should be construed to represent the cell per se with no limitation of use. Therefore, in this case, the difference between “A-cell for the treatment of cardiac infarction” and publicly known “A-cell” with no limitation of use cannot be acknowledged in view of composition of matters (refer to Examination Guidelines, Part II; Chapter 2, 1.5.2(2)).

**[Example 3] Medicine characterized in a medicinal use of the cells specified by manufacturing process**

**Claims**

[Claim 1] An anticancer agent comprising the cells as an active ingredient obtained by the following process consisting of the steps of;

- (1) culturing W-cells obtained from a human body in medium A containing 0.1~0.2 weight % of protein X for 5 to 10 hours and collecting them, and
- (2) disseminating the collected cells in the step (1) on an extracellular matrix Y, culturing them in medium B containing 0.1~0.2 weight % of protein Z for 24 to 48 hours, and collecting them.

[Claim 2] A method of manufacturing an anticancer agent consisting of the steps of;

- (1) culturing W cells obtained from a human body in medium A containing 0.1~0.2 weight % of protein X for 5 to 10 hours and collecting them,
- (2) disseminating the collected cells in the step (1) on an extracellular matrix Y, culturing them in medium B containing 0.1~0.2 weight % of protein Z for 24 to 48 hours, and collecting them, and
- (3) a step of producing a pharmaceutical formulation by using the cells collected in the step (2), wherein the anticancer agent contains the cells obtained by the process consisting of the steps (1) and (2) as an active ingredient.

**Outline of Detailed Explanation of the Invention**

It was found that the anticancer agent containing cells obtained by the process consisting of the steps of (1) and (2) as an active ingredient inhibited angiogenesis peculiar to a cancer tissue and diminished the cancer growth.

It is described in the example with the result of the pharmacological test that the cells obtained by a process consisting of the steps of (1) and (2) in the example have an excellent inhibitory effect of angiogenesis and of diminishing effect of the cancer growth.

**Result of Prior Art Search**

It is publicly known that W-cell obtained from a human body is processed through the steps of (1) and (2) and that cells processed through the steps have an immunosuppressive effect. However, it has not been known that W-cell itself or the cells processed through the steps consisting of (1) and (2) has an inhibitory effect of angiogenesis and an anticancer effect.

Furthermore, from the state of the art as of the filing, it is not possible to predict that the cells obtained by processing W-cells derived from the human body through the steps consisting of (1) and (2) have an inhibitory effect of angiogenesis and an anticancer effect.

**Outline of Reasons for Refusal**

No reason for refusal.

**[Explanation]**

The medicinal invention of claim 1 is considered to be novel because a medicinal use (anticancer) of cells obtained from the steps consisting of (1) and (2) is different from the conventionally-known medicinal use (immunosuppression).

The medicinal invention of the claim 1 is considered to involve the inventive step because the prior art documents have not been publicly known which disclose the relationship between an immunosuppressive effect and angiogenesis and then motivate the use of the cells obtained by the steps consisting of (1) and (2) as an anticancer agent.

In addition, the invention of claim 2 is considered to be novel and to involve inventive step

based on the same idea of the invention of the claim 1.

It should be noted the cells could be specified by manufacturing process, even when it is difficult to specify the cells with cell markers etc. In this example, the inventions of claim 1 and 2 are considered to be clear, because original cells and culture condition are identified in details in the steps consisting of (1) and (2). As for handling of claims including specification of a product by the manufacturing process, please refer to Part I Chapter 1, 2.2.2.4(2), Part II Chapter 2, 1.5.5(4) and 2.7

### 3.2 Medicine characterized in a medicinal use of an application to a specific disease in which dosage and administration is specified

#### [Example 4] Medicine performing remarkable effect by an application to a specific disease in which dosage and administration is specified

##### Claim

[Claim 1] A therapeutic agent for asthma containing compound A wherein 30~40 µg/kg of compound A is orally administered to humans once per 3 months.

##### Outline of Detailed Explanation of the Invention

Although it has been publicly known that the symptom of asthma is reduced by daily oral administration of 1µg/kg/day of compound A to asthma patients, the reduction of the symptom is only during the administration period of compound A. It was necessary thus to continue to administer compound A daily, because the symptom relapses if the administration is stopped. In addition, in case of the daily oral administration of 1µg/kg/day of compound A, it has been pointed out that the side effect B arises with high frequency.

It was found in this invention that the symptom of asthma is improved for a long term and the incidence of side effect B is reduced compared to before, by orally administering 30~40µg/kg of compound A to asthma patients once per 3 months.

It is described in the example with the result of the pharmacological test that the symptom of asthma was reduced at least for 3 months by every single oral administration of 30~40 µg/kg of compound A to a group of asthma patients (weighing 30kg to 90kg), that body weights didn't bring clear difference in pharmacological efficacy, and that the incidence of side effect B significantly decreased from the case of daily oral administration of 1µg/kg/day of compound A.

##### Result of Prior Art Search

It is publicly known that the symptom of asthma is reduced by daily oral administration of 1µg/kg/day of compound A and that side effect B arises with high frequency in that case. However, administering 30~40µg/kg of compound A once per 3 months is not described in the prior art documents.

Furthermore, from the state of the art as of the filing, it is not possible to predict that the symptom of asthma decreases at least for 3 months by a single oral administration of 30~40µg/kg of compound A and that the incidence of side effect B decreases compared to the prior art.

##### Outline of Reasons for Refusal

No reason for refusal.

##### [Explanation]

Regarding dosage and administration of compound A for asthma treatment, dosage and administration of this invention is different from the already known dosage and administration. Therefore, the medicinal invention of claim 1 is novel.

Furthermore, by a single administration of 30~40µg/kg of compound A, the symptom of asthma is reduced at least for 3 months and the incidence of side effect B significantly decreases compared to the case of the daily oral administration of 1µg/kg/day of compound A. As they are remarkable effects which cannot be foreseen from the state of the art as of the filing, the medicinal invention of claim 1 involves an inventive step.

**[Example 5] Medicine performing remarkable effect by an application to a specific disease in which dosage and administration is specified**

**Claim**

[Claim 1] A therapeutic agent for ovary cancer containing compound A as an active ingredient wherein 100~120 $\mu$ g/kg of compound A is administered to the particular site Z in human brain.

**Outline of Detailed Explanation of the Invention**

It has been known that compound A exhibits growth-inhibitory effect against ovary cancer by intravenous administration to humans but arises hepatotoxicity as a side effect at the same time.

In this invention, it is found that the blood level of hormone Y secreted from the pituitary gland changes by administration of compound A to the particular site Z in the human brain, and consequently ovary cancer significantly diminishes compared to the conventional treatment by intravenous administration.

It is described in the example with the result of the pharmacological test that the blood level of hormone Y secreted by the pituitary gland changes by administration of compound A to the particular site Z in the human brain, and that as a result ovary cancer diminishes more compared to the conventional treatment by intravenous administration. It is also described in the example with the result of the pharmacological test that compound A is not delivered to the liver and does not show hepatotoxicity when it is administered to the particular site Z in the brain.

**Result of Prior Art Search**

It is publicly known that compound A exhibits growth-inhibitory effect against ovary cancer by intravenous administration to humans and hepatotoxicity as a side effect. However, it is not described in the prior art documents that the intravenously administered compound A is delivered to the brain through the blood brain barrier, or the administration of compound A to the particular site Z in the human brain results in more shrinking of ovary cancer than the prior art.

Furthermore, from the state of the art as of the filing, it is not possible to predict that ovary cancer diminishes without causing a side effect of hepatotoxicity by administering compound A to the particular site Z in the human brain.

**Outline of Reasons for Refusal**

No reason for refusal.

**[Explanation]**

Regarding dosage and administration of compound A for ovary cancer treatment, dosage and administration (administration to the particular site Z in the human brain) of this invention is different from the already known dosage and administration (intravenous administration). Therefore, the medicinal invention of claim 1 is novel.

Moreover, as it is a remarkable effect which cannot be foreseen from the state of the art as of the filing that compound A does not cause a side effect of hepatotoxicity by administration to the particular site Z in the brain, or ovary cancer diminishes more compared to the treatment by intravenous administration, the medicinal invention of claim 1 has an inventive step.



**[Example 6] Medicine characterized in an application to a specific disease in which dosage and administration is specified****Claim**

[Claim 1] An antitussive agent containing compound A wherein 400~450 $\mu$ g/kg per dose of compound A is orally administered to humans once per day.

**Outline of Detailed Explanation of the Invention**

Although it has been known that orally administering 160 $\mu$ g/kg per dose of compound A to humans three times a day has the antitussive effect, it was found in this invention that the antitussive effect improves compared to before by oral administration of 400~450 $\mu$ g/kg per dose of compound A to humans.

It is described in the example with the result of the pharmacological test that oral administration of 400 $\mu$ g/kg per dose of compound A to a patient once per day improves the antitussive effect compared to the oral administration of 160 $\mu$ g/kg per dose of compound A to a patient three times per day. Furthermore, it is also described that drug compliance improves because the number of doses per day decreases.

**Result of Prior Art Search**

It is publicly known that the antitussive effect is obtained by oral administration of 160 $\mu$ g/kg per dose of compound A three times per day. Furthermore, the degree of the antitussive effect and improvement of drug compliance disclosed in the detailed explanation of the invention falls under the predictable range in the light of the state of the art as of the filing.

**Outline of Reasons for Refusal**

It is publicly known that an antitussive agent including compound A as an active ingredient is orally administered. In general, in order to solve a problem well known to a person skilled in the art, such as an increase in a medicinal effect and improvement of drug compliance, optimization of dosage and administration of a medicine is among exercise of ordinary creativity of a person skilled in the art. Therefore, it would have been easily arrived at by a person skilled in the art to experimentally decide appropriate dosage and administration of compound A.

Furthermore, that a medicinal effect and drug compliance can be improved by optimizing dosage and administration of a medicine can normally be foreseen to a person skilled in the art, and the degree of improvement in this invention is not remarkable one unforeseeable from the state of the art as of the filing.

**Measures for Reasons for Refusal**

Ordinarily, the above-described reason for refusal is not overcome.

**[Remark]**

How much effect is “remarkable one unforeseeable from the state of the art as of the filing” is judged individually taking into consideration the content of disclosure of the description, results of the prior art search, and common general technical knowledge as of the filing or the like.

### **3.3 Medicine characterized by combination of materials having a specific attribute**

#### **[Example 7] A medicinal drug performing remarkable effect by combination of active ingredients**

##### **Claim**

[Claim 1] An antidiabetic composition containing a compound A and a compound B at a ratio by weight 5:1 to 4:1.

##### **Outline of Detailed Explanation of the Invention**

In this invention, reduction of the side effects such as a weight gain or the like, which have conventionally been observed when the compound A is independently used, is found to be the result of combining and using of the compound A and the compound B at a ratio by weight 5:1 to 4:1.

In the example the result of the pharmacological test is described, which shows the reduction of the side effects in case that using a combination of a compound A and a compound B at a specific ratio.

##### **Result of Prior Art Search**

Although it is publicly known that the compound A and the compound B are respectively used as antidiabetic agents, the prior art documents do not describe the antidiabetic agent composition by combining and using the compound A and the compound B. Furthermore, decrease in the side effects such as a weight gain or the like by combining and using compound A and compound B at the specific ratio cannot be foreseen from the state of the art as of the filing.

##### **Outline of Reasons for Refusal**

No reason for refusal.

##### **[Explanation]**

As the result of the pharmacological test or the like shows a remarkable effect of reducing the side effects that cannot be foreseen by a person skilled in the art from the state of the art as of the filing by combining and using of the compound A and the compound B at the specific ratio, the invention involves an inventive step.

**[Example 8] Combination of a component with another component having the same major effect which is publicly known**

**Claim**

[Claim 1] A liquid antifatulent containing 1 to 30g of dietary fiber and  $1 \times 10^6$  to  $1 \times 10^8$  cells of the YY bacterium.

**Outline of Detailed Explanation of the Invention**

In this invention, an antifatulent, which fortifies the intestine regulating function, is formulated by combining the dietary fiber and the YY bacterium, both affecting the functions of the intestines. Furthermore, in the description, the result of the pharmacological test of an antifatulent having this combination is shown. However, the result of the pharmacological test in case that using the dietary fiber and the YY bacterium respectively is not described.

**Result of Prior Art Search**

It is publicly known that there is an intestine regulating function when 1 to 30g of the dietary fiber is taken or when  $1 \times 10^6$  to  $1 \times 10^8$  cells of the YY bacterium are taken. And it is also publicly known to make the bacterium and the dietary fiber co-exist in order to maintain the activity of the bacterium having the intestine regulating function and fortify intestine regulating function.

**Outline of Reasons for Refusal**

It is publicly known that there is an intestine regulating function when 1 to 30g of the dietary fiber is taken or when  $1 \times 10^6$  to  $1 \times 10^8$  cells of the YY bacterium are taken. Furthermore it is publicly known to make the bacterium and the dietary fiber co-exist, in order to maintain the activity of the bacterium having the intestine regulating function and to fortify the intestine regulating function, it would have been easily arrived at by a person skilled in the art to formulate medicine for intestinal disorder by combining  $1 \times 10^6$  to  $1 \times 10^8$  cells of the YY bacteria having the intestine regulating function with 1 to 30g of the dietary fiber also having the intestine regulating function. Furthermore, it is considered as a mere exercise of ordinary creativity of a person skilled in the art to formulate a liquid medicine in view of the ease of taking medicine or the like, and in addition, the effect thereof cannot be found to be remarkable one.

**Measures for Reasons for Refusal**

In the detailed explanation of the invention in this example, the result of the pharmacological test on the antifatulent of this invention formulated by combining the dietary fiber and the YY bacterium is shown, and a fortification of the intestine regulating function is also described. Therefore, in a written opinion etc., it is possible to insist and demonstrate that there is the advantageous effect of the antifatulent composed of the combination of the dietary fiber and the YY bacterium compared to a cited invention, with showing the experimental result in case of the administration of the dietary fiber and the YY bacterium respectively. However, reasons for refusal should be sustained if the effect does not exceed beyond the scope expected from the state of the art as of the filing.

**[Example 9] Combination of a publicly known main component having a side effect with a publicly known sub-component having the ability to reduce the side effect**

**Claim**

[Claim 1] Therapeutic agent for a paclitaxel responsive tumor formulated by combining paclitaxel with a compound X in a effective dose for suppressing a vomiting caused by administration of paclitaxel.

**Outline of Detailed Explanation of the Invention**

In this invention, it is found that the paclitaxel responsive tumor can be cured while suppressing the vomiting which is the side effect caused at the time of administering the paclitaxel by using the paclitaxel together with the compound X at the same time.

In the example, the result of the pharmacological test is described which shows the reduction of the side effect by using the paclitaxel together with the compound X at the same time.

**Result of Prior Art Search**

Although the paclitaxel is an excellent anti-tumor agent, it is publicly known that vomiting is a side effect caused by the paclitaxel at the time of administration, and using the paclitaxel together with sub-component reducing vomiting. On the other hand, it is publicly known that the compound X generally weakens the vomiting. Furthermore, the effect of reducing the vomiting disclosed in the detailed explanation of the invention falls under the predictable range from the state of the art as of the filing.

**Outline of Reasons for Refusal**

Since it is known that paclitaxel is used together, at the same time, with the sub-component for weakening the vomiting which is the side effect of the administration of paclitaxel, and furthermore the compound X is well known as a compound for generally weakening the vomiting, the combined use of the paclitaxel with the compound X can be easily made by a person skilled in the art, in order to weaken the vomiting which is the side effect of the administration of paclitaxel. Furthermore, there is no remarkable effect that cannot be foreseen as a result of the combined use as described.

**Measures for Reasons for Refusal**

Ordinarily, the above-described reason for refusal is not overcome.

**[Example 10] Combination with a publicly known sub-component having the ability to eliminate a problem related to the efficacy of a publicly known main component**

**Claim**

[Claim 1] A combination drug for anti-inflammation formulated by compounding 1 to 100 weight parts of compound X and 0.2 to 20 weight parts of compound Y for the total 100 weights parts of diclofenac or its salts and acetaminophen.

**Outline of Detailed Explanation of the Invention**

In this invention, it is shown that the pain threshold value can be increased and the duration time of the function can be extended in a test for painkiller functions by adding compound X and compound Y in the anti-inflammatory drug formulated by combining diclofenac or its salts with acetaminophen.

In the embodiment, the result of the pharmacological test is described, which shows the said effects by adding compound X and compound Y at a specific ratio to the combination of the diclofenac or its salts and acetaminophen.

**Result of Prior Art Search**

A combination drug for anti-inflammation formulated by combining diclofenac or its salts with acetaminophen is publicly known, and it is also known that there is a so-called ceiling effect in which the anti-inflammatory and painkiller effect does not increase while only the side effect increases, even if the dose thereof is increased by more than a certain dose, generally, in the non-steroidal type anti-inflammatory drug.

In general, it is publicly known that, by adding compound X and compound Y to the non-steroidal type anti-inflammation drugs, the pain threshold value can be increased to the same degree as the invention of the present application and the duration time of the effect can also be extended to the same degree as the invention of the present application in a test for painkiller functions.

**Outline of Reasons for Refusal**

A non-steroidal type anti-inflammation drugs formulated by combining diclofenac or its salts with acetaminophen is publicly known, and it is known that the pain threshold value can be increased and the duration time of the effect can be extended in the analgesic effect test by adding compound X and compound Y to the non-steroidal type anti-inflammation drugs. Accordingly, adding compound X and compound Y to the non-steroidal type anti-inflammation drugs formulated by combining the diclofenac or its salts with acetaminophen in order to increase the pain threshold value and extend the duration time of the function would have been easily arrived at by a person skilled in the art, and it is considered that the range of the compounding ratio of the components would have been experimentally optimized by a person skilled in the art. In addition, the effect thereof cannot be found to be remarkable one.

**Measures for Reasons for Refusal**

Ordinarily, the above-described reason for refusal is not deemed overcome.

**[Example 11] Combination of publicly known components having respective efficacy for various symptoms caused by major disease**

**Claim**

[Claim 1] Therapeutic agent for AIDS formulated by combining azidothymidine (AZT), an anti-HIV medicine, with compound Z.

**Outline of Detailed Explanation of the Invention**

In this invention, it is shown that, in order to cure a patient with AIDS which appears after the patient has been infected by HIV, the combination of the anti-HIV medicine AZT and compound Z which is effective in curing pneumonia caused as a symptom of the AIDS inhibits the proliferation of the HIV and cures pneumonia.

**Result of Prior Art Search**

It is publicly known that azidothymidine (AZT) can be used as therapeutic agent for AIDS. It is also publicly known that the pneumonia is caused as one mode of the AIDS. Furthermore, the inhibitory effect of the proliferation of the HIV and curing effect of pneumonia disclosed in the detailed explanation of the invention falls under the predictable range from the state of the art as of the filing.

**Outline of Reasons for Refusal**

It is known that the azidothymidine (AZT) is effective as therapeutic agent for AIDS, and also known that the pneumonia is easily caused as a symptom of the AIDS. Furthermore, curing the pneumonia by use of compound Z is widely practiced.

Accordingly, it is among exercises of ordinary creativity of a person skilled in the art to use a combination of the anti-HIV medicine AZT with the compound Z when medicinally treating AIDS patients for the purpose of suppressing the proliferation of the HIV which causes the AIDS while curing also the pneumonia which is caused as a symptom of the AIDS. Furthermore, remarkable effects that cannot be foreseen are not shown by the combined use.

**Measures for Reasons for Refusal**

Ordinarily, the above-described reason for refusal is not overcome.