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

Chapter 2 Biological Inventions

（Applied to any patent applications filed on or after January 1, 2015）

In this chapter, matters requiring special judgement and handling in examining patent applications relating to biological inventions are mainly explained.

Here, the term "organisms" means microorganisms, animals as well as plants, including reproducible animal or plant cells.

1. Genetic Engineering

This section deals with inventions relating to genetic engineering in biological inventions. The term "genetic engineering" here means the technology which manipulates genes artificially by gene recombination, cell fusion, etc.

Inventions relating to genetic engineering include those of a gene, a vector, a recombinant vector, a transformant, a fused cell, a protein which are obtained by transformation (hereinafter, referred to as "a recombinant protein"), a monoclonal antibody, etc.

Inventions relating to microorganisms, plants and animals, and which are obtained using genetic engineering are treated here in this section, in principle.

1.1 Description Requirements of the Specification

1.1.1 Scope of Claim

According to Section 36(6)(ii) of the Patent Act, the invention for which a patent is sought shall be clear, therefore, scope of claim shall be described so that an invention is clearly identified on the basis of statements of each claim.

In a claim, a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein and a monoclonal antibody should be described as indicated below.

(1) Genes

① A gene may be described by specifying its nucleotide sequence.

② A structural gene may be described by specifying an amino acid sequence of the protein encoded by the said gene.

Example:

A gene encoding a protein consisting of an amino acid sequence represented by Met-Asp-Lys-Glu.

③ A gene may be described by a combination of the terms "substitution, deletion or addition" or "hybridize" with functions of the gene, and if necessary, origin or source of the gene in a generic form as follows (provided that the claimed invention is clear and the enablement requirement is met (See 1.1.2.1 below)).

Example1:

A gene encoding a protein of (a) or (b) as follows:

(a) a protein whose amino acid sequence is represented by Met-Tyr-Cys-Leu

(b) a protein derived from the protein of (a) by substitution, deletion or addition of one or several amino acids in the amino acid sequence defined in (a) and having the activity of enzyme A.

[Note]

The protein (a) has the activity of enzyme A.

The gene encoding the protein (b) is described in the detailed description of the invention in such a manner that a person skilled in the art can make the said gene without large amount of trials and errors or complicated experimentation beyond the reasonable extent that can be expected from a person skilled in the art who is supposed to have ordinary skill.

Example 2:

A gene selected from the group consisting of:

(a) a DNA whose nucleotide sequence is represented by ATGTATCGG･･･TGCCT

(b) a DNA which hybridizes under stringent conditions to the DNA, whose nucleotide sequence is complementary to that of the DNA defined in (a) and encodes the human protein having the activity of enzyme B.

[Note]

A protein encoded by the DNA (a) has the activity of enzyme B.

"Stringent conditions" are described in the detailed description of the invention.

④ A gene may be described by specifying functions, physiochemical properties, origin or source of the said gene, a process for producing the said gene, etc. (provided that the claimed invention is clear and the enablement requirement is met (See 1.1.2.1 below)).

(2) Vectors

A vector should be described by specifying a base sequence of its DNA, a cleavage map of DNA, molecular weight, number of base pairs, source of the vector, process for producing the vector, function or characteristics of the vector, etc.

[Note] A cleavage map is a map which shows the relative location and distance of the cleavage sites by various restriction enzymes.

(3) Recombinant vectors

A recombinant vector may be described by specifying at least one of the gene and the vector.

Example:

A recombinant vector containing a DNA whose base sequence is represented by ACAGCA･･････ AGTCAC.

(4) Transformants

A transformant may be described by specifying at least one of ① its host and ② the gene which is introduced (or the recombinant vector) (provided the that the claimed invention is clear and enablement requirement is met (See 1.1.2.1 below)).

Example 1:
A transformant comprising a recombinant vector containing a gene encoding a protein whose amino acid sequence is represented by Met-Asp-‥‥‥Lys-Glu.

Example 2:
A plant wherein a toxin gene having a base sequence of ATGACT‥‥‥ is inserted and the said gene is expressed.

Example 3:
A transgenic non-human mammal, having a recombinant DNA obtained by linking a structural gene encoding any protein to the regulatory region of a gene involved in the production of milk protein, and secreting the said protein into milk.

(5) Fused cells

A fused cell may be described by specifying parent cells, function and characteristics of the fused cell, or a process for producing the fused cell, etc.

(6) Recombinant proteins

① A recombinant protein may be described by specifying an amino acid sequence or a base sequence of structural gene encoding the said amino acid sequence.

Example:

A recombinant protein consisting of an amino acid sequence represented by Met-Tyr-Cys-Leu.

② A recombinant protein may be described by a combination of the terms "substitution, deletion or addition" and functions of the recombinant protein, and if necessary, origin or source of the recombinant protein in a generic form as follows (provided that the claimed invention is clear and the enablement requirement is met (See 1.1.2.1 below)).

Example:

A recombinant protein of (a) or (b) as follows:

(a) a protein whose amino acid sequence is represented by Met-Tyr-Cys-Leu

(b) a protein derived from the protein of (a) by substitution, deletion or addition of one or several amino acids in the amino acid sequence in(a) and having the activity of enzyme A.

[Note]

A protein (a) has the activity of enzyme A.

The protein (b) is described in the detailed description of the invention in such a manner that a person skilled in the art can make the said protein without a large amount of trials and errors or complicated experimentation beyond the reasonable extent that can be expected from a person skilled in the art who is supposed to have ordinary skill.

③ A recombinant protein may be described by specifying functions, physiochemical, origin or source of the said recombinant protein, a process for producing the said recombinant protein, etc.

(provided that the claimed invention is clear and the enablement requirement is met (See 1.1.2.1 below)).

(7) Monoclonal antibodies

A claim directed a monoclonal antibody may be defined by specifying any of antigen recognized by it, hybridoma which produces it, or cross-reactivity, etc.

Example 1:

A monoclonal antibody to antigen A.

[Note] Antigen A is necessary to be defined by specifying as a substance.

Example 2:

A monoclonal antibody to antigen A, produced by a hybridoma having ATCC Deposit No. HB-xxxx.

[Note] Antigen A is necessary to be defined by specifying as a substance.

Example 3:

A monoclonal antibody which binds not to antigen B but to antigen A.

[Note] Antigen A and antigen B are necessary to be defined by specifying as substances.

1.1.2 Detailed Description of the Invention

The detailed description of the invention shall be stated in such a manner sufficiently clear and complete for the invention to be carried out by a person having ordinary skill in the art to which the invention pertains (the enablement requirement), and shall be stated that the problem to be solved by the invention and its solution, or other matters necessary for a person having ordinary skill in the art to understand the technical significance of the invention (the Ministerial Ordinance Requirement).

The detailed description of the invention which does not meet the above requirements violates Section 36(4)(i) of the Patent Act.

1.1.2.1 Enablement Requirement

Section 36(4)(i) of the Patent Act states that "the detailed description of the invention shall be stated....in such a manner sufficiently clear and complete for the invention to be carried out by a person having ordinary skill in the art to which the invention pertains." This means that "the detailed description of the invention shall be described in such a manner that a person who has ability to use ordinary technical means for research and development (including comprehension of document, experimentation, analysis and manufacture) and to exercise ordinary creativity in the art to which the invention pertains can carry out the claimed invention on the basis of matters described in the specification (excluding claims) and drawings taking into consideration the common general knowledge as of the filing."

Therefore, if "a person skilled in the art" who is supposed to have ordinary skill cannot understand how to carry out the invention on the basis of teachings in the specification (excluding claims) and drawings taking into consideration the common general knowledge as of the filing, then, such a description of the invention should be deemed insufficient for enabling such a person to

carry out the invention. For example, if a large amount of trials and errors or complicated experimentation are needed to find a way of carrying out the invention beyond the reasonable extent that can be expected from a person skilled in the art who is supposed to have ordinary skill, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to carry out the invention.

(1) Invention of a Product

For an invention of a product, the definition of "being able to carry out the invention" is to make and use the product. Therefore, the "mode for carrying out the (claimed) invention" should be described in so that this becomes possible.

Also, the said invention of a product should be explained clearly in the detailed description of the invention.

Therefore, an invention of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein, a monoclonal antibody, etc. should be described as follows.

①"An invention of a product" being explained clearly

If an invention of a product can be identified by a person skilled in the art based on the statements of a claim and can be understood from the statements and implications in the detailed description of the invention, then, the invention will be deemed as being explained clearly.

②"Can be made"

For an invention of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein or a monoclonal antibody, the way of making the product shall be described in the detailed description of the invention except where the product could be made by a person skilled in the art without such description when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(i) Genes, vectors or recombinant vectors

A process for producing a gene, a vector or a recombinant vector should be described by respective origin or source, means for obtaining a vector to be used, an enzyme to be used, treatment conditions, steps for collecting and purifying it, or means for identification, etc.

If genes are claimed in a generic form (See 1.1.1(1)) and a large amount of trials and errors or complicated experimentation are needed to produce those genes beyond the reasonable extent that can be expected from a person skilled in the art, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to make the product.

For example, in cases where a claimed invention includes the gene actually obtained and many of genes whose identity is extremely low to the said gene obtained and is specified by their function and that as a result, many of genes which do not have the same function as the said gene obtained are included in the genes whose identity is extremely low, a large amount of trials and errors or complicated experimentation are generally needed to select the genes with the same function as the said gene obtained among the genes whose identity is extremely low

beyond the reasonable extent that can be expected from a person skilled in the art, and therefore, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to make the product.

[Example]

A gene selected from the group consisting of:

(a) a DNA whose nucleotide sequence is represented by ATGTATCGG…TGCCT

(b) a DNA whose nucleotide sequence has more than X% identity to that of (a) and which encodes the protein having the activity of enzyme B.

[Note]

A protein encoded by the DNA (a) has the activity of enzyme B.

X% represents extremely low identity.

(Explanation)

Genes whose identity is extremely low to the gene actually obtained are included in the (b), although (b) is specified by its function. In case that " A DNA whose nucleotide sequence has more than X % identity to that of (a)" includes many of genes which do not have the activity of enzyme B, a large amount of trials and errors or complicated experimentation are generally needed to select the genes with the activity of enzyme B beyond the reasonable extent that can be expected from a person skilled in the art. Therefore, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to make the product.

(ii) Transformants

A process for producing a transformant should be described by a gene or a recombinant vector introduced, a host (a microorganism, a plant or an animal), a method of introducing gene or the recombinant vector into the host, a method of selectively collecting the transformant, or means for identification, etc.

If the transformant is the one described by a generic taxonomical unit (e.g., a transformed plant, a transformed non-human vertebrate, a transformant (including microorganisms, plants and animals)), and if a large amount of trials and errors or complicated experimentation are needed to produce those transformants beyond the reasonable extent that can be expected from a person skilled in the art, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to make the product.

(iii) Fused cells

A process for producing a fused cell should be described by stating pretreatment of the parent cells, fusion condition, a method of selectively collecting the fused cell, or means for identification, etc.

(iv) Recombinant proteins

A process for producing a recombinant protein should be described by stating means for obtaining a gene encoding the recombinant protein means for obtaining, an expression vector used, means for obtaining a host, a method for introducing the gene into the host, steps for

collecting and purifying the recombinant protein from the transformant into which the gene has been introduced, or means for identification of the obtained recombinant protein, etc.

(See “(i) Gene, vector or recombinant vector" mentioned above for the treatment of enablement requirement in cases wherein recombinant proteins are claimed in a generic form.)

(v) Monoclonal antibodies

A process for producing a monoclonal antibody should be described by stating means for obtaining or producing immunogen, a method for immunization, a process for selectively obtaining antibody producing cells, or means for identification of the monoclonal antibody, etc.

(vi) Deposit of microorganisms, etc. (For information on the deposit and furnishing of microorganisms, see "5.1 Deposit and Furnishing of Microorganisms")

(a) For an invention of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein, a monoclonal antibody, etc. produced by the use of a microorganism, etc. ("a microorganism, etc." here includes a microorganism, a plant and an animal), a process for producing the said product should be described in the specification as filed so that a person skilled in the art can make it. Further, the microorganism used in the process should be deposited and its accession number should be described in the specification as filed unless the microorganisms readily available to a person skilled in the art (See 5.1(ii)(b)).

(b) For an invention of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein, a monoclonal antibody, etc., when it is not possible to describe a process for producing the said product in the specification in such a manner that a person skilled in the art can make it, the obtained transformant (including a transformant which produces a recombinant protein) or the fused cell (including a hybridoma which produces a monoclonal antibody) into which the gene, the vector, the recombinant vector has been introduced, should be deposited and its accession number should be described in the specification as filed.

(c) Generally, the acquisition of a hybridoma producing a monoclonal antibody which satisfies limitative conditions, (e.g., a monoclonal antibody whose affinity to the antigen A is specified by the limitative coupling constant,) is not reproducible. Therefore, in case that the claimed invention is related to a monoclonal antibody which satisfies limitative conditions or a hybridoma producing the said monoclonal antibody, the said hybridoma should be deposited and its accession number should be described in the specification as filed, except where the hybridoma can be created by a person skilled in the art on the basis of the description in the specification.

③"Can be used"

An invention of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein, a monoclonal antibody, etc., must be described so that invention can be used by the person skilled in the art. Knowledge of how the invention can be used shall be described in the detailed description of the invention, except where it could be understood by the

person skilled in the art without such description, when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

For instance, in order to show how an invention of a gene can be used, it should be described in the detailed description of the invention that the gene has a specific function (the "specific function" here means a "function from which a specific application with technical meanings can be assumed"; in case of a structural gene, the protein encoded by the said gene has the specific function).

In case that genes are claimed in a generic form and the function is not specified in the claim (genes specified only by "substituted, deleted or added," "hybridized" or "having more than X% identity," etc.), the genes claimed in a generic form contain the ones which do not have the said function and the part of the said genes cannot be used, and therefore, the detailed description of the invention is not described in such a manner that enables a person skilled in the art to use the product.

(2) Invention of a Process

For an invention of a process, the definition of "being able to carry out the invention" is that the process can be used. Further, the said invention of a process should be explained clearly in the detailed description of the invention. In order to describe the invention of the process in such a manner that the process can be used, the enablement requirement in "(1) Invention of a Product" should be referred to, if necessary. For instance, "5.1 Deposit and Furnishing of Microorganisms" should be referred to if deposit of microorganisms, etc. is necessary.

(3) Invention of a Process for Manufacturing a Product

Where an invention of a process is directed to "a process for manufacturing a product," the definition of "the process can be used" means that the product can be manufactured by the process. Further, the said invention of a process for manufacturing a product should be explained clearly.

Therefore, for an invention of a process for producing a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein, a monoclonal antibody, etc., the said process should be explained clearly and the description shall be stated so as to enable a person skilled in the art to produce the product by using the said process. In order to be stated so as to enable a person skilled in the art to produce the product by using the said process, the enablement requirement in "(1) Invention of a Product" should be referred to, if necessary. For instance, "5.1 Deposit of microorganisms, etc." should be referred to if deposit of microorganisms, etc. is necessary.

Further, it is necessary to describe how said process can be used or at least one use of the said product.

(4) How Specifically Must the Detailed Description of the Invention Be Described?

It is necessary for the applicant to describe at least one mode for showing how to carry out the claimed invention in the detailed description of the invention. When embodiments or working

examples are necessary in order to explain the invention in such a way that a person skilled in the art can carry out the invention, "the mode for carrying out the invention" should be described in terms of embodiments or working examples. Embodiments or working examples are those which specifically show the mode for carrying out the invention (in case of an invention of a product, for instance, those which specifically show how to make the product, what structure it has, or how to use it, etc.)

In the case of inventions in technical fields where it is generally difficult to infer how to make and use a product on the basis of its structure, normally one or more representative embodiments or working examples are necessary which enable a person skilled in the art to carry out the invention.

Since this technical field (i.e., genetic engineering) is the one where it is difficult to infer how to make and use a product on the basis of its structure, normally one or more representative embodiments or working examples are necessary.

(5) Balance of the Claim and the Detailed Description of the Invention

In the detailed description of the invention, at least one mode for carrying out the invention needs to be described in terms of "claimed invention." For not all embodiments nor all alternatives within the extent (or the metes and bounds) of the claimed invention, the mode for carrying out the invention needs to be described.

However, when the examiner can show well-founded reason that a person skilled in the art would be unable to extend the particular mode for carrying out the invention in the detailed description of the invention to the whole of the field within the extent (or the metes and bounds) of the claimed invention, the examiner should determine that the claimed invention is not described in such a manner sufficiently clear and complete to be carried out by a person skilled in the art. In such a case, the examiner should specifically point out a concrete reason and preferably the reason above should be supported by reference documents.

1.1.2.2 Ministerial Ordinance Requirement

Matters required under the Ministerial Ordinance are (1) technical field to which an invention pertains and (2) problem to be solved by the invention and its solution.

(1) Technical field to which an invention pertains

As "technical field to which an invention pertains," at least one technical field to which a claimed invention pertains shall be stated in a specification, in principle.

In the inventions of genetic engineering, "technical field to which an invention pertains" should be described such as pharmaceuticals, analytical agents, production of plants, for example.

(2) Problem to be solved by the invention and its solution

As "problem to be solved by the invention," an application shall state at least one technical problem to be solved by a claimed invention, in principle. As "its solution," an application shall explain how the technical problem has been solved by the claimed invention.

For example, in the case of the invention of the process for the production of a plant resistant to disease A by using a vector into which disease A-resistant gene B has been inserted, the problem to be solved by the invention should be described as "to produce a plant resistant to disease A" and

the means for solving the problem should be described as "cloning disease-resistant gene B from the chromosomal DNA of another plant resistant to disease A, obtaining a recombinant vector inserted by the said gene, and regenerating the plant body from the plant cell transformed by the said vector."

1.1.2.3 Prior Art and Advantageous Effects

(1) Prior art

An applicant should describe background prior art, as far as he knows, which is deemed to contribute to understanding the technical significance of the claimed invention and examination of patentability of the invention, because such descriptions of prior art could teach the problem to be solved and could substitute the descriptions of the problems.

(2) Advantageous effects over prior art

It is an applicant's advantage to describe an advantageous effect of a claimed invention over the relevant prior art because such advantageous effect, if any, is taken into consideration as a fact to support to affirmatively infer the existence of an inventive step. Therefore, an applicant should describe an advantageous effect of a claimed invention over the relevant prior art, if any, as far as he knows.

1.1.3 Sequence Listing

(1) When a nucleotide sequence consisting of 10 or more nucleotides, or an amino acid sequence of a protein or peptide consisting of 4 or more L-amino acids is described in a specification, a "Sequence Listing" of the sequence prepared in accordance with "Guidelines for the preparation of specifications which contain nucleotide and/or amino acid sequences" ([Appendix 3]; *omitted in this English translation*) published in the Public Notice of Japan Patent Office should be described at the end of the detailed description of the invention as a part of it (See Note 15"Ho" of Form 29, Section 24 of Regulations under the Patent Act).

(2) When a nucleotide sequence or an amino acid sequence is described in the scope of claim, the sequence described in the "Sequence Listing" prepared in accordance with "Guidelines for the preparation of specification which contain nucleotide and/or amino acid sequence" may be cited.

1.2 Unity of Invention

A single application may be filed for a set of claims describing inventions shown in the following examples, because these inventions have the same or corresponding special technical features among them.

These examples below are explained under the presumption that each invention in claims has a contribution over the prior art.

[Example 1]

Claim1: A protein X

Claim2: A structural gene Y encoding the protein X

Claim3: A recombinant vector Z containing the structural gene Y

Claim4: A transformant A containing the recombinant vector Z

(Explanation)

As a protein X was encoded and expressed by a structural gene Y, it can be said that they have a special technical feature. Further, a structural gene Y, a recombinant vector Z containing the structural gene Y, and a transformant A containing the recombinant vector Z also have a structural gene Y as a special technical feature. Therefore the inventions in claims 1 to 4 have special technical features, and they comply with the requirement of unity of invention.

[Example 2]

Claim1: A parent cell A

Claim2: A fused cell prepared from the parent cell A

(Explanation)

Since a fused cell contains essential genetic materials which express characteristics similar to a parent cell A, as a part of its genetic materials, A parent cell A and the fused cell have the same or corresponding special technical feature. Accordingly, the inventions in claims 1 and 2 have a special technical feature, and they comply with the requirement of unity of invention.

[Example 3]

Claim1: A transformant A

Claim2: A process for manufacturing a chemical substance X using the transformant A

(Explanation)

A process for producing a chemical substance X using a transformant A utilizes properties and functions particular to a transformant A. Accordingly, the inventions in claims 1 and 2 have a special technical feature, and they comply with the requirement of unity of invention.

[Example 4]

Claim1: A gene Y

Claim2: A process for producing a recombinant vector Z using a gene Y

Claim3: A process for producing a transformant A using a recombinant vector Z

(Explanation)

the inventions in claims 1 to3 all have a gene Y as a special technical feature, Accordingly, they comply with the requirement of unity of invention.

[Example 5]

Claim1: An antigenic protein X

Claim2: A monoclonal antibody against the antigenic protein X

(Explanation)

A monoclonal antibody in claim 2 obtained for the frist time by using an antigenic protein X in claim 1. Further a monoclonal antibody in claim 2 is used for detecting and/or purifying an antigen protein X in claim 1. Therefore the invention of an antigenic protein X has a very close relationship with the monoclonal antibody. Accordingly the inventions in claims 1 and 2 have a special technical feature, and they comply with the requirement of unity of invention.

However, the patent application does not comply with the requirements of Section 37 of the Patent Act in the following case.

[Example 6]

Claim1: A transformant A

Claim2: A process using a chemical substance X produced with the use of the transformant A

(Note) a chemical substance X is publicly known.

(Explanation)

A process using a chemical substance X produced with the use of the transformant A does not utilize properties and functions particular to a transformant A, and providing a transformant A does not have a close relationship with using a chemical substance X. Therefore they do not have special technical features. Accordingly the inventions in claims 1 and 2 do not comply with the requirement of unity of invention.

1.3 Requirements for Patentability

1.3.1 Invention Not Falling under "Industrially Applicable Invention"

Inventions of a gene, a vector, a recombinant vector, a transformant, a fused cell, a recombinant protein and a monoclonal antibody whose utility is not described in a specification or cannot be inferred, do not meet the requirements set forth in the first sentence in Section 29(1) of the Patent Act.

1.3.2 Novelty

(1) Recombinant proteins

① Where a protein X as an isolated and purified single substance is publicly known, a claimed invention concerning a recombinant protein X specified by a process of production, the said recombinant protein being identical as a chemical substance with the publicly known protein X, is not novel.

② In case where a recombinant process inevitably leads to a different product, for example in its sugar chain or the like, due to the difference of the host cells, even though the recombinant

protein has the same amino acid sequence as the publicly known one, a claimed invention concerning the recombinant protein specified by a process of production is novel.

(2) Monoclonal antibodies

① If antigen A is novel, a monoclonal antibody to the antigen A is generally considered novel. However, if a monoclonal antibody to publicly known antigen A' is publicly known and if the antigen A has the same epitope as that of A' because the antigen A is partially modified from publicly known antigen A' or the like, a monoclonal antibody to antigen A' also binds to antigen A. Therefore, in such a case, the claimed invention of "a monoclonal antibody to antigen A" is not novel.

② The claimed invention of a monoclonal antibody specified by a cross-reactivity, such as "a monoclonal antibody which binds not to antigen B but to antigen A" is not novel, if a monoclonal antibody to antigen A is publicly known and if there is no particular technical significance to specify the monoclonal antibody described by such a cross-reactivity (e.g., when it is clear that the publicly known monoclonal antibody to antigen A does not bind to antigen B either, because antigen B has no similarities to antigen A in the function, structure, etc.).

1.3.3 Inventive Step

(1) Genes

① In invention of a gene encoding Protein A has an inventive step, if Protein A has novelty and an inventive step.

② Where Protein A is publicly known but its amino acid sequence is not publicly known, an invention of a gene encoding Protein A does not have an inventive step, provided that a person skilled in the art could determine the amino acid sequence easily at the time of filing. However, when it is considered that the gene is specified by a specific base sequence and has advantageous effects that a person skilled in the art cannot foresee in comparison with other genes having a different base sequence encoding the Protein A, the invention of the said gene has an inventive step.

③ When an amino acid sequence of Protein A is publicly known, an invention of a gene encoding the Protein A does not have an inventive step. However, when it is considered that the gene is specified by a specific base sequence and has advantageous effects that a person skilled in the art cannot foresee in comparison with other genes having a different base sequence encoding the Protein A, the invention of the said gene has an inventive step.

④ When a structural gene is publicly known, an invention relating to a structural gene of naturally obtainable mutant (allelic mutant, etc.) of the said publicly known structural gene and which is derived from the same species as the said structural gene and has the same properties and

functions as the said structural gene does not have an inventive step. However, if the claimed structural gene has advantageous effects that a person skilled in the art cannot foreseen in comparison with the said publicly known structural gene, the claimed invention of the structural gene has an inventive step.

(2) Recombinant vectors

In case where both a vector and a gene to be introduced are publicly known, a claimed invention concerning a recombinant vector obtained by a combination of them does not have an inventive step. However, even if both a vector and a gene to be introduced are publicly known, a claimed invention concerning a recombinant vector with a specific combination of them, which leads to an advantageous effect that a person skilled in the art cannot foresee, has an inventive step.

(3) Transformants

If both a host and a gene to be introduced are publicly known, a claimed invention concerning the transformant obtained by a combination of them does not have an inventive step. However, even if both of a host and a gene to be introduced are publicly known, a claimed invention concerning a transformant with a specific combination of them, which leads to an advantageous effect that a person skilled in the art cannot foresee, has an inventive step.

(4) Fused cells

If both of parent cells are publicly known, a claimed invention concerning a fused cell produced by fusing both of the parent cells does not have an inventive step. However, if the fused cell has advantageous effects that a person skilled in the art cannot foresee, the claimed invention of the fused cell has an inventive step.

(5) Monoclonal antibodies

If antigen A is publicly known and it is clear that the antigen A has immunogenicity (for example, antigen A clearly has immunogenicity because a polyclonal antibody to the antigen A is publicly known or because the antigen A is a polypeptide with a large molecular weight, etc.), the claimed invention of "a monoclonal antibody to the antigen A " does not have an inventive step. However, if the claimed invention is further specified by other features, etc. which leads to an advantageous effect that a person skilled in the art cannot foresee, the claimed invention has an inventive step.

1.4 Amendment of Description, Claims or Drawings

Amendment of the description, claims or drawings relating to the deposit of microorganisms, etc. is handled as described in "2.3 Amendment of Description, Claims or Drawings" below.

2. Microorganisms

This section deals with inventions related to microorganisms per se as well as those related to the use of microorganisms, etc. Inventions relating to the use of microorganisms include not only those using a novel microorganism but also those based on finding of a method for using a publicly known microorganism (e.g., an invention of a process for producing a publicly known substance using a publicly known microorganism, an invention of a process for treating a material (e.g., water treatment, soil improvement) using a publicly known microorganism, an invention of use for a publicly known microorganism as a treating agent (e.g., water treating agent, soil improving agent).

The term "microorganisms" means yeasts, molds, mushrooms, bacteria, actinomycetes, unicellular algae, viruses, protozoa, etc. and further includes undifferentiated animal or plant cells as well as animal or plant tissue cultures.

Matters relating to genetic engineering are referred to "1. Genetic Engineering" even if they are inventions relating to microorganisms.

2.1 Description Requirements of the Specification

2.1.1 Designation of Microorganisms

In principle, microorganisms should be specified by scientific names in accordance with microbiological nomenclature. In case of designating a strain of a microorganism, it should be specified by the strain name following the species name (in accordance with microbiological nomenclature). When a microorganism cannot be specified by the species name, it may be specified by the strain name along with the genus name.

In case that a strain of a microorganism has been deposited, the said strain may be specified by the description of the accession number in addition to the species name or the strain name following the species name.

Example: Bacillus subtilis FERM P-xxxxx strain

Undifferentiated animal or plant cells should be specified, in principle, by scientific names in accordance with zoological or botanical nomenclature or standard Japanese names, respectively.

2.1.2 Scope of Claim

According to Section 36(6)(ii) of the Patent Act, the invention for which a patent is sought shall be clear, therefore, scope of claim shall be described that an invention shall be clearly identified on the basis of statements of each claim.

2.1.3 Detailed Description of the Invention

(See 1.1.2 above)

2.1.3.1 Enablement Requirement

(See 1.1.2.1 above)

(1) Invention of a Product

As to an invention of a product, a microorganism to be created or a microorganism to be used should be described as follows.

① A microorganism being explained clearly

In order to explain a microorganism clearly, the microorganism should be described as indicated below.

As to a new microorganism, the microorganism should be specified by the species name or the strain name following the species name in accordance with microbiological nomenclature, and also the microbiological characteristics should be described. As microbiological characteristics, it is desirable that taxonomic characteristics generally used in the field (Appendix1) are described, however, other microbiological characteristics (e.g., selective productivity of metabolites) may be described.

A microorganism which cannot be specified by the species name should be specified by the strain name along with the genus name, after clarifying the reason why the species name cannot be specified.

Microbiological characteristics of a microorganism should be described as follows, depending on whether it is a new strain or a new species.

(i) New strain

It should be clearly described that the characteristics of the strain as well as the difference in the microbiological characteristics of the strain from the publicly known strains within the same species to which the new strain belongs.

(ii) New species

The taxonomic characteristics of the species should be described in detail, and the reason why the microorganism is judged to be a new species should be clarified. That is, the difference of the species from the existing similar species should be expressly described, and the relevant literature used on the basis of the judgement should be indicated.

② "Can be made"

As to an invention relating to a microorganism per se or relating to the use of a novel microorganism, means for creating the microorganism should be described so that a person skilled in the art can create the said microorganism.

Means for creating microorganisms includes means for screening, means for mutagenesis, means for gene recombination, etc.

If the means for creating the microorganism cannot be described in the detailed description of the invention so that a person skilled in the art can create the said microorganism, it is necessary to deposit the microorganism in accordance with Section 27bis of Regulations under the Patent Act (For the details, see "5.1 Deposit and furnishing of microorganisms.").

③ "Can be used"

An invention of a microorganism per se or of the use of a microorganism must be

described so that invention can be used by the person skilled in the art. Knowledge of how the invention can be used shall be described in the detailed description of the invention, except where it could be understood by the person skilled in the art without such description, when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(2) Invention of a Process

Of those inventions related to the use of a microorganism, an invention of a process for the use of a microorganism (e.g. an invention of a process for treating a material with a microorganism) should be described as follows.

For an invention of a process, the definition of "being able to carry out the invention" is that the process can be used. Further, "the said invention of a process" should be explained clearly in the detailed description of the invention.

In order to describe the invention of the process in such a manner that the process can be used, the enablement requirement in "(1) Invention of a Product" should be referred to, if necessary. For instance, "5.1 Deposit and Furnishing of Microorganisms." should be referred to if deposit of microorganisms, etc. is necessary.

(3) Invention of a Process for Manufacturing a Product

Of those inventions related to the use of a microorganism, an invention of a process for producing a substance using a microorganism should be described as follows.

Where an invention of a process is directed to "a process for manufacturing a product," the definition of "the process can be used" means that the product can be manufactured by the process. Further, the said invention of a process for manufacturing a product should be explained clearly in the detailed description of the invention.

Accordingly, for the invention of a process for producing a substance by using a microorganism, a process for producing the said substance shall be described in the detailed description of the invention so that a person skilled in the art can produce the said substance taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing. In order to describe the process in such a manner that a person skilled in the art can produce the said substance by the process, the enablement requirement described in "(1) Invention of a Product" should be referred to, if necessary. For instance, "5.1 Deposit and furnishing of microorganisms" should be referred to, if the deposit of microorganisms is necessary.

Further, it is necessary to describe how the said process can be used or at least one use of the said substance.

As to "How Specifically Must the Detailed Description of the Invention Be Described?" and "Balance of the Claim and the Detailed Description of the Invention," see the relevant portions (1.1.2.1(4) and (5)) in "1. Genetic Engineering."

2.1.3.2 Ministerial Ordinance Requirement

Matters required under the Ministerial Ordinance are (1) technical field to which an invention

pertains and (2) problem to be solved by the invention and its solution.

(1) Technical field to which an invention pertains

As "technical field to which an invention pertains," at least one technical field to which a claimed invention pertains shall be stated in a specification, in principle.

In the inventions related to a microorganism, "technical field to which an invention pertains" should be described such as pharmaceuticals, feed, food, water treatment, for example.

(2) Problem to be solved by the invention and its solution

As "problem to be solved by the invention," an application shall state at least one technical problem to be solved by a claimed invention, in principle. As "its solution," an application shall explain how the technical problem has been solved by the claimed invention.

As to "Prior Art and Advantageous Effects," see 1.1.2.3 in "1. Genetic Engineering."

2.2 Requirements for Patentability

2.2.1 Invention Not Falling under "Industrially Applicable Invention"

The following inventions do not meet the requirement provided in the first sentence in Section 29(1) of the Patent Act.

(1) A mere discovery which is not a creation

Example: A merely discovered microorganism existing in nature.

However, an invention of a microorganism which is isolated from nature artificially involves creativity.

(2) Inventions incapable of industrial application

An invention of a microorganism per se whose utility is not described or cannot be inferred.

2.2.2 Inventive Step

(1) Invention of a microorganism per se

An inventive step of an invention of a microorganism per se should be examined based on taxonomic characteristics of the microorganism as well as effects produced by the use of the microorganism.

①An invention of a microorganism whose taxonomic characteristics are remarkably different from those of publicly known species (i.e., a new species) has an inventive step.

②An invention involving a microorganism producing advantageous effects that a person skilled in the art cannot foresee, though the taxonomic characteristics of the microorganism are not substantially different from those of publicly known species, has an inventive step.

Example:

A microorganism which was obtained by mutating a publicly known species and which has

remarkably high productivity of metabolite.

(2) Invention relating to the use of a microorganism

①An invention relating to the use of a microorganism (e.g., an invention of a process for producing a substance) does not have an inventive step, if the microorganism used in the invention is a taxonomically known species and belongs to the same genus as another microorganism for which the same mode of use (e.g., producing the aimed substance) is known. However, if it is found that the invention using the former microorganism has advantageous effects that a person skilled in the art cannot foresee in comparison with the invention using the latter microorganism, the invention using the former microorganism has an inventive step.

(Explanation)

Between publicly known species in the same genus, it is usually easy for a person skilled in the art to culture each microorganism and confirm its utility (e.g., substance productivity) and its effects.

②An invention relating to the use of a microorganism (e.g., an invention of a process for producing a substance) has an inventive step, if the microorganism used in the invention is remarkably different from publicly known species in taxonomic characteristics (i.e., a new species), even if the mode of use (e.g., the aimed substance) is the same.

(Explanation)

Since the used microorganism per se has an inventive step as described (1)① above, a process using the microorganism has also an inventive step.

2.3 Amendment of Description, Claims or Drawings

(1) An amendment to convert or add an accession number of a microorganism is acceptable because it does not introduce any new technical matter, if microbiological characteristics of the microorganism are described in the description, scope of claims or drawings as of filing, to the extent that the microorganism can be specified, and deposit of the microorganism can be specified based on the name of the depositary institution, etc.

(2) An amendment converting a storage number of a microorganism to an accession number based on the deposit of the microorganism with a depositary institution for the purpose of patent procedure, is acceptable because it does not introduce any new technical matter, if the microorganism used is stored at a reliable public culture collection and the storage number of the microorganism is explicitly stated in the description, scope of claims or drawings as of the filing and that it is clear that the identity of the microorganism is not lost.

In such a case, the applicant should make an amendment of the accession number without delay.

(3) An amendment converting a reference number of a microorganism to a corresponding accession number is obviously acceptable, if the reference number issued by the depositary

institution designated by the Commissioner of the Patent Office is described in the description, scope of claims or drawings as of the filing (A reference number corresponds to the number adding “A” to the head of an accession number in a depositary institution designated by the Commissioner of the Patent Office).

(4) An amendment adding microbiological characteristics of a microorganism is not acceptable because it introduces new technical matter unless those characteristics are inherently presented in the original description, even if the accession number of the microorganism stated in the description, scope of claims or drawings as of the filing is not changed and microbiological characteristics of the microorganism are described in the description, scope of claims or drawings as of the filing to the extent that the taxonomic species of the microorganism can be specified.

3. Plants

This section deals with inventions of plants per se, those relating to parts of plants (e.g., a fruit), those of a process for creating plants, those relating to use of plants, etc. The term "plants" means the plants under the classification where organisms are classified into three groups, namely microorganisms, plants and animals.

As to undifferentiated plant cells as well as plant tissue cultures, which are treated as microorganisms, reference should be made to relevant parts in "2. Microorganisms."

Matters relating to genetic engineering are referred to "1. Genetic Engineering" even if they are inventions relating to plants.

3.1 Description Requirements of the Specification

3.1.1 Designation of Plants

In principle, plants should be specified by scientific names in accordance with the botanical nomenclature or standard Japanese names.

3.1.2 Scope of Claim

As to an invention relating to a plant, a claim should be described as follows.

In the case of an invention of a plant per se, the plant should be specified by, for example, a combination of any of the species, the distinctive gene of the plant, characteristics of the plant, etc. and may be further specified by the process for creating the plants.

Example 1:

A plant belonging to Castanea crenata (Japanese chestnut) having the ATCC Accession No. xxxx whose bark contains catechol tannin and pyrogallol tannin in the ratio of X1-X2: Y1-Y2 and has a catechol tannin content of z1-z2 ppm (weight ratio), or its mutatnt having the said characteristics.

Example 2:

A watermelon obtained by crossing a diploid watermelon with a tetraploid watermelon obtained by polyploidizing a diploid watermelon, whose somatic cell has 33 chromosomes.

As to an invention of a process for creating a plant, the process for creating the plant should be described in the claim step by step. In the case where selection is performed as one step of creation based on characteristics or the like, the characteristics or the like necessary for the selection should be additionally described. Where conditions such as environment are necessary for creating the plant, such conditions should be also described.

Example:

A process for creating a cabbage characterized by crossing a cabbage strain having the ATCC Accession No.xxxx as a seed parent with another cabbage as a pollen parent by having resistance for the herbicide X.

3.1.3 Detailed Description of the Invention

(See 1.1.2 above)

3.1.3.1 Enablement Requirement

(See 1.1.2.1 above)

(1) Invention of a Product

An invention of a plant per se should be described as follows.

① A plant being explained clearly

In order to explain a plant clearly, for example, (i) matters regarding species of the plant created and (ii) matters relating to characteristic properties of the created plant should be described.

(i) Species of the plant created

In principle, the created plant should be specified by the scientific name in accordance with the botanical nomenclature or standard Japanese name.

(ii) Characteristic properties of the plant created

In the case that properties of the created plant are characteristic, they should be described specifically stating by numeric values actually obtained by measuring or the like and it is desirable that they are described in comparison with those of publicly known plants, if necessary.

For instance, it should be described not by a mere statement that the plant is high-yielding, but concrete numeric values commonly used in conventional yield surveys, such as total number of fruits produced per stock, total weight of fruits produced per stock, gross yield per are, etc., and they should be described in comparison with those of publicly known plants, if necessary.

Colors, such as leaf color, fruit color, and flower color should be expressed in accordance with official standards, such as the color atlas JIS Z8721 which is a specification of colours according to their three attributes, JIS Z8102 concerning color names and the R.H.S. color chart.

Where characteristic properties of the created plant cannot be expressed by a conventional cultivation method which a person skilled in the art usually conducts, or where characteristic properties of the created plant are expressed only in specific environments and under specific cultivation method though the method is conventional, such specific cultivation conditions should be specifically described.

② "Can be made"

As to an invention of a plant per se, a process for creating the plant should be described step by step including species of parent plant(s), a step of selecting the plant to be aimed at based on objective indicators or the like.

Where it is not possible to describe a process for creating the plant in the specification in such a manner that enables a person skilled in the art to create the plant, the created plant which is reproducible (seeds, cells, etc.) should be deposited with a depositary institution prior to filing and its accession number should be described in a specification as filed similarly to the deposit under Section 27bis of Regulations under the Patent Act. (For the details of the deposit and furnishing of plants, see "5.2 Deposit and Furnishing of Plants.")

③ "Can be used"

An invention of a plant per se must be described so that invention can be used by the person skilled in the art. Knowledge of how the invention can be used shall be described in the detailed description of the invention, except where it could be understood by the person skilled in the art without such description, when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(2) Invention of a Process for Manufacturing a Product

An invention of a process for creating a plant should be described as follows.

An invention of a process for creating a plant should be described in such a manner that enables a person skilled in the art to create the plant by the said process.

In order to describe the process in such a manner that a person skilled in the art can produce the said plant by the process, the enablement requirement described in "(1)Invention of a Product" should be referred to, if necessary. For example, in case that deposit of a plant is necessary, "5.2 Deposit and Furnishing of Plants" should be referred to.

Further, in an invention of a process for creating a plant, how the process or the plant created by the process can be used should be described in the detailed description of the invention, except where it could be understood by a person skilled in the art without such description when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(3) Invention of a Process

An invention of a process should be described as follows.

For an invention of a process, the definition of "being able to carry out the invention" is that the process can be used. Further, "the said invention of a process" should be explained clearly in the detailed description of the invention.

In order to describe for the person skilled in the art can use the process, the enablement requirement described in "(1)Invention of a Product" should be referred to, if necessary. For instance, "5.2 Deposit and furnishing of plants" should be referred to, if the deposit of plants are necessary.

As to "How Specifically Must the Detailed Description of the Invention Be Described?", "Balance of the Claim and the Detailed Description of the Invention," "Ministerial Ordinance Requirement" and "Prior Art and Advantageous Effects," see the relevant portions (1.1.2.1(4) and (5), 1.1.2.2 and 1.1.2.3) in "1. Genetic Engineering."

3.1.4 Drawings

When photographs are attached as drawings, black-and-white photographs should be used. Color photographs may be submitted as reference materials.

3.2 Requirements for Patentability

3.2.1 Invention Not Falling within "Industrially Applicable Invention"

The following inventions do not meet the requirement provided in the first sentence in Section 29(1) of the Patent Act.

(1) Mere discovery which is not a creation

Example: A newly discovered plant per se.

(2) Inventions incapable of industrial application

Inventions whose utility is not described or cannot be inferred.

3.2.2 Inventive Step

(1) An invention of a plant per se does not have an inventive step, where characteristics of the plant created can be easily predicted from the characteristics of publicly known plants within the species to which the plant belongs and where the invention does not have advantageous effects that a person skilled in the art cannot foresee.

Example 1:

A plant whose shape or color is similar to that of publicly known plants within the species to which the plant belongs.

Example 2:

Mere combination of the characteristics of publicly known plants within the species to which the plant belongs.

(Plants obtained by mere crossing: for instance, suppose that it is publicly known that *Pisum sativum* A (pea A) has a single-locus-controlling characteristics that the legume is yellow when premature and *Pisum sativum* B has a single-locus-controlling characteristics that it bears blossoms at each knot through the full length. In such a case, a new *Pisum sativum*, obtained by merely crossing *Pisum sativum* A and *Pisum sativum* B and fixing their characteristics, having characteristics that the legume is yellow when premature and it bears blossoms at each knot, does not have an inventive step.)

(2) An invention of a process for creating a plant does not have an inventive step, where the selection of parent plants, means, conditions or the like is not considered to be difficult and where the created plant does not have advantageous effects that a person skilled in the art cannot foresee.

3.3 Amendment of Description, Claims or Drawings

Amendment of the description, claims or drawings relating to the deposit of plants is handled as described in "2.3 Amendment of Description, Claims or Drawings" above.

4. Animals

This section deals with inventions of animals per se, those relating to parts of animals, those of a process for creating animals, those relating to use of animals, etc. The term "animals" means the animals (excluding humans) under the classification where organisms are classified into three groups, namely microorganisms, plants and animals.

As to undifferentiated animal cells as well as animal tissue cultures, which are treated as microorganisms, reference should be made to relevant parts in "2. Microorganisms."

Matters relating to genetic engineering are referred to "1. Genetic Engineering" even if they are inventions relating to animals.

4.1 Description Requirements of the Specification

4.1.1 Designation of Animals

In principle, animals should be specified by scientific names in accordance with the zoological nomenclature or standard Japanese names.

4.1.2 Scope of Claim

As to an invention relating to an animal, a claim should be described as follows.

In the case of an invention of an animal per se, the animal should be specified by, for example, a combination of any of the species, the distinctive gene of the animal, characteristics of the animal, etc. and may be further specified by the process for creating the animals.

Example:

A mouse having DSM Accession No.xxxxx characterized by the occurrence of degeneration and swelling of anterior lens cortical fibers at 8 weeks of age, appearance of opacity of the lens at 5 or 6 months of age and rapid completion of cataract immediately after that, or its mutant having the said characteristics.

As to an invention of a process for creating an animal, the process for creating the animal should be described in the claim step by step. In the case where selection is performed as one step of creation based on characteristics or the like, the characteristics or the like necessary for the selection should be additionally described. Where conditions such as environment are necessary for creating the animal, such conditions should be described.

4.1.3 Detailed Description of the Invention

(See 1.1.2 above)

4.1.3.1 Enablement Requirement

(See 1.1.2.1 above)

(1) Invention of a Product

An invention of an animal per se should be described as follows.

① An animal being explained clearly

In order to explain an animal clearly, for example, (i) matters regarding species of the animal created and (ii) matters relating to characteristic properties of the created animal should be described.

(i) Species of the animal created

In principle, the created animal should be specified by the scientific name in accordance with the zoological nomenclature or standard Japanese name.

(ii) Characteristic properties of the animal created

In the case that properties of the created animal are characteristic, they should be described specifically stating by numeric values actually obtained by measuring or the like and it is desirable that they are described in comparison with those of publicly known animals, if necessary.

Where characteristic properties of the created animal cannot be expressed by a conventional breeding method which a person skilled in the art usually conducts and they are expressed only in specific environments or only under specific breeding method, such specific conditions should be specifically described.

② "Can be made"

As to an invention of an animal per se, the process for creating the animal should be described step by step including species of parent animal(s), a step of selecting an animal to be aimed at based on objective indicators or the like.

Where it is not possible to describe the process for creating the animal in the specification in such a manner that enables a person skilled in the art to create the animal, the created animal which is reproducible (fertilized ovum, etc.) should be deposited with a depositary institution prior to filing and its accession number should be described in a specification as filed similarly to the deposit under Section 27bis of Regulations under the Patent Act. For the details of the deposit and furnishing of animals, see "5.3 Deposit and Furnishing of Animals."

③ "Can be used"

An invention of an animal per se must be described so that invention can be used by the person skilled in the art. Knowledge of how the invention can be used shall be described in the detailed description of the invention, except where it could be understood by the person skilled in the art without such description, when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(2) Invention of a Process for Manufacturing a Product

An invention of a process for creating an animal should be described as follows.

An invention of a process for creating an animal should be described in such a manner that enables a person skilled in the art to create the animal by the said process.

In order to describe the process in such a manner that a person skilled in the art can produce the said animal by the process, the enablement requirement described in "(1) Invention of a Product" should be referred to, if necessary. For example, in case that deposit of an animal is necessary, see "5.3 Deposit and Furnishing of Animals."

Further, in an invention of a process for creating an animal, how the process or the animal created by the process can be used should be described in the detailed description of the invention, except where it could be understood by a person skilled in the art without such description when taking into account the overall descriptions of the specification (excluding claims), drawings and common general knowledge as of the filing.

(3) Invention of a process

An invention of a process should be described as follows.

For an invention of a process, the definition of "being able to carry out the invention" is that the process can be used. Further, "the said invention of a process" should be explained clearly in the detailed description of the invention.

In order to describe for the person skilled in the art can use the process, the enablement requirement described in "(1)Invention of a Product" should be referred to, if necessary. For instance, "5.3 Deposit and furnishing of Animals" should be referred to, if the deposit of animals is necessary.

As to "How Specifically Must the Detailed Description of the Invention Be Described?", "Balance of the Claim and the Detailed Description of the Invention," "Ministerial Ordinance Requirement" and "Prior Art and Advantageous Effects," see the relevant portions (1.1.2.1(4) and (5), 1.1.2.2 and 1.1.2.3) in "1. Genetic Engineering."

4.1.4 Drawings

When photographs are attached as drawings, black-and-white photographs should be used. Color photographs may be submitted as reference materials.

4.2 Requirements for Patentability

4.2.1 Invention Not Falling under "Industrially Applicable Invention"

The following inventions do not meet the requirement provided in the first sentence in Section 29(1) of the Patent Act.

(1) Mere discovery which is not a creation

Example: A newly discovered animal per se.

(2) Inventions incapable of industrial application

Inventions whose utility is not described or cannot be inferred.

4.2.2 Invention Contravening Public Order, Morality or Public Health

When working of an invention inevitably contravenes public order, morality or public health, the invention falls under the invention as provided in Section 32 of the Patent Act.

4.2.3 Inventive Step

(1) An invention of an animal per se does not have an inventive step, where characteristics of the animal created can be easily predicted from the characteristics of publicly known animals within the species to which the animal belongs and where the invention does not have advantageous effects that a person skilled in the art cannot foresee.

(2) An invention of a process for creating an animal does not have an inventive step, where the selection of parent animal(s), means, conditions or the like is not considered to be difficult and where the created animal does not have advantageous effects that a person skilled in the art cannot foresee.

4.3 Amendment of Description, Claims or Drawings

Amendment of the description, claims or drawings relating to the deposit of animals is handled as described in "2.3 Amendment of Specification" above.

5. Deposit

This section deals with inventions related to microorganisms, plants, and animals which need to be deposited.

5.1 Deposit and Furnishing of Microorganisms

When describing inventions involving a microorganism itself or a use for a novel microorganism, and when it is impossible to describe how to originate the microorganism so that the person skilled in the art can produce the microorganism, the microorganism must be deposited according to Section 27bis of Regulations under the Patent Act. (For specific information, see below. Also see "(Reference) With Regard to the Change of Practices Related to the Expansion of Scope of Deposit by the Patent and Bio-Resource Center ")

Section 27bis of Regulations under the Patent Act (Deposition of microorganisms)

1 A person desiring to file a patent application for an invention involving or using a microorganism shall attach to the request a copy of the latest receipt referred to in Rule 7 of the Regulations under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (hereinafter referred to as "Treaty") for the deposit of the microorganism issued by the International Depositary Authority defined in Article 2(viii) of the Treaty, or a document certifying the fact that the microorganism has been deposited with an institution designated by the Commissioner of the Patent Office (hereinafter referred to as "designation by the institution") or with an institution received a designation or another certification which is equivalent to a "designation by the institution" by a country that is not a party to Treaty (the country is limited one which allows Japanese nationals to perform a procedure of the deposit of a microorganism for the purposes of patent procedure under the same conditions as in Japan and that is designated by the Commissioner of the Patent Office) , except where the microorganism is readily available to a person skilled in the art to which the invention pertains.

2 Where an accession number is newly given after the filing of a patent application to the deposit of a microorganism under the preceding paragraph, the applicant for a patent or the patentee shall notify the Commissioner of the Patent Office without delay.

3 The notification under the preceding paragraph shall be made in accordance with Form 32 with respect to a patent application, or Form 33 with respect to an International Patent Application.

Section 27ter of Regulations under the Patent Act (Furnishing of microbiological samples)

1 A person who intends to work for the purpose of tests or experiments an invention involving or using a microorganism deposited in accordance with the preceding section may be furnished with a sample of the microorganism provided that:

(i) registration for the establishment of a patent right to the invention involving or using the microorganism has been made;

(ii) the person received a warning given in the form of a document describing the contents of the invention involving or using the microorganism in accordance with Section 65(1) of the Patent Act; or

(iii) such is necessary in order to prepare a written argument referred to in Section 50 of the Patent Act (including its application under Section 159(2) (including its application under Section 174(2)) and Section 163(2)).

2 A person who has been furnished with a sample of the microorganism in accordance with the preceding paragraph shall not permit a third party to utilize the sample of the microorganism.

(i) Deposit and Furnishing

A person desiring to file a patent application for an invention involving or using a microorganism (hereinafter "an applicant"), shall deposit the microorganism with a depositary institution designated by the Commissioner of the Patent Office (hereinafter referred to as "designation by the institution"), an institution received a designation or another certification which is equivalent to a "designation by the institution" by a country that is not a party to Treaty (the country is limited one which allows Japanese nationals to perform a procedure of the deposit of a microorganism for the purposes of patent procedure under the same conditions as in Japan and that is designated by the Commissioner of the Patent Office) or International Depositary Authorities (hereinafter, these are referred to as "depositary institution for the purposes of patent procedure"), unless a person skilled in the art can easily obtain the microorganism, shall state the accession number in the specification as filed, and shall attach a document certifying the fact that the microorganism has been deposited (hereinafter referred to as a "copy of the Receipt of an Original Deposit") to the patent appliction.

The depositary institution for the purposes of patent procedure issues a receipt of a reception immediately after receiving the application of patent depositary, and then it issues a Receipt of an Original Deposit after testing the microorganism and finding them to be viable. As a receipt of a reception is not a document certifying the fact that the microorganism has been deposited, provided in Section 27bis of Regulations under the Patent Act, a receipt of a reception shall not be attached to the patent application.

An applicant may file a patent application stating a reference number which is written in a receipt of a reception, in the specification as filed. In this case, an applicant shall submit a copy of the Receipt of an Original Deposit immediately after being issued the Receipt of an Original Deposit.

When a copy of the Receipt of an Original Deposit is issued, the date of the original deposit shall be the date on which the microorganism was received by the depositary institution for the purposes of patent procedure.

The application is not treated as having been deposited from the received date, in case that the depositary institution for the purposes of patent procedure couldn't find the microorganism to be viable, and did not issue the Receipt of an Original Deposit.

When a new accession number is given to the microorganism after filing, for the reason that, e.g., re-deposit was made, samples of the microorganism were transferred to another International Depositary Authority or the deposit was converted from the deposit under the national act to that under the Budapest Treaty, the applicant or the patentee shall give a notice to that effect to the

Commissioner of the Patent Office without delay.

Where a microorganism which was deposited with a depositary institution designated by the Commissioner of the Patent Office and was confirmed to be viable is found to be no longer viable, the depositor, upon receipt of the "Notice that the microorganism cannot be furnished" (Official Gazette of MITI No.178 Section 15) from the depositary institution, should deposit immediately the same microorganism as that originally deposited. Where the microorganism is related to a patent application or a patent, the applicant or the patentee should give a notice to that effect to the Commissioner of the Patent Office without delay. In such a case, the newly deposited microorganism is treated as having been deposited without intermission since the original deposit was made.

The deposited microorganism can be furnished simultaneously with the registration for establishment of a patent right. Even prior to the registration for establishment of a patent right, though, in the case where Section 27ter (1)(ii) or (iii) of Regulations under the Patent Act is applied, the microorganism can be furnished.

The deposit of a microorganism should be maintained at least during the term of the patent for the invention related to the microorganism so that the microorganism can be furnished.

For reference, a list of International Depositary Authorities and kinds of microorganisms accepted by the IDAs is shown in [Appendix 2]. *(Omitted in this English translation version)*

(ii) Microorganisms Excluded from Obligation to be Deposited

(a) Microorganisms which cannot be stored or maintained by the depositary institution for the purpose of patent procedure for technical reasons or the like

In such a case, however, furnishing of the microorganisms provided in Section 27ter of Regulations under the Patent Act should be guaranteed by the applicant. (Such microorganisms should be preferably deposited with a reliable culture collection.)

(b) Microorganisms readily available to the persons skilled in the art stated in "Section 27bis of Regulations under the Patent Act"

More specifically, the following microorganisms are included for example:

(b-1) Commercially available microorganisms, such as baker's yeast, koji (*Aspergillus oryzae*), *Bacillus natto*, etc.

(b-2) A stored microorganism in the case where it has been confirmed, prior to filing, that the microorganism has been stored at a reliable culture collection and is freely accessible from a catalog or the like issued by the said culture collection

In this case, the storage number of the microorganism should be described in the specification as filed.

(b-3) Microorganisms which can be created by a person skilled in the art on the basis of the description in the specification

(iii) Applications Claiming Priority Rights

Where a claimed invention in an application claiming priority relates to a microorganism which is

not readily available to a person skilled in the art, the application can enjoy advantages of the priority provided that the microorganism has been deposited with a depositary institution for the purpose of patent procedure or a reliable public culture collection, and that the accession number or storage number of the microorganism is stated in the specification contained in the first application being the basis for priority rights, or in the specification contained in the earlier application being the basis for internal priority rights.

(iv) Omission of submission of a "copy of the Receipt of an Original Deposit"

In cases when there are two or more applications concerning the same copy of the Receipt of an Original Deposit are made at the same time, or when making applications concerning a copy of the Receipt of an Original Deposit that has been already submitted, the applicant may omit the submission of the document by stating either of the two reasons above, according to Section 10 (1) and (2) of Regulations under the Patent Act.

For example, in cases like the ones below, the applicant may omit submission of a copy of the Receipt of an Original Deposit:

(1) When dividing an application
(2) When making an application claiming internal priority rights
(3) When the same applicant is making a second application and the submission of the same copy of the Receipt of an Original Deposit is necessary.
(4) When the applicant is making two or more applications and the submission of the same copy of the Receipt of an Original Deposit is necessary.
(5) When the applicant is submitting a notice for the change of accession number

Section 10 (1) of Regulations under the Patent Act (Omission of submission of documents)

When two or more procedures (Utility Model Act (Act No.123 of 1959), Design Act (Act No.125 of 1959), Trademark Act (Act No.127 of 1959), Act Concerning the Special Provisions to the Procedure, etc. Relating to an Industrial Property Right (Act No.30 of 1990; hereinafter referred to as the "Special Provisions Act") or procedures prescribed in orders in accordance to the aforesaid Acts) are taken at the same time, and when the contents of certifying documents necessary to be submitted under Sections 4ter through 7, 8(1), 9(4) [Submission of Certifying Documents], or 27bis(1) [Deposition of microorganisms] are the same, it is possible to submit the document in one procedure, and by stating this fact, omit submission of the document in other procedures.

Section 10 (2) of Regulations under the Patent Act (Omission of submission of documents)

When an applicant has already submitted a certifying document concerned in a previous case, and when there is no change in the matters certified by the document, the applicant may state these facts and omit submission of the certifying documents stated in Section

4ter through 7, 8(1), 9(4), the above Paragarph [Submission of Certifying Documents], or 27bis (1) [Deposition of microorganisms] in the procedure concerned.

5.2 Deposit and Furnishing of Plants

When describing inventions involving a plant itself, a part of a plant, a method of producing a plant, or a use for a novel plant, and when it is impossible to describe how to originate the plant so that the person skilled in the art can produce the plant, the plant must be deposited according to Section 27bis of Regulations under the Patent Act. (For specific information, see "5.1 Deposit and Furnishing of Microorganisms")

(a) Even when the specification describes the step-by-step process of producing a plant, in cases where the person skilled in the art cannot work the invention due to difficulties in obtaining the parent plant, the applicant must deposit the parent plant (its seeds, cells, etc.) prior to the application, and state the accession number in the original specification, according to Section 27bis of Regulations under the Patent Act.

(b) In cases when it is impossible to describe the process of producing a plant so that the person skilled in the art can produce the plant, the applicant must deposit the plant produced in a reproducible state (its seeds, cells, etc.), and state the accession number in the original specification, according to Section 27bis of Regulations under the Patent Act.

However, in cases when it is not possible to deposit the plant, due to technical reasons of the institution designated by the Commissioner of the Patent Office, the applicant shall guarantee the furnishing of the plant, in proportion with Section 27ter of Regulations under the Patent Act. (It is desirable to take measures such as storing the plant at a reliable public culture collection.)

5.3 Deposit and Furnishing of Animals

When describing inventions involving an animal itself, a part of an animal, a method of producing an animal, or a use for a novel animal, and when it is impossible to describe how to originate the animal so that the person skilled in the art can produce the animal, the animal must be deposited according to Section 27bis of Regulations under the Patent Act. (For specific information, see "5.1 Deposit and Furnishing of Microorganisms")

(a) Even when the specification describes the step-by-step process of producing an animal, in cases where the person skilled in the art cannot work the invention due to difficulties in obtaining the parent animal, the applicant must deposit the parent animal (its embryos, etc.) prior to the application, and state the accession number in the original specification, according to Section 27bis of Regulations under the Patent Act.

(b) In cases when it is impossible to describe the process of producing an animal so that the person

skilled in the art can produce the animal, the applicant must deposit the animal produced in a reproducible state (its embryos, etc.), and state the accession number in the original specification, according to Section 27bis of Regulations under the Patent Act.

However, in cases when it is not possible to deposit the animal, due to technical reasons of the institution designated by the Commissioner of the Patent Office, the applicant shall guarantee the furnishing of the animal, in proportion with Section 27ter of Regulations under the Patent Act. (It is desirable to take measures such as storing the animal at a reliable public culture collection.)

6. Examples of Inventions Relating to Genes

[Note]

The requirement of the first sentence of Patent Act Section 29(1) is not considered within the examples below.

Within each case, the method of calculating "homology" of sequences is described in the specification, and said method is technically proper.

6.1 Unity of Invention

For examples of unity of invention, see examples of unity of invention relating to biotechnological inventions (Part 1 Chapter 2 Requirements of Unity of Invention). (to be prepared)

6.2 Cases Lacking Enablement

Case 1 Full-length cDNA

[Claim1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 5.

[Description of the invention]

The claimed polynucleotide is 3000bp cDNA obtained from human liver cDNA library. It encodes a polypeptide of amino acid sequence of SEQ ID NO:6. As a result of similarity search, no known sequences showed over 30% similarity to the nucleotide sequence of SEQ ID NO:5 or the amino acid sequence of SEQ ID NO:6. The amino acid sequence of SEQ ID NO:6 was proved to have a potential site of glycosylation.

Therefore, the claimed polynucleotide is assumed to be a structural gene encoding a new glycoprotein, whose specific function is unknown, and may be used for obtaining a new drug.

[Result of the prior-art search]

There is no known nucleotide sequence with over 30% similarity to that of SEQ ID NO:5. There is no known amino acid sequence with over 30% similarity to that of SEQ ID NO:6.

[Reason for refusal]

Even if the claimed polynucleotide encodes glycoprotein, the corresponding glycoprotein's specific function cannot be recognized because there are so many glycoproteins whose specific function differs from each other. The specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge. As the specific function of the claimed polynucleotide is not clear, it is not clear how to use the claimed polynucleotide.

Therefore, there is no disclosure concerning the use of the claimed polynucleotide, thus, the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

[Responses to the Notice of reason for refusal]

The above mentioned reason for refusal normally shall not be overcome.

(Supplementary Explanation)

The "specific function" stated here means a "function from which a specific application with technical meanings can be assumed."

Case 2 Full-length cDNA

[Claim1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:7.

[Description of the invention]

The claimed polynucleotide is 2400bp cDNA obtained from human liver cDNA library. It encodes a polypeptide of 800 amino acids of SEQ ID NO.8. As a result of similarity search using a known DNA and amino acid database, the claimed polynucleotide showed 20 to 30% homology to the polynucleotides encoding factor WW1 of mammalians such as rats. The polynucleotides are written in document A, document B, etc. And the amino acid sequence of SEQ ID NO.8 showed 20 to 30% homology to the amino acid sequences of factor WW1 of mammalians such as rats. The amino acid sequences are also written in document A, document B, etc.

Therefore, the claimed polynucleotide was assumed to encode human factor WW1 and to be useful.

[Result of the prior-art search]

There is no known sequence with over 40% similarity to the nucleotide sequence of SEQ ID NO:7 or the amino acid sequence of SEQ ID NO:8.

[Reason for refusal]

The given reason by the applicant that this polynucleotide encodes human factor WW1 is only based on the fact that the claimed polynucleotide has 20 to 30% homology to other mammalian polynucleotides encoding factor WW1 and that the amino acid sequence of SEQ ID NO:8 has 20 to 30% homology to amino acid sequences of factor WW1 of other mammalians.

In general, when two polynucleotides (polypeptides) show only 20-30% homology to each other,

they probably do not have any specific function in common. And there is no common general knowledge that the human polynucleotide, with only 20-30% homology to the polynucleotide of factor WW1, encodes human factor WW1. As the claimed polynucleotide probably does not encode human factor WW1, the specific function of the claimed nucleotide is not clear and no one can assume the specific function of the protein encoded by the nucleotide.

Therefore, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

[Responses to the Notice of reason for refusal]

If the claimed polynucleotide is proved as encoding human factor WW1 by written argument describing the activity of the protein actually expressed, or describing a logical explanation, the above mentioned reason for refusal may be overcome.

(Supplementary Explanation)

In cases where the above mentioned "logical explanation" is based on publicly known knowledge of the preserved regions within the factor WW1 gene, it would be easy, on the other hand, for the person skilled in the art to obtain a nucleotide encoding "factor WW1" by constructing a DNA primer probe based on the DNA sequence of the preserved regions, and using the primer probe in methods such as PCR. Under these circumstances, unless it is found that the polynucleotide has unexpected advantageous effects, claim 1 lacks inventive step.

The "specific function" stated here means a "function from which a specific application with technical meanings can be assumed."

The "specific function," i.e. the "function from which a specific application with technical meanings can be assumed" of factor WW1, is known.

Case 3 Full-length cDNA

[Claim1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:9.

[Description of the invention]

The claimed polynucleotide is 2400bp cDNA obtained from human liver cDNA library. It encodes a polypeptide of 800 amino acids of SEQ ID NO:10. As a result of similarity search using a known DNA and amino acid database, the claimed polynucleotide showed 20 to 30% homology to the polynucleotide encoding factor ZZ1 of rat, factor ZZ2 of pig and an antagonist of factor ZZ1 receptor of monkey. And the amino acid sequence of SEQ ID NO:10 showed 20 to 30% homology to factor ZZ1 of rat, factor ZZ2 of pig and an antagonist of factor ZZ1 receptor.

Therefore, this polynucleotide encodes a human protein related to factor ZZ and may be used to diagnose patients with disease related to factor ZZ.

[Result of the prior-art search]

There is no known sequence with over 40% similarity to the nucleotide sequence of SEQ ID NO:9 or the amino acid sequence of SEQ ID NO:10.

[Reason for refusal]

As factor ZZ1, factor ZZ2, and antagonist of factor ZZ1 receptor have a different specific function to each other, mere description that the claimed polynucleotide encodes protein relating to factor ZZ does not indicate any specific function of the claimed polynucleotide. And the specific function of the corresponding protein cannot be assumed considering the state of the art as of the filing.

Therefore we consider there is no disclosure concerning the use of this polypeptide, and thus the description of the invention is deemed as insufficient, for enabling a person skilled in the art to carry out the invention.

[Responses to the Notice of reasons for refusal]

Even if the claimed polynucleotide is proved as encoding human protein ZZ1 by written argument or certified experiment results, the reason for refusal above may not be overcome.

(Supplementary Explanation)

Even though the description states that polypeptide in this case "showed 20 to 30% homology to factor ZZ1 of rat, factor ZZ2 of pig and an antagonist of factor ZZ1 receptor", or that the nucleic acid "encodes a human protein related to factor ZZ", we cannot assume, taking into consideration common general knowledge as of the filing, that the nucleic acid encodes "human factor ZZ1."

The "specific function" stated here means a "function from which a specific application with technical meanings can be assumed."

Proteins related to factor ZZ, namely factors ZZ1 and ZZ2, and antagonist of factor ZZ1 receptor each are known to have different "specific functions," i.e. "functions from which a specific application with technical meanings can be assumed."

6.3 Case Lacking Inventive Step

Case 4 Full-length cDNA

[Claim 1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:11.

[Description of the invention]

The claimed polynucleotide is 2700bp cDNA obtained from human liver cDNA library. It encodes a polypeptide of 900 amino acids of SEQ ID NO:12. As a result of similarity search, the amino acid sequence of SEQ ID NO:12 showed 85% homology to rat factor XX1(written in document A) and

the polynucleotide sequence of SEQ ID NO:11 showed 80% homology to the polynucleotide encoding rat factor XX1(written in document A).

Therefore, this polynucleotide was assumed to encode human factor XX1 and to be useful.

[Result of the prior-art search]

There was no other sequence detected with over 80% similarity to that nucleotide sequence or polypeptide sequence except for rat polynucleotide encoding rat factor XX1 or the amino acid sequence of rat factor XX1. It is a well-known fact that mammalians including human have factor XX1.

[Reason for refusal]

It is a well-known object to prepare human DNAs encoding proteins. It is also common general knowledge to isolate the human DNA encoding a certain protein by using a partial nucleotide sequence of a mammal other than human encoding the same protein as a primer probe. Since polynucleotide encoding proteins with the same biological activities are in general highly homologous between mammalian species.

Therefore, it is obvious that the DNA encoding human factor XX1 can be isolated from human cDNA library using the partial polynucleotide encoding rat factor XX1 written in document A as a primer. And any advantageous effect cannot be acknowledged from document A or common general knowledge, hence this invention cannot be regarded as involving an inventive step.

[Responses to the Notice of reason for refusal]

The reason for refusal above may be overcome if the applicant proves in written arguments that there was specific difficulty to obtain the claimed polynucleotide, considering the state of the art as of the filing.

(Supplement)

The "specific function," i.e., the "function from which a specific application with technical meanings can be assumed" for factor XX1, is known.

6.4 Cases Lacking Both Inventive Step and Enablement

Case 5 DNA fragment

[Claim 1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:13.

[Description of the invention]

A cDNA library was constructed from human liver using oligo (dT) primers. The nucleotide sequence of SEQ ID NO:13 is one of the sequences (500 bp) which were analyzed using an automated DNA sequencer. The polynucleotide consisting of the nucleotide sequence of SEQ ID NO:13 is part of a structural gene, and it can be used as a probe in one of the steps to obtain the

full-length DNA.

However, there is no working example indicating that the full-length DNA was actually obtained, and there is no description of the function or biological activity of the DNA and its corresponding protein.

[Result of the prior-art search]

There is no known sequence with over 30% similarity to the nucleotide sequence of SEQ ID NO:13 or the amino acid sequence of SEQ ID NO:14.

[Reason for refusal]

1. Inventive Step: No

It is a well-known object to obtain cDNAs from human cells and sequence them. It is also a well-known art to construct cDNA libraries from human organs, such as the liver, and to analyze the sequence of cDNA randomly chosen from the library with the use of an automated sequencer.

Therefore, for a person skilled in the art, it would have been easy to prepare cDNA library and to sequence cDNAs derived from the library using conventional methods. And the obtained DNA does not have an unexpected advantageous effect.

Hence, this invention cannot be regarded as involving an inventive step.

2. Enablement Requirement: No

An invention of a product should be described in a way enabling for a person skilled in the art to make and to use the product.

There is a description that the claimed DNA can be used as a probe in one of the steps to obtain a full-length DNA. However, there is no description on function or biological activity of the protein encoded by the corresponding full-length DNA. Moreover, function or biological activity of the full-length DNA cannot be assumed with common general knowledge as of the filing. The use of a DNA fragment in obtaining the full-length DNA, whose corresponding protein's function and biological activity are unknown, is not considered to be a "use" as stated above. We consider that the description of the invention is insufficient for enabling a person skilled in the art to carry out the invention.

[Responses to the Notice of reason for refusal]

Reason 2 above normally shall not be overcome.

Case 6 SNPs

[Claim1]

A polynucleotide of between 20 and 100 bases including position 100 (polymorphic site) of the nucleotide sequence of SEQ ID NO:14 or SEQ ID NO:15.

[Description of the invention]

The polynucleotide of the locus of the human genome DNAs derived from 10 persons was compared to each other. Six of 10 polynucleotide were SEQ ID NO:14 and four of 10 were SEQ ID NO:15. The nucleotide at position 100 of SEQ ID NO:14 is g. On the other hand, that of SEQ ID NO:15 is c. These two nucleotide sequences are the same except for the nucleotide at position 100. The claimed polynucleotide can be used as a forensic marker.

[Result of the prior-art search]

The nucleotide sequence of SEQ ID NO:14 and NO:15 are unknown. The claimed polyuncleotide is also unknown.

[Reason for refusal]

1. Inventive step: No

It is a well-known object to detect polymorphic site in human genome DNA. It is a well-known art to analyze and compare the sequences of genome DNAs of many persons, to detect a polymorphic site.

Therefore, for a person skilled in the art, it would have been easy to analyze and compare the sequences of a certain part of genome DNAs of several persons and to detect the polymorphic site.

And any unexpected advantageous effect cannot be acknowledged, hence this invention cannot be regarded as involving an inventive step.

2. Enablement requirement: No

An invention of a product should be described in a way enabling for a person skilled in the art to make and to use the product

Though, there is a description that the claimed nucleotide can be used as a forensic marker, only one SNP itself is not usually utilized as a forensic marker. Therefore, the mere description that the polynucleotide can be used as a forensic marker does not indicate any use of the claimed polynucleotide.

[Responses to the Notice of reason for refusal]

Reason 2 above normally shall not be overcome.

6.5 Cases Where Inventive Step is Involved and Enablement Requirement is Satisfied

Case 7 DNA fragment

[Claim 1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:16.

[Description of the invention]

The polynucleotide is one of the 500bp cDNAs which were found in a cDNA library derived from the hepatocyte of patients with disease Y, but not found in those of normal persons. It was confirmed by northern hybridization that the corresponding mRNAs were expressed only in the patients' hepatocyte. Therefore, the polynucleotide can be used to diagnose disease Y.

[Result of the prior-art search]

There is no known DNA and polypeptide which are unique in the patients with disease Y. There is no known sequence with over 30% similarity to the nucleotide sequence of SEQ ID NO:16.

[Reason for refusal]

No reason for refusal

(Supplemental Explanations)

1. The polynucleotide in claim 1 has the unexpected advantageous effect that it can be used to diagnose disease Y.
2. There also may be cases in which claim 1 is "A polynucleotide comprising the nucleotide sequence of SEQ ID NO:16." In this case, the claim contains any polynucleotide which contains the DNA sequence of SEQ ID NO:16. We can logically assume that there should be some polynucleotides unsuitable for the diagnosis of disease Y, among polynucleotides belonging to claim 1, but contain a very long sequence that has nothing in common with the claimed sequence. Therefore, a notice of reason for refusal will be made to the effect that claim 1 in part is not workable. (This notice, however, does not mean that all polynucleotides which have polynucleotides attached to the sequence of SEQ ID NO:16 cannot be used as a diagnostic probe.)

Case 8 Full-length cDNA

[Claim1]

A polynucleotide consisting of the nucleotide sequence of SEQ ID NO:17.

[Description of the invention]

The claimed polynucleotide is 2700bp cDNA obtained from human liver cDNA library. It encodes a polypeptide of 900 amino acids of SEQ ID NO:18. This polypeptide was expressed and it showed the activity of human factor YY1.

[Result of the prior-art search]

There is no known sequence with over 80% similarity to the nucleotide sequence of SEQ ID NO:17 or the amino acid sequence of SEQ ID NO:18. And no prior art was found about the human factor YY1.

[Reason for refusal]

No reason for refusal

(Supplementary Explanation)

The "specific function", i.e., the "function from which a specific application with technical meanings can be assumed" of the factor YY1 is known.

Case 9 SNP

[Claim1]

A polynucleotide of between 20 and 100 bases including position 50("g") (polymorphic site) of the nucleotide sequence of SEQ ID NO:19.

[Description of the invention]

A polynucleotide identical to SEQ ID NO:19 (500bp length DNA), except that the nucleotide "g" in position 50 of SEQ ID NO:19 is "c", is known. Position 50 of the polynucleotide of SEQ ID NO:19 is proved to be a polymorphic site, and a polynucleotide of between 20 and 100 bases including position 50 (g) of the nucleotide sequence of SEQ ID NO:19 is experimentally proved to be suitable to diagnose disease Z.

[Result of the prior-art search]

The polynucleotide sequence of SEQ ID NO:19 was not known. The claimed polynucleotide was neither known. Relationship between the polymorphic site at position 50 and disease Z was neither known as well. Though the polynucleotide of with "c" in position 50 is known to be a part of structural gene, the relationship between the protein encoded by the structural gene and disease Z was not known.

[Reason for refusal]

No reason for refusal

(Supplemental Explanation)

The polynucleotide in claim 1 has the advantageous effect that it can be used to diagnose disease Z.

7. Examples of Inventions Relating to Protein Conformtion

(to be prepared)

8. Examples Relating to Judgment of Necessity for Deposit of Microorganisms, etc.

This section explains about the judgment on whether microorganisms, etc. ("microorganisms, etc." here include microorganisms, plants and animals) are necessary to be deposited or not prior to filing of the application, based on specific cases.

For information on general matters relating to the judgment of necessity for Deposit, see "5. Deposit".

The present Examples include the following Cases.

8.1 Inventions Relating to Bacteria

Case 1-1 A case where the bacteria are readily available to a person skilled in the art (No need to deposit)

Case 1-2 A case where the bacteria are not readily available to a person skilled in the art (Need to deposit)

Case 1-3 A case of the invention relating to a DNA derived from bacteria (No need to deposit)

8.2 Inventions Relating to Antibodies

Case 2-1 A case where the hybridoma can be prepared by a person skilled in the art on the basis of the description in the specification (No need to deposit)

Case 2-2 A case where the hybridoma can be prepared by a person skilled in the art on the basis of the description in the specification (No need to deposit)

Case 2-3 A case where the hybridoma is not readily available to a person skilled in the art (Need to deposit)

8.3 Inventions Relating to Cells

Case 3-1 A case where the cells can be produced by a person skilled in the art on the basis of the description in the specification (No need to deposit)

Case 3-2 A case where the cells are not readily available to a person skilled in the art (Need to deposit)

8.4 Inventions Relating to Animals

Case 4-1 A case where the animal can be produced by a person skilled in the art on the basis of the description in the specification (No need to deposit)

Case 4-2 A case where the animal is not readily available to a person skilled in the art (Need to deposit)

(Points of concern)

In the present Examples, each case shall not mean that there are no other reasons for refusal such as lack of novelty/inventive step.

8.1 Inventions Relating to Bacteria

Case 1-1 A case where the bacteria are readily available to a person skilled in the art (No need to deposit)

[Claims]

1. A β-galactosidase derived from a Streptomyces lividans strain xyz-1; ATCC ******, having the following physicochemical properties:

(a) function and substrate specificity: to hydrolyze a substrate having β-D-galactoside bond and to release a D-galactoside group;

(b) optimum pH: 4.5;

(c) stable pH: 3.0 to 5.5;

(d) optimum temperature: 55°C;

(e) stable temperature: 50°C; and

(f) molecular weight: 200 kD as measured by gel filtration chromatography.

[Outline of Description of the invention]

Since neutral or acidic material such as milk, cheese whey, lactose solution and the like is the subject of processing by a β-galactosidase, the β-galactosidase with sufficient enzyme activity in an acidic condition is required. But a microorganism that produces the β-galactosidase with sufficient enzyme activity in an acidic condition was not known at the filing.

The inventors isolated the β-galactosidase described in claim 1 from a *Streptomyces lividans* strain xyz-1 with a specific technique. Further, the *Streptomyces lividans* strain xyz-1 is listed in a catalog issued by ATCC with the storage number ATCC ******, and freely accessible prior to the filing.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In the present case, based on the Description of the invention, it was confirmed prior to the filing that the *Streptomyces lividans* strain xyz-1 was a microorganism stored in ATCC that is a reliable culture collection and freely accessible from the catalog issued by ATCC. Further, the storage ATCC number of xyz-1 was also described in the Description of the invention.

Therefore, the *Streptomyces lividans* strain xyz-1 is readily available to a person skilled in the art, and any person skilled in the art can isolate the β-galactosidase described in claim 1 with the specific technique described in the specification.

Accordingly, the *Streptomyces lividans* strain xyz-1 is not required to be deposited.

Case 1-2 A case where the bacteria are not readily available to a person skilled in the art (Need to deposit)

[Claims]
1. A Bacillus subtilis strain T-169 capable of decomposing dioxin.

[Outline of Description of the invention]

A *Bacillus subtilis* strain T-169 was isolated from the sample, which was collected from muddy sediment of seabed of Toyama Bay in Japan, with a method known to a person skilled in the art. The taxonomic characteristic of T-169 was analyzed in detail, and the difference between T-169 and any other strains in the same species was examined. The *Bacillus subtilis* strain T-169 proved to be a new strain, and with further experiments, it was verified that T-169 has an ability to decompose dioxin with high efficiency.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In general, variety and quantity of microorganisms inhabiting soil, seawater or the like are not always stable even though the soil and seawater were obtained from a certain area.

Therefore, even when a novel microorganism is isolated from a sample of the soil, seawater or the like from a certain area, it is difficult to obtain the same novel microorganism reproducibly in the absence of a reasonable ground that the novel microorganism is present in the sample collected again from the soil, seawater or the like.

In the present case, there is no description about the reasonable ground that the *Bacillus subtilis* strain T-169 is present in the sample collected again from muddy sediment of seabed of Toyama Bay in the Description of the invention.

Consequently, the *Bacillus subtilis* strain T-169 is not reproducible in confirmatory studies conducted by a person skilled in the art. Therefore, the *Bacillus subtilis* strain T-169 is not a microorganism that can be prepared by a person skilled in the art on the basis of the description in the specification.

Accordingly, the *Bacillus subtilis* strain T-169 is required to be deposited, since the *Bacillus subtilis* strain T-169 is not a microorganism readily available to a person skilled in the art.

Case 1-3 A case of the invention relating to DNA derived from bacteria (No need to deposit)

[Claims]

1. A DNA comprising the nucleic acid sequence represented by SEQ ID NO: 1, encoding an argininosuccinate synthase derived from a coryneform bacterium strain K-336.
2. An expression vector containing the DNA described in claim 1.
3. A transformant, retaining the vector described in claim 2 in a state that the vector is capable of expression.

[Outline of Description of the invention]

A coryneform bacterium strain K-336 producing L-arginine was isolated from soil based on the drug tolerance. Its taxonomic characteristic was analyzed in detail, and the difference between K-336 and the similar species was examined. The coryneform bacterium strain K-336 proved to be a new species.

It had been known at the filing that ArgA to ArgH genes are involved in an L-arginine biosynthetic pathway of the coryneform bacterium. The inventors for the first time identified an ArgG gene comprising the nucleic acid sequence represented by SEQ ID NO: 1 from the coryneform bacterium strain K-336, made to express the ArgG gene with a known genetic technology, and verified that the protein encoded by the ArgG gene is an argininosuccinate synthase.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In the present case, the invention described in claim 1 is not a coryneform bacterium strain K-336 but a DNA. Further, since the nucleic acid sequence of the DNA is specifically described in the specification, the DNA can be obtained based on the nucleic acid sequence by a person skilled in the art through an artificial synthesis method and the like. In addition, a person skilled in the art can incorporate the DNA into a suitable expression vector and prepare a transformant retaining the expression vector in a state capable of expressing.

Accordingly, the coryneform bacterium strain K-336 is not required to be deposited.

8.2 Inventions Relating to Antibodies

Case 2-1 A case where the hybridoma can be prepared by a person skilled in the art on the basis of the description in the specification (No need to deposit)

[Claims]
1. An antigenic protein A consisting of the amino acid sequence represented by SEQ ID NO: 1.
2. A monoclonal antibody against the antigenic protein A described in claim 1.
3. A hybridoma producing the monoclonal antibody described in claim 2.

[Outline of Description of the invention]

A novel antigenic protein A was isolated and purified from the outer membrane of virus X. Since the antigenic protein A was found to react only with a serum derived from a person infected with virus X, the antigenic protein A is useful for identifying a person infected with virus X.

Further, a partial amino acid sequence of the antigenic protein A was determined, and a gene encoding the antigenic protein A consisting of the amino acid sequence represented by SEQ ID NO: 1 was cloned by a known genetic engineering technique based on the partial amino acid sequence.

[Note]

There is no example in the specification that a monoclonal antibody specifically reacting with the antigenic protein A was prepared.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In the present case, the monoclonal antibody described in claim 2 is a monoclonal antibody specified only by an antigen.

Generally, there is common general knowledge that, when a protein having immunogenicity is obtained, a monoclonal antibody binding to the protein can be obtained by using the protein as an immunogen based on a known hybridoma method.

Further, a person skilled in the art can prepare an antigenic protein A consisting of the amino acid sequence represented by SEQ ID NO: 1 by means of obtaining a gene encoding the antigenic protein A and expressing the gene using a known genetic technology, on the basis of the description in the specification. In addition, it is obvious that the antigenic protein A has immunogenicity.

Consequently, a person skilled in the art can obtain the monoclonal antibody described in claim 2 and a hybridoma producing the monoclonal antibody by the means of preparing the antigenic protein A and using the antigenic protein A as an immunogen by a known hybridoma method, on the basis of the description in the specification.

Therefore, the hybridoma described in claim 3 is a microorganism that can be prepared by a person skilled in the art on the basis of the description in the specification.

Accordingly, the hybridoma described in claim 3 is not required to be deposited, since the hybridoma described in claim 3 is a microorganism readily available to a person skilled in the art.

Case 2-2 A case where the hybridoma can be prepared by a person skilled in the art on the basis of the description in the specification (No need to deposit)

[Claims]

1. A monoclonal antibody of IgM isotype, reacting with a surface antigen P of a virus Y with an association constant of $10^{10}M^{-1}$ or more.

2. A hybridoma producing the monoclonal antibody described in claim 1.

[Outline of Description of the invention]

The surface antigen P of a virus Y was already isolated and purified, and the antibody detecting the surface antigen P was publicly known at the filing. However, the monoclonal antibody of IgM isotype had not been considered suitable for detection of the surface antigen P due to its properties of easy aggregation and the other. The inventors obtained for the first time a monoclonal antibody of IgM isotype capable of detecting the surface antigen P of a virus Y with high sensitivity.

The inventors selected a specific partial amino acid sequence from an amino acid sequence encoding the surface antigen P, and prepared a polypeptide consisting of the specific partial amino acid sequence, and confirmed that the polypeptide functions as an immunogen. Further, using the polypeptide as an immunogen, they prepared a hybridoma producing the monoclonal antibody based on a known hybridoma method. As a result, there were obtained 149 lines of the hybridoma in which the antibody production was confirmed. From these, 10 lines were selected, an association constant of the antibody produced by the selected hybridoma was measured, and only 3 lines of the hybridoma were confirmed to satisfy the conditions of being an IgM isotype and having an association constant of $10^{10}M^{-1}$ or more. However, when a set of these experiments was performed three times repeatedly for preparing the hybridoma in a similar manner, at least one line of the hybridoma producing an antibody, which satisfies the conditions of being an IgM isotype and having an association constant of $10^{10}M^{-1}$ or more, was obtained in every experiment.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In the present case, the monoclonal antibody described in claim 1 is a monoclonal antibody satisfying limitative conditions, "reacting with a surface antigen P of a virus Y with an association constant of $10^{10}M^{-1}$ or more".

Generally, there is common general knowledge that it is in many cases not reproducible to obtain a hybridoma producing a monoclonal antibody that satisfies limitative conditions.

However, in the Description of the invention, there is a description that plural lines of a hybridoma producing a monoclonal antibody of IgM isotype that satisfy the limitative conditions, "reacting with a surface antigen P of a virus Y with a association constant of $10^{10}M^{-1}$ or more" can be obtained by selecting a certain specific partial amino acid sequence from the amino acid sequence encoding a surface antigen P of a virus Y. Further, there is also a description that a hybridoma producing the monoclonal antibody of IgM isotype that satisfies the limitative conditions can be reproducible by repeatedly performing the experiments of preparing the hybridoma in a similar manner using a polypeptide consisting of the specific partial amino acid sequence as an immunogen.

Consequently, the monoclonal antibody described in claim 1 and the hybridoma producing the

monoclonal antibody are reproducible in confirmatory studies conducted by a person skilled in the art.

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Therefore, the hybridoma described in claim 2 is a microorganism that can be prepared by a person skilled in the art on the basis of the description in the specification.

Accordingly, the hybridoma described in claim 2 is not required to be deposited, since the hybridoma described in claim 2 is a microorganism readily available to a person skilled in the art.

Case 2-3 A case where the hybridoma is not readily available to a person skilled in the art (Need to deposit)

[Claims]

1. A monoclonal antibody ABC-1, suppressing cell proliferation by binding to receptor Z.
2. A hybridoma H- ABC-1 producing the monoclonal antibody described in claim 1.

[Outline of Description of the invention]

Receptor Z was already isolated and purified, and it was publicly known at the filing that cell proliferation was suppressed by agonist binding to receptor Z. Further, an attempt to prepare a monoclonal antibody that suppresses the cell proliferation by binding to receptor Z was performed prior to the filing. However, an antibody suppressing the cell proliferation by binding to receptor Z was not obtained prior to the filing.

When the inventors prepared a monoclonal antibody based on a known hybridoma method using receptor Z as an immunogen, they obtained numerous hybridomas producing a monoclonal antibody that binds to receptor Z. Among them, however, only one line was the hybridoma producing the monoclonal antibody that suppresses the cell proliferation. Further, the monoclonal antibody suppressing the cell proliferation was named "monoclonal antibody ABC-1" and the hybridoma producing the "monoclonal antibody ABC-1" was named "hybridoma H-ABC-1".

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

In the present case, the monoclonal antibody ABC-1 described in claim 1 is a monoclonal antibody produced by the specific hybridoma line, hybridoma H-ABC-1.

Generally, there is common general knowledge that it is difficult to obtain a specific hybridoma line by design based on a known hybridoma method.

Further, in the Description of the invention, there is only a description that one line of the hybridoma H-ABC-1 producing the monoclonal antibody ABC-1 was obtained based on a known hybridoma method, and there is no description of a method for obtaining the hybridoma H-ABC-1 reproducibly.

Consequently, the monoclonal antibody ABC-1 or hybridoma H-ABC-1 is not reproducible in confirmatory studies conducted by a person skilled in the art. Therefore, the hybridoma H-ABC-1 is not a microorganism that can be prepared by a person skilled in the art on the basis of the description in the specification.

Accordingly, the hybridoma H-ABC-1 is required to be deposited, since the hybridoma H-ABC-1 is not a microorganism readily available to a person skilled in the art.

8.3 Inventions Relating to Cells

Case 3-1 A case where the cells can be produced by a person skilled in the art on the basis of the description in the specification (No need to deposit)

[Claims]
1. A method for isolating mouse lung cancer cells from a heterogeneous cell population containing the mouse lung cancer cells, comprising:
(1) a step of preparing a vector ligated to a nucleic acid molecule encoding a fluorescent protein under the control of a lung cancer cell-specific promoter consisting of the nucleic acid sequence represented by SEQ ID NO: 1;
(2) a step of introducing the vector into the cell population; and
(3) a step of identifying and isolating mouse lung cancer cells as cells generating fluorescence from the cell population.
2. The mouse lung cancer cells, isolated by the method described in claim 1.

[Outline of Description of the invention]
A novel promoter that functions specifically in lung cancer cells was cloned from a mouse. The nucleic acid sequence of the promoter is represented by SEQ ID NO: 1. In addition, based on a known technique, a heterogeneous cell population containing lung cancer cells was prepared from a mouse. Further, a vector ligated to a nucleic acid molecule encoding GFP, that is well-known as a kind of fluorescent protein, under the control of the promoter was introduced into the cell population, GFP was expressed only in lung cancer cells in the cell population, and mouse lung cancer cells were identified and isolated as fluorescing cells among the cell population.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]
In the present case, in the Description of the invention, the nucleic acid sequence of a promoter specifically functioning in lung cancer cells is disclosed. It is also disclosed that mouse lung cancer cells were identified and isolated from a heterogeneous cell population by using a vector ligated to a nucleic acid molecule encoding GFP under the control of the promoter.

Consequently, the mouse lung cancer cells can be identified/isolated reproducibly in confirmatory studies conducted by a person skilled in the art.

Therefore, the mouse lung cancer cells described in claim 2 are microorganisms that can be produced by a person skilled in the art on the basis of the description in the specification.

Accordingly, the mouse lung cancer cells described in claim 2 are not required to be deposited, since the mouse lung cancer cells are microorganisms readily available to a person skilled in the art.

Case 3-2 A case where the cells are not readily available to a person skilled in the art (Need to deposit)

[Claims]

1. A mesenchymal stem cell line H-01, derived from a mouse mesenchymal stem cell, capable of subculturing in a serum-free medium, exhibiting fibrous form when cultured in the serum-free medium, and being induced to differentiate into target cells at a rate of 80 % or more by culturing in a medium containing a conditioned medium of the target cells.

[Outline of Description of the invention]

Mesenchymal stem cells obtained from mouse bone marrow were cultured for three weeks in a serum-free medium and dead cells were removed. Subsequently, by repeatedly subculturing the remaining cells for examining the differentiation potential, a mutant cell line differentiating into astrocyte-like cells was fortuitously obtained by culturing in a medium containing an astrocyte-conditioned medium. Further, the mutant cell line was named "mesenchymal stem cell line H-01". Here, by performing a further analysis of the differentiation potential of the mesenchymal stem cell line H-01, the mesenchymal stem cells were induced to differentiate into adipocytes, smooth muscle cells, fibroblasts and the like respectively at the rate of nearly 100% by culturing in medium each containing a conditioned medium of the corresponding cells.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]

Generally, there is common general knowledge that it is difficult to obtain a specific mutant cell line intentionally during the cell culture since the mutation in a genome of a cell occurs randomly during the cell culture.

In the present case, in the Description of the invention, there is only a description that the mesenchymal stem cell line H-01 was established from a mutant cell line that was obtained fortuitously in the process of subculturing the mesenchymal stem cells obtained from mouse bone marrow, and there is no description about a method for obtaining the mesenchymal stem cell line H-01 reproducibly.

Consequently, the mesenchymal stem cell line H-01 is not reproducible in confirmatory studies conducted by a person skilled in the art. Therefore, the mesenchymal stem cell line H-01 is not a microorganism that can be produced by a person skilled in the art on the basis of the description in the specification.

Accordingly, the mesenchymal stem cell line H-01 is required to be deposited, since the mesenchymal stem cell line H-01 is not a microorganism readily available to a person skilled in the art.

8.4 Inventions Relating to Animals

Case 4-1 A case where the animal can be produced by a person skilled in the art on the basis of the description in the specification (No need to deposit)

[Claims]
1. A transgenic mouse introduced with a proto-oncogene comprising the base sequence represented by SEQ ID NO: 1.

[Outline of Description of the invention]
A novel proto-oncogene consisting of the base sequence represented by SEQ ID NO: 1 was cloned from human. Further, a plurality of transgenic mice were prepared based on a known gene transfer method by introducing the gene into a commercially available fertilized BALB/c mouse ovum to create transgenic mice. These mice developed tumors at an average age of 5 months old.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]
In the present case, in the Description of the invention, a novel proto-oncogene consisting of the nucleic acid sequence SEQ ID NO: 1 is described. The description also describes that transgenic mice were prepared based on a known gene transfer method, using said proto-oncogene and a commercially available mouse.

Consequently, a transgenic mouse introduced with a proto-oncogene consisting of the base sequence represented by SEQ ID NO: 1 is reproducible in confirmatory studies conducted by a person skilled in the art.

Therefore, the transgenic mouse described in claim 1 is an animal that can be produced by a person skilled in the art on the basis of the description in the specification.

Accordingly, the prepared transgenic mouse (a fertilized egg thereof and the like) is not required to be deposited, since the transgenic mouse described in claim 1 is an animal readily available to a person skilled in the art.

Case 4-2 A case where the animal is not readily available to a person skilled in the art (Need to deposit)

[Claims]
1. An RFG mouse spontaneously developing dermatitis, developing periocular edema as an incipient lesion at 3 weeks old.

[Outline of Description of the invention]
In the process of maintaining the strain of BALB/c mouse, a mutant individual which developed periocular edema as an incipient lesion at 3 weeks old and spontaneously developing dermatitis under a clean condition was fortuitously obtained. Subsequently, an inbred mouse strain was established from the mutant individual and named "RFG mouse". After establishing the inbred mouse strain, in the process of 25 generations, an RFG mouse spontaneously developed dermatitis while maintaining a characteristic of developing periocular edema as an incipient lesion at 3 weeks old.

[Explanation on judgment of necessity for deposit of microorganisms, etc.]
Generally, it is common general knowledge that it is difficult to obtain a specific mutant individual reproducibly in a process of maintaining a mouse strain, since the mutation occurring in a genome of a mouse randomly occurs in a process of maintaining the mouse strain.

In the present case, in the Description of the invention, there is only a description that the RFG mouse is an inbred mouse established from a mutant individual obtained fortuitously in the process of maintaining the strain of BALB/c mouse, and there is no description about a method for obtaining the RFG mouse with repeatability.

Consequently, the RFG mouse is not reproducible in confirmatory studies conducted by a person skilled in the art.. Therefore, the RFG mouse is not an animal that can be produced by a person skilled in the art on the basis of the description in the specification.

Accordingly, the RFG mouse (a fertilized egg thereof and the like) is required to be deposited, since the RFG mouse is not an animal readily available to a person skilled in the art.

[Appendix 1]

The Guidelines for Describing Taxonomic Characters

It is required to describe in detail taxonomic characters of a microorganism belonging to a new species (including ones designated by their strain) and append a micrograph or electron micrograph as necessary. The description should mention differences from other similar known species, make clear the reason why the microorganism was judged as new, and cite relevant literature on which the judgement based. It is desirable that a new species is named in accordance with the applicable international rules of nomenclature.

In the following, microorganisms are divided into four categories, namely yeast, mold or mushroom, bacteria and actinomycetes. Items to be described are shown below. In describing such items, experiments and observations should be performed on normally grown microorganism. It is necessary to describe cultivation conditions, such as the kind of culture media used (or the composition of the media), incubation temperature, incubation time, etc. Further, it is desirable to describe the date, the source (its scientific name should be shown, when the source is an animal or a plant) and the place of isolation of the strain.

Besides, the items listed here are only a guidance for specifying microorganisms. Which items must be described to sufficiently specify a microorganism should be judged depending on microorganisms involved in each patent application.

1. If the new species belongs to yeasts, the following should be described.

(a)Cultural and morphological characters

a)Wort or YM liquid medium

b)Wort agar medium or YM agar medium

c)Dalmau plate culture or slide culture using potato or corn meal agar culture media

It is necessary to describe the appearance, color, luster, diffusion pigment, etc. of those grown on agar media, as well as the surface growth, turbidity of the media, etc. of those grown on liquid media, in addition to the size, shape and mode of multiplication of vegetative cells (indicate whether it multiplies by budding or fission, it has mycelia or pseudohyphae) grown on these media. Further, it is desirable to describe in detail the above characters observed through the use of a medium which reveals the characteristics of the strain.

(b)Formation of spores

a)Sexual spore

1) The presence of ascosporogenesis should be examined with the use of Gorodkowa medium, gypsum sodium acetate medium, malt extract agar medium, vegetable extract agar medium, carrot piece, etc. The form of the ascus and the ascospore should be described when the formation of spores is found.

2) It is necessary to describe the shape of dicaryon mycelia, basidia (teliospore, premycelia) or basidiospore when it is found with the use of malt extract agar medium,

vegetable extract agar medium, corn meal agar medium, potato yeast exudate glucose agar medium, etc.

b)Ballistospore

The presence of ballistospore should be examined with the use of wort agar medium, potato agar medium, corn meal agar medium and the like. The shape of the ballistospore should be described when it is found.

(c)Physiological and chemotaxonomical characters

a) Optimal growth conditions (pH, temperature)
b) Range of growth (pH, temperature)
c) Utilization of nitrate
d) Lipolysis
e) Decomposition of urea
f) Color reaction to diazonium blue B
g) Liquefaction of gelatin
h) Optimal or maximal concentration of sucrose or sodium chloride if it is osmophilic or osmotolerant
i) Formation of carotinoid
j) Remarkable formation of organic acid
k) Formation of starch-like substance
l) Requirement for vitamins
m) Utilization of 15 or more of the following carbon sources (for the saccharides marked with *, both utilization and fermentativeness should be described.)

1) D-arabinose
2) L-arabinose
3) D-ribose
4) D-xylose
5) *D-glucose
6) D-mannose
7) *D-galactose
8) L-rhamnose
9) D-fructose
10)L-sorbose
11)*maltose
12)*sucrose
13)*lactose
14)*melibiose
15)cellobiose
16)trehalose
17)*raffinose

18)melezitose
19)α-methyl-D-glucoside
20)D-glucosamine
21)N-acetyl glucosamine
22)arbutin or esculin
23)dextrin
24)soluble starch
25)inulin
26)methanol
27)ethanol
28)adonitol
29)erythritol
30)*inositol
31)D-mannitol
32)D-sorbitol
33)dulcitol
34)D-gluconate
35)glycerin
36)DL-lactate
37)succinate
38)citrate
39)hexadecane
40)other carbon compounds necessary to show characteristics of new species

n)It is desirable to describe the base composition (GC content) of DNA and type of ubiquinone (coenzyme Q).

o)Other physiological and chemotaxonomical characters necessary to characterize the new species, if any, should also be described.

The following are examples.

1)Sugar composition of cell wall (presence of xylose, rhamnose, fucose and galactose)
2)DNA-DNA homology with analogous species

(d)In addition to the above characters, other characteristics characterizing the microorganism, if any, should be described.

2. If the new species belongs to mold or mushroom, the following should be described.

(a)Cultural and morphological characters

a) Wort (or malt extract) agar medium
b) Potato glucose agar medium
c) Czapek agar medium

d) Sabouraud agar medium

e) Oatmeal agar medium

f) Synthetic mucor agar medium

g) YpSs agar medium

h) Glucose dry yeast agar medium (for mycorrhiza forming fungi)

i) corn meal agar medium

Two or more of the above media should be selected. It is necessary to describe the state of growth of strains grown on each selected medium, namely the teleomorphic (sexual stage) and anamorphic (asexual stage) morphological characters, shape and color tone of the surface of colonies, color tone of the back side of colonies.

Further, it is desirable to describe in detail the above characters observed with the use of a medium which reveals the characteristics of the strain very well.

(b)Physiological and chemotaxonomical characters

a) Optimal growth conditions (pH, temperature)

b) Range of growth (pH, temperature)

c) Phenol oxidase reaction (only for wood-rotting fungi)

d) Other physiological and chemotaxonomical characteristics necessary to characterize the new species, if any, should also be described.

The following are examples.

1) Base composition (GC content) of DNA

2) Electrophoretogram of enzyme and protein

3) DNA-DNA identity with analogous species

4) Type of ubiquinone (coenzyme Q)

(c) When the above characters are insufficient to determine the microorganism to be new, it is necessary to describe teleomorphic or anamorphic morphological characters and the shape, color tone of a microorganism on the substrate on the basis of dry specimens,

[Note] It is desirable to state the storage facility (culture collection) and the specimen number of the standard type specimen.

(d) In addition to the above, other characteristics characterizing the microorganism, if any, should be described.

3. If the new species belongs to bacteria, the following should be described.

(a) Morphological characters

Following items should be described in respect of cells grown on agar media and liquid media. In principle, the standard medium formulation is broth or broth agar, but other appropriate media may be used for cells which do not grow well on such media.

a) Shape and size of cells

b) Polymorphism of cells, the details of the polymorphism if present.

c) Motility, the state of adherence of flagella if the cell has motility.

d) Spores, the shape and size of the spores and sporangia as well as site of spores if the cell has spores.

(b) Cultural characters

a) Broth agar plate culture

b) Broth liquid culture

c) Broth gelatin stab culture

d) Litmus milk

It is required to describe the appearance, color, luster, diffusible pigment, etc. of cells grown on agar media; the presence of surface growth, turbidity of media and the like of those grown on liquid media, the state of growth, gelatin liquefaction and the like of those grown on gelatin stab culture, as well as the change of color (alkaline or acid), coagulation and liquefaction of litmus milk. It is recommended to describe the state of growth on any other media suitable for growth when the microorganism does not grow on the media listed above.

(c) Physiological characters

a) Gram stain

b) Reduction of nitrate

c) Denitrification

d) MR test

e) VP test

f) Production of indole

g) Production of hydrogen sulfide

h) Hydrolysis of starch

i) Utilization of citric acid (Both Koser (or Simmons) medium and Christensen medium should be used)

j) Utilization of inorganic nitrogen sources (nitrate and ammonium salt)

k) Production of pigment (indicate whether the pigment is water soluble or not)

l) Urease

m) Oxidase

n) Catalase

o) Range of growth (pH, temperature)

p) Behavior toward oxygen (aerobic or anaerobic)

q) O-F test (according to Hugh Leifson method)

r)The formation of acids or gases from the saccharides below should be described.

1) L-arabinose

2) D-xylose

3) D-glucose

4) D-mannose

5) D-fructose

6) D-galactose

7) maltose
8) sucrose
9) lactose
10) trehalose
11) D-sorbitol
12) D-mannitol
13) inositol
14) glycerin
15) starch

Descriptions should also include the formation of gas or acid from any other sugars, if necessary to show the characteristics of the new species.

(d) It is desirable to describe items selected from the following necessary for showing characteristics of the new species.

a) Decomposition products of saccharides
b) Oxidation of gluconic acid
c) Oxidation of alcohol
d) Formation of dihydroxyacetone
e) Decomposition of esculin
f) Decomposition of cellulose
g) Decomposition of hippuric acid
h) Utilization of malonic acid
i) Decomposition of arginine
j) Decarboxylation of lysine
k) Decarboxylation of ornithine
l) Deamination of phenylalanine
m) Coagulase
n) Hemolysis
o) Temperature sensitivity
p) Tolerance to sodium chloride
q) Tolerance to potassium cyanide
r) Phosphatase
s) Pectinase
t) Lipase
u) Lecithinase
v) Auxotrophy
w) Acid fastness
x) Other necessary characters

(e) Chemotaxonomic characters

a) It is desirable to describe the base composition (GC content) of DNA.

b) Other chemotaxonomical characteristics necessary to characterize the new species, if any, should be described.

The following are examples.

1) Amino acid composition of cell wall peptide glycan

2) Kind of reducing sugars in cell wall hydrolysate

3) Kind of lipids (isoprenoid quinone, phospholipid, fatty acid including mycolic acid)

4) DNA-DNA identity with analogous species

(f) Obligate anaerobes, lithotrophic bacteria, photosynthetic bacteria should be described in accordance with the above with reference to the Bergey's Manual of Systematic Bacteriology or recent studies.

(g)In addition to the above characters, other characteristics to characterize, if any, should be described.

4. If the new species belongs to actinomycetes, the followings should be described. In principle, the medium stated below should be used. However, if there is any other medium on which the new species reveals the characteristic features, it may additionally be used. Hereinafter, the International Streptomyces Project is abbreviated as "ISP".

(a) Morphological characters

It is required to describe morphological characters of mycelia, spores, etc. which differentiate the taxonomic genus or species of the actinomycetes, based on observation of the species grown on yeast malt agar medium (ISP medium No.2), oatmeal agar medium (ISP medium No.3), starch inorganic salt agar medium (ISP medium No.4) or glycerin asparagine agar medium (ISP medium No.5).

The following are examples.

a) Hypha

The formation of aerial hypha, septation (fragmentation) of aerial or substrate hypha and the motility of septated (fragmented) hypha

b) Spores

1) The formation of spores or sporangia as well as their adhering site (on aerial or substrate hypha)

2) The number of spores per chain on sporophore and the shape of the chain (linear, curving, circular, spiral, trochoidal)

3) Shape and size of sporangia, as well as the number sporangiospore per sporangium, when sporangia exist.

4) Characteristics (surface structure, size, motility, flagella) of spores (including sporangiospore)

c) Others

The formation of chlamydospores, coremia, rhizomorph, pseudosporangia or sclerotia, type of fission of mycelia, etc.

(b) Cultivation characters

It is recommended to describe the state of growth on yeast malt agar medium (ISP medium No.2), oatmeal agar medium (ISP medium No.3), starch inorganic salt agar medium (ISP medium No.4) or glycerin asparagine agar medium (ISP medium No.5), the state of adhesion and the color tone of aerial mycelia, the color tone of substrate mycelia, the production of pigment diffusing into media, etc.

(c) Physiological characters

a) Range of growing temperature

b) Formation of melanin like pigments

Peptone yeast iron agar medium (ISP medium No.6) and tyrosine agar medium (ISP medium No.7) should be used.

c) Utilization of carbon sources

At least, the utilization of the carbon sources below shall be described.

1) L-arabinose
2) D-fructose
3) D-glucose
4) D-inositol
5) D-mannitol
6) raffinose
7) L-rhamnose
8) sucrose
9) D-xylose

In principle, Pridham & Gottlieb agar medium (ISP medium No.9) should be used as a base medium. When any other medium is used, the medium used should be expressly described.

(d) Chemotaxonomic characters

a) It is preferable to identify optical isomers (LL- and meso-type) of diaminopimelic acid when it is present in a cell.

b) Other chemotaxonomical characteristics necessary to characterize new species, if any, should also be described.

The following are examples.

1) Amino acid composition of cell wall peptidoglycan
2) Kind of reducing sugars in hydrolysate of the whole cell or cell wall
3) Kind of lipids (isoprenoid quinone, phospholipid, fatty acid including as mycolic acid)
4) DNA-DNA identity with analogous species
5) Base composition (GC content) of DNA

(e) In addition to the above, other characteristics characterizing the microorganism, if any, should

be described.

The following are examples of media formulation used in identifying yeasts, mold, mushroom, bacteria and actinomycetes. Commercially available media may also be used. In such cases the manufacturer and the trade name of the product should be described.

1.Yeast

(1) YM medium

Peptone	5 g
Yeast extract	3 g
Malt extract	3 g
D-glucose	10 g
Deionized water	1000ml

(2) Potato glucose agar medium

Mash 100g of potato, immerse in 300 ml of water and allow to stand for several hours in a cold dark place. Filter this mash through a piece of cloth and boil the filtrate at 120 ℃ for one hour. After cooling, add water to 1000 ml, and further add 20 g of D-glucose and 20 g of agar.

(3) Gorodkowa medium

Peptone	1 %
Bouillon	1 %
D-glucose	0.25 %
NaCl	0.5 %
Agar	2.5 %

(4) Sodium acetate medium

CH_3COONa	0.4 %
Agar	1.5 %
（Raffinose	0.04 %）

(5) Malt extract agar medium

Powdered malt extract	20 g
Agar	12 g
Deionized water	400 ml

(6) Vegetable extract agar medium

Vegetable extract	500 ml
Baker's yeast	10 g
Agar	20 g
Deionized water	500 ml

pH 7.0

(7) Gypsum medium

Impaste calcined gypsum by adding an equal volume of water. Pour the paste into a suitable frame (a conical trapezoid frame made of copper, of which inner surface has been thinly coated with vaseline beforehand). Immediately after that, tap the frame on the desk in order to let gases out of the gypsum. Allow the gypsum to stand for about 30 minutes until it solidifies. Take the gypsum out of the frame, shave its surface smoothly and bore a small hole for placing a sample of yeast. After solidification, wipe off vaseline from the gypsum. Boil the gypsum for about 30 minutes, while changing water once or twice.

Immediately after that, take out the gypsum using a sterile pincette and put into a previously sterilized large petri dish. Add sterilized water to the half of the height of the gypsum block. Preculture yeast on wort, koji soup, YM or Miller media two or three times. Collect fresh yeast by removing the supernatant of the liquid culture, dispense the fresh yeast into the small hole of the gypsum using a platinum loop or a microspoon and incubate at 20 to 25 ℃.

(8) Corn meal agar medium

Corn meal	12.5 g
Deionized water	300 ml
(After heating in warm bath at 60℃ for 1 hour, filter and make up its filtrate to 300 ml)	
Agar	3.8 g

(9)Potato yeast exudate glucose agar medium

Potato (peeled and diced)	200 g
Baker's yeast	30 g
Deionized water	1000 ml
(boil for 30 minutes to obtain exudate)	
Glucose	20 g
Agar	15 g

2. Mold or mushroom

(1) Malt extract agar medium

Malt extract	20 g
Glucose	20 g
Peptone	1 g
Agar	25 g
Deionized water	1000 ml

(2) Potato glucose agar medium

Potato (peeled and diced)	200 g
Deionized water	1000 ml

(prepare exudate using the above)

Glucose	20 g
Agar	15 g

(3) Czapek agar medium

$NaNO_3$	3 g
K_2HPO_4	1 g
$MgSO_4 \cdot 7\ H_2O$	0.5 g
KCl	0.5 g
$FeSO_4 \cdot 7\ H_2O$	0.01 g
Sucrose	30 g
Agar	15 g
Deionized water	1000 ml

(4) Sabouraud agar medium

Maltose or glucose	40 g
Peptone	10 g
Agar	15 g
Deionized water	1000 ml

(5) Oatmeal agar medium

Oatmeal	30 g
Deionized water	1000 ml
(prepare exudate using the above)	
Agar	20 g

(6) Synthetic mucor agar medium

Glucose	40 g
Asparagine	2 g
KH_2PO_4	0.5 g
$MgSO_4 \cdot 7\ H_2O$	0.025 g
Thiamin chloride	0.5 mg
Agar	15 g
Deionized water	1000 ml

(7) YpSs agar medium

Soluble starch	15 g
Yeast extract	4 g
K_2HPO_4	1 g
$MgSO_4 \cdot 7\ H_2O$	0.5 g
Agar	15 g
Deionized water	1000 ml

(8) Glucose dry yeast agar medium (for mycorrhiza forming fungi)

Glucose	10 g
Dry yeast	5 g
KH_2PO_4	1 g
$MgSO_4 \cdot 7\ H_2O$	0.5 g
Agar	15 g
Deionized water	1000 ml
pH (adjusted by 1 N HCl)	5.0

(9) Medium for assaying phenol oxidase reaction

Add 0.5 % of tannic acid and 0.5 % of gallic acid to wort agar medium or potato glucose agar medium.

3. Bacteria

(1) Broth medium

Broth	10 g
Peptone	10 g
NaCl	5 g
Deionized water	1000 ml
pH 7.2	

(2) Broth agar medium

Broth	10 g
Peptone	10 g
NaCl	5 g
Agar	15-20 g
Deionized water	1000 ml
pH 7.2	

(3) Broth gelatin medium

Broth	10 g
Peptone	10 g
NaCl	5 g
Gelatin	100-300 g
Deionized water	1000 ml
pH 7.2	

(4) Litmus milk

Add adequate amount of litmus to fresh skim milk or reconstituted skim milk adjusted to the density of original milk.

4. Actinomycetes

Sterilization should be performed under high pressure at 121°C for 20 minutes, unless otherwise stated.

(1) Yeast malt agar medium (ISP medium No.2)

Yeast extract	4 g
Malt extract	10 g
Glucose	4 g
Deionized water	1000 ml
Agar	15-20 g
pH 7.3	

(2) Oatmeal agar medium（ISP medium No.3）

Oatmeal	20 g
Trace salts solution	1 ml
$FeSO_4 \cdot 7\ H_2O$	0.1 g
$MnCl_2 \cdot 4\ H_2O$	0.1 g
$ZnSO_4 \cdot 7\ H_2O$	0.1 g
Deionized water	100 ml
Agar	18 g
pH 7.2	

Boil oatmeal in 1000 ml of deionized water for 20 minutes and filtrate through cheese cloth. Supplement the loss with deionized water. Adjust pH by adding trace salts solution, then add agar.

(3) Starch inorganic salt agar medium（ISP medium No.4）

Liquid I: Impaste 10 g of soluble starch by adding small amount of cold deionized water and dilute to make 500 ml.

Liquid II:

K_2HPO_4	1 g
$MgSO_4 \cdot 7\ H_2O$	1 g
NaCl	1 g
$(NH_4)_2SO_4$	2 g
$CaCO_3$	2 g
Deionized water	500 ml
Trace salts solution	1 ml (same as(2))

Mix Liquid I and Liquid II, and add 15-20 g of agar.

(4) Glycerin asparagine agar medium（ISP medium No.5）

Glycerin	10 g
L-asparagine	1 g
K_2HPO_4	1 g

Deionized water	1000 ml
Trace salts solution (same as(2))	1 ml
Agar	15-20 g
pH 7.0-7.4	

(5) Peptone yeast iron agar medium (ISP medium No.6)

1) Peptone iron agar	36.58 g
Peptone	15 g
Proteose peptone	5 g
Iron ammonium citrate	0.5 g
K_2HPO_4	1 g
Na_2S2O_3	0.08 g
Agar	15 g
2) Yeast extract	1 g
3) Deionized water	1000 ml

Mix 1), 2) and 3), and adjust pH to 7.0-7.2.

(6) Tyrosine agar medium (ISP medium No.7)

Glycerin	15 g
L-tyrosine	0.5 g
L-asparagine	1 g
K_2HPO_4	0.5 g
$MgSO_4 \cdot 7\ H_2O$	0.5 g
NaCl	0.5 g
$FeSO_4 \cdot 7\ H_2O$	10 mg
Deionized water	1000 ml
Trace salts solution (same as(2))	1 ml
Agar	15-20 g
pH 7.2-7.4	

(7) Pridham & Gottlieb agar medium (ISP medium No.9)

$(NH_4)_2SO_4$	2.64 g
KH_2PO_4	2.38 g
K_2HPO_4	5.65 g
$MgSO_4 \cdot 7\ H_2O$	1 g
Deionized water	1000 ml
Pridham Gottlieb trace salts solution	1 ml
$CuSO_4 \cdot 5H_2O$	0.64 g
$FeSO_4 \cdot 7\ H_2O$	0.11 g
$MnCl_2 \cdot 4\ H_2O$	0.79 g
$ZnSO_4 \cdot 7\ H_2O$	0.15 g
Deionized water	100 ml

Dissolve all the ingredients, adjust pH to 6.8-7.0 (use 1 N NaOH or 1 N HCl as required) and add 15-20 g of agar. Sterilize the agar medium and cool it down to 60 ℃, and add 10 % of various carbon sources sterilized separately (filtration sterilization, ether sterilization, ethylene oxide sterilization etc.) to the agar medium in the ratio of 1:10.

Trace salts solution should be stored at 3 to 5 ℃ and returned to room temperature before use. Do not use a trace salt solution which was stored more than one month after prepared or which produced precipitate during storage.

[Appendix 2] (Omitted)
[Appendix 3] (Omitted)