ARTICLES

Introduction to Decisions Aspect of "Biotechnology Field Invention"*

Biotechnology Committee

Contents

1. Introduction

In the field of biotechnology, with the rapid advancement in genetic discoveries and technological innovations, there is now discussion about how to protect intellectual property of such innovations.

In this paper, we introduce recent decisions of the Tokyo High Court in Japan, the Federal Circuit in the United States and the Boards of Appeal of the European Patent Office concerning the patentability of innovations in biotechnology, and attempt to provide the inquirer with an understanding of current thinking on the subject of intellectual property in this field.

2. Case Digests

In this paper, we introduce 6 decisions the Boards of Appeal of the Patent Offices and court decisions, each 2 cases from Japan, the United States and Europe.

Each of 2 cases in Japan includes the judgment concerning action against trial decision. In the first case, a case on a method of controlling male fertility in plants, it was determined that the description of the patent specification dose not meet the enabling requirement of the invention. It would not be recognized that an invention is recited in the patent specification so that a person skilled in the art is enable to carry out it readily, because none actual successful experience is known in cases that no concrete technique is disclosed in the specification, even though there is a probability of success in exploitation of the invention through unspecified method. It would say that it was decided in the present case example that such a case which would require no embodiment for invention would be limited to the case which contains each process of claim comprising well-known techniques only and the case in which the claimed invention can be achieved by combining these techniques according to the description of the specification.

In the second case, a case of recombinant human protein hormone, it was judged upon judgment of novelty of chemical substances that one invented substance differs from another invention in such a case that the differences in purity between the chemical substances are important as usefulness of the invention. Even if the presence of natural substance was known,

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the invention relating to a recombinant protein was judged as novel. A human protein hormone having been publicly known at the time of the patent application was filed must be identified only by raw materials or purification methods thereof at that time. The Court found in the present case of invention that the invention could not be identified only by chemical structure of the substance because usefulness of the invention would be dependent on the extent of the contents of impurities. Consequently, the court adopted a limitation of the claim on that "No other human protein or no other hormone is contained" concerning the gist of the invention.

The next 2 cases in the United States introduced here include decisions of the United States Court of Appeals for the Federal Circuit (the CAFC) in which validity of patents was disputed in appeal trials on patent infringement suits. In the second case, there is first ruling that the relation of the timing of operation of the invention by defendant and the time of patent registration, relating to 35 U.S.C §271(g). The scope covered by claims of this patent in this case was also provided.

The first case held by the CAFC, a case on a random screening method, is a patent infringement suit relating to research tools which gain recognition mainly in the discovery processes of pharmaceutical drugs and with which the invention is operated in laboratories. It was an appeal case from the decision of district court which also aroused interest in Japan because the decision of the district court made a pronouncement on very high damage. Upon decision of non-obviousness of the patent in this case, the CAFC found that it would be obvious to apply the known methods used for determining a specified substance merely for screening of unknown substances.

In the second case, a case on an insecticidal protein, the time covered by a patent relating to a product manufactured in a foreign country became a main issue. It was a case for which such a decision was held that the product would not be subject under intended for 35 U.S.C. §271(g), even if the product was manufactured by operating the method was brought in the US after beginning the US patent in such a case that the method had been operated (the product had been manufactured) before beginning the US patent. It points out a possibility that the timing of operation of the invention relating to process patents for screening methods would affect on the determination of the presence of infringement in the field of biotechnology. This court decision will create a precedent case where the time of infringement for process invention is determined in the future. In addition, another issue in this case was an application of a doctrine of the precedent Festo case decision stating that the doctrine of equivalents would not be applied, unexceptionally in the field of biotechnology, in such a case that the scope of claims was narrowed in the process of examination.

Both of two cases in Europe include trial decisions in the boards of appeal of the European Patent Office. In the first case, a case on a novel thrombolytic protein, the Board held that enabling requirements of the patent specification would satisfy the EPC 83 and 84, since there are no doubts that the invention could be tested unambiguously without any undue burden and inventive skills despite the fact that the patent specification contained no experimental data which would support the claimed invention. With respect to the inventive step, the applicant complemented the argument on surprising effects of this invention by post-published documents, and hence the Board adopted such documents as expert opinions and affirmed the inventive step of this invention, because a solution of technical problem relating the invention were sufficiently provided in the patented specification.

In the second case, a case on an astaxanthin producing yeast, the Board considered that it was obvious for the skilled person to enter the route of treating a naturally occurring yeast (Phaffia rhodozyma strain) with an ordinary mutagen pertaining to the methods for "production". Nevertheless, the Board found that the invention of the mutants with high productivity claimed by auxiliary request, albeit achieved by conventional mutagenesis techniques, constituted a contribution to the art which deserved patent protection because it contained elements of surprise which justified the recognition of an inventive step.

3. Decisions of the Tokyo High Court in Japan

3.1 Case Title: A Method of Controlling Male Fertility in Plants

Case number:	1998 (Gyo-ke) No.28
Type of case:	Judgment concerning action against trial decision of rejection (Revocation suit of trial decision of rejection)
Date of decision:	May 17, 2001
Country name:	Japan
Parties concerned:	Pioneer Hi-Bred International Inc.
Document:	The court opinion

(1) Main legal decision

1) Description requirements (Japanese Patent Law, Sec. 36(4))

Such a situation that any skilled person can carry out the process readily must have been produced as a requirement for considering that there is no particular need for recitation of a concrete embodiment in the specification, since each process, for which no operative example is recited, is a well-known technique at the time of claim of priority.

With respect to the technique of gene manipulation relevant to the present invention, the technique as it is can not always be applied to any other gene or any other living organism as a matter of course, even though application of the technique became successful in a specific gene of a specific living organism. Accordingly, presence of common general technical knowledge can not be admitted even from the proofs produced.

As for the present invention, as for at least a part of the processes, it is difficult to say that the technique was recited to such extent to which a skilled person is able to carry out it readily. Consequently, the specification does not meet the description requirements.

(2) Outline of the case

The present invention refers to a method of utilizing a male sterility plant as a female on mating. The male sterility plant would be produced by tying up a promoter introducible from outside with a gene relating to microsporogenesis and by allowing the plant to remain usually in the off-state to form a male sterility plant with a controllable gene which was transduced into a plant.

Request for trial of the application was made after decision of its final rejection, but it was rejected for the reason of inadequate description of the patent specification.

Plaintiff (applicant) appealed that the invention could be carried out without any particular recitation of its concrete embodiment in the specification, since the techniques used in the processes a) - e) of the present invention were well-known techniques.

The court supported the Department of Appeal finding that there was no good reason of the revocation of trial decision appealed by the plaintiff.

(3) Details of the legal decision

Court affirmed that successful examples of identification or transformation of unknown valuable genes were recited in publication A of the Patent Office with specifying the methods, species of organism, and type of gene or characters used in the cases.

It was described in publication A that it is sometimes unknown whether a technique is applicable to other organisms or things often turn out to be different from those in the application even if the technique is a routine one for a specific organism in the technical field of gene manipulation at the time of priority claim of the application.

Namely, a sporadic success in a technique relevant to a specific gene or property of a specific organism does not always lead to the success in application of the art to genes or properties of other organisms as a matter of course. It has been recognized that whether a technique invented successfully could be applied or not is unclear without any trial with taking time and labor, and hence, whether application of the technique to another item is successful or not depends on the respective concrete means. Above all, it is said that application of genetic manipulation technique of monocotyledons is one of the most difficult matters among those relevant to higher eukaryotes. Application of this type of gene manipulation technique was behind not only those in animals but those in

dicotyledonous plants. Moreover, it had been acknowledged by skilled persons that application of gene manipulation techniques targeting such properties which are said to be generated via complicated mechanisms would be very difficult.

According to the finding on the techniques at the time of priority claim of the application based on the description in publication A, it was decided that the specification does not describe the contents of the invention so that a skilled person can operate readily the methods of the invention even though abstract means were described for each step in the specification, in consideration of the objective of the present invention aiming to manipulate the complicated mechanisms of actions relating to reproductive behaviors of plants as such living organisms as monocotyledons.

Even though abstract methods which may have a chance of success, but not concrete means, are described for each step of the present invention, skilled persons have to repeat tests and faults since no actual successful example is known, and since they have to go through processes with which they do not know whether they can succeed or not. Consequently, it is obviously illogical to admit that the specification includes such a disclosure which deserves providing exclusive right called patent right.

(4) Main claim

A method for providing the genetic male sterility controllable from outside to plants and a method comprising the following processes of a), b), c), d) and e):

a) A step of selecting gene encoding a gene product on which microsporogenesis of said plant depends;

b) A step of cloning said gene selected

c) A step of tying up said cloned gene to the expressed sequence containing an inducible promoter responding to the control from outside

d) A step of removing the gene which encodes the gene product of said cloned gene from the original nuclear genome of said plant; and

e) A step of inserting an expressed sequence (DNA) into the nuclear genome of said plant

(5) References

1) File history
- Date of filing: June 12, 1991 [Japanese Patent Application, No.140379/1991] (Date of priority of claim: June 12, 1990 [USP Application No.537183])
- Date of decision of final rejection: April 3, 1995
- Appeal of an examiner's decision to reject: Appeal trial No.14416 in 1995
- Date of trial decision: August 7, 1997 (Failure of claim)

2) Patent family
- Europe: EP 465024B

3) Publication A

Plant biotechnology II, Special number of Gendai Kagaku (Modern chemistry) 20 (published in September 20, 1991)

3.2 Case Title: Recombinant Human Protein Hormone [Heteropolymeric Protein]

Case number:	1997 (Gyo-ke) No.302
Type of case:	Judgment concerning action against trial decision of rejection (Revocation suit of appeal trial of rejection)
Date of decision:	February 17, 2000
Country name:	Japan
Parties concerned:	Applied Research Systems ARS Holding N.V.
Document:	The court opinion

(1) Main legal decision

1) Novelty (Japanese Patent Law Sec. 29(1))

Human protein hormone has no other choice but to be identified by raw materials or a purification method thereof at the time of filing. It is not correct to consider that human protein hormone is "a compound that would be specified by its chemical structure".

Accordingly, it is considered that assertion of plaintiff should be accepted for the reasons that there is an error in the gist finding of the present invention and there is a good reason of the revocation of trial decision asserted by the plaintiff.

(2) Outline of the case

The invention refers to recombinant human protein hormones, human chrionic gonado-

tropin (hCG) and luteinizing hormone (LH).

Finding of the Patent Office was as follows.

Said "recombinant human protein hormone" is a compound which would be specified by its chemical structure. In addition, the claim, "containing no other human protein and no other hormones but for proteins derived from the host cell which might be used for producing the human protein hormone", does not affect on the chemical structure of said "recombinant human protein hormone". Accordingly, said description, "it contains no other human protein but proteins derived from host cell which might be used for producing of the human protein hormone, and it contains no other hormones", can not be accepted as an indispensable constituent of the present invention.

Then, the Patent Office made a decision of final rejection because the recombinant hCG in the present invention can not be distinguished as a different chemical compound from the hCG (naturally occurring hCG) purified by fractional precipitation, ion exchange chromatography and gel filtration described in the cited document 1 or 2.

Plaintiff filed a suit expressing dissatisfaction against the trail decision. As a consequence, the court revoked the trial decision of final rejection for the reason that the trial decision had been made by improper gist finding on the present invention.

(3) Details of the legal decision

1) Novelty (Japanese Patent Law Sec. 29(1))

Opinion of the Patent Office is as follows. "Chemical substance" in an invention of chemical substance would be enough to have "sufficient purity (grade of purification) for identifying it as a individual chemical substance". On the other hand, the recombinant protein of the present invention can be identified as a single "chemical substance" like the protein purified with prior arts and these compounds are obviously identical each other in their physical properties. Namely, the difference in the methods for producing these compounds does not affect the chemical structure thereof, and hence the difference only includes expressive medium to identify the chemical compounds. As a consequence, the proteins identified by these processes are identical and there is no novelty in the protein of the present invention.

Nevertheless, chemical structure of protein varies by conformation or sugar chains thereof, and hence it is not easy for a skilled person to elucidate the structure with the techniques known at the time of application of the patent. Moreover, there is a possibility that the protein to be identified by these processes may vary by origin of raw materials. Therefore, "the recombinant human protein hormone" of the present invention can not be based on the premise that "it is a compound which can be identified by its chemical structure", and it is improper to find the gist of the present patent based on the above premise.

Furthermore, compounds such as hCG and LH which would be used for medical uses including diagnostic and therapeutic products may cause unfavorable effects on diagnosis or medical treatment, if these compounds contain impurities beyond certain limit, even though their contents are very small. This concept is the common general technical knowledge in the technical filed to which the invention belongs. Consequently, usefulness of "recombinant human protein hormone" including hCG and LH depends not only on chemical structure thereof but also sometimes on constituent features other than chemical structure of the said chemical compounds, for example, contents of impurities.

Accordingly, limiting on "Containing no other human protein and no other hormones but for proteins derived from host cell which might be used for producing the human protein hormone" can not be disregarded upon gist finding of invention.

(4) Main claim

In a recombinant human protein hormone being selected from a group of compounds comprising hCG and LH, said recombinant human protein hormone containing no other human protein and no other hormones but for proteins derived from host cell which would be used for producing the human protein hormone and being modified after translation and being biologically active.

(5) Reference

1) File history

- Date of filing: October 31, 1984 [Divi-

sional application of Japanese Patent Application No.504232/1984: Japanese Patent Application No.162620/1993]
(Date of priority claim: November 2, 1983 [USP application No.548228])

- Date of decision of final rejection: March 28, 1995
- Date of trial decision: May 30, 1997

2) Patent family
- PCT: WO85/01959
- Japan: Examined patent application publication No.32244/1996, Patent No. 2573817, Patent No.3091673 and Patent No.3126348
- Europe: EP 160699B, EP 487512B, DE 3485869G, DE 3484669G and DK 8502971A
- USA: USP 4840869

3) References
- Citation 1: Endocrinology Vol.88 (1971) p.1045-1053
- Citation 2: Endocrinology Vol.94 (1974) p.1601-1606

4. Decisions of the Federal Circuit in the U.S.

4.1 Case Title: Random Screening Method

Case number:	CAFC No.99-1381
Type of case:	Appeal trial of patent infringement suit
Date of trial decision:	September 6, 2000
Country name:	USA
Parties concerned:	SIBIA Neurosciences, Inc. v. Cadus Pharmaceutical Corporation
Document name:	The court opinion

(1) Main legal decision [Obviousness (35 U.S.C. §103)]

The main point of the issue was presence or absence of a motivation to modify a known assay method to a random screening method.

The present invention discloses a method for screening a large number of compounds and identifying drugs with the use of cells having a cell surface protein and a reporter gene. A method similar to that of the present invention was disclosed as an assay method in a cited reference. The CAFC recognized that motivation to modify the assay method of the reference to the screening method can be derived from the level of skill in the art at the time when the invention was made or from other cited references, and decided that the present invention is obvious over teachings in a plurality of the prior art references.

(2) Outline of the case

SIBIA Neurosciences, Inc. (hereinafter "SIBIA") is the owner of U.S. Patent No. 5401629 (hereinafter "the '629 patent"), which is directed to a cell-based screening method useful for identification of compounds that bind to heterologous cell surface protein. Cadus Pharmaceutical Corporation (hereinafter "Cadus") was sued by SIBIA for infringement of the '629 patent.

The United States District Court for the Southern District of California set aside the claim of Cadus which appeals that the invention of the '629 patent is obvious for the teachings of a single reference or a combination of more than one references, and the court affirmed infringement of the '629 patent by Cadus. Cadus filed post-trial motions but they were denied. Then, Cadus filed an appeal to the CAFC.

The CAFC concluded that the invention of the '629 patent is obvious against the teachings of the said cited references and reversed the judgement of the district court.

(3) Details of legal decision [Obviousness]

1) Comparison with an assay method taught by the Stumpo's article

The CAFC stated that the Stumpo's article which had not been cited at the time of examination of the '629 patent would teach recombinant cells containing a heterologous cell surface receptor and a reporter gene which are identical to the recombinant cells in the claimed method of the '629 patent and that the said cells have been used in order to detect activation of the receptor using the reporter gene transcript as an indicator. Furthermore, the CAFC asserted that the difference between the assay method described in the Stumpo's article and the drug screening method of the '629 patent would be in the respective sample to be tested, that is, those in the former was a known receptor ligand but

those in the latter were large numbers of compounds, not previously known to interact with the cell surface proteins.

Accordingly, it was discussed whether or not there was a motivation to modify a simple assay method using a known receptor ligand to a screening method for compounds which were not previously known to interact the cell surface receptors.

2) Motivation to modify the cited references

The CAFC said that a motivation to modify teaching contents of a cited reference could come from the knowledge which a skilled person in the art had at the time of invention, from a reference itself or from the nature of the problems to be resolved. And then, the CAFC further affirmed it was known at the time of invention that the heterologous cell surface receptors would be ideal candidates for drug screening methods, and examined the following two cited references.

3) Two citations: the Lester's article and the Dull patent

The CAFC states that the Lester's article taught a drug screening method utilizing cells which express heterologous cell surface receptors in order to overcome such a condition in which highly empirical approaches is necessary for the drug design and in which there was no specific functional assay method for the receptors, and that the article taught the screening method which could be widely used in the physiological and pharmacological fields. Further, the CAFC said that such a teaching is identical to the problems to be solved in the '629 patent, that is, to enable to screen a large number of samples to be tested and to identify desired drugs by providing rapid and effective means to identify compounds which interact with receptors localized in cell surface. The CAFC stated also that there was a teaching of a similar drug screening method with the use of cells having cell surface receptors in the Dull patent.

SIBIA argued that there was no teaching on cells having a reporter gene in the Lester's article and the Dull patent. The CAFC, however, affirmed that such an argument was confusing obviousness with anticipation and that cells having a reporter gene construct were known to be useful for drug screening methods in the art at the time of the invention.

4) Conclusion

The CAFC reversed the decision of district court for the reasons that the claims on the '629 patent were obvious because teachings in the Lester's article and the Dull patent provided the motivation to modify a method taught in the Stumpo's article to the method of the '629 patent in consideration of the nature of the problems in the '629 patent.

(4) Claims (Abstract)

1. A method for identifying compounds that modulate cell surface protein-mediated activity by detecting intracellular transduction of a signal generated upon interaction of the compound with the cell surface protein, comprising: comparing the amount of transcription of a reporter gene or the amount of reporter gene product expressed in a first recombinant cell in the presence of the compound with the amount of transcription or product in the absence of the compound, or with the amount of transcription or product in a second recombinant cell ;and selecting compounds that change the amount of transcription of a reporter gene or the amount of reporter gene product expressed in the first recombinant cell in the presence of the compound compared to the amount of transcription or product in the absence of the compound, or compared to the amount of transcription or product in the second recombinant cell, wherein;

(5) References

1) File history
- Date of filing: August 7, 1990 [US Patent Application No.563751]
- Date of issue of patent: March 28, 1995 [USP 5401629]
- Date of request of reexamination: October 9, 1998
- Date of change of name: August 2, 1996 (from Salk Institute to Sibia Neurosciences)

2) Patent family
- Japan: PCT Application No.502527/1994, Appeal trial for examiner's decision
- Europe: EP 542830A, under examination
- USA: USP 5436128

3) References
- Stumpo's article: J. Biol. Chem., 263, p.1611
- Lester's article: Science, 241, p.1058
- Dull patent: USP 4859609

4.2 Case Title: A Synthetic Insecticidal Crystal Protein

Case number:	CAFC No.00-1127
Type of case:	Patent infringement suit
Date of trial decision:	May 30, 2001
Country name:	USA
Parties concerned:	Mycogen Plant Science, Inc. and Agrigenetics, Inc. v. Monsanto Company
Document name:	The court opinion

(1) Main legal decision

1) Infringement of process patent against a section imported (35 U.S.C. §271(g))

Requirements for a fact to correspond to sell or use of a product "which is made by a process patented in the United States" under Section 271(g) is that the patent must have been issued and in force at the time of manufacturing of the product by the patented process. Accordingly, in cases that the process had been used before the patent issued, selling or using product dose not infringe the process claims under Section 271 (g).

2) Doctrine of equivalents

In a case that claims defining the synthetic gene by a broadly specified DNA sequence were cancelled and replaced with claims containing a more narrowly specified DNA sequence, prosecution history estoppel barred application of the doctrine of equivalents. Accordingly, the product claims would not be infringed by equivalents in this case.

(2) Outline of the case

Mycogen Plant Science, Inc. (hereinafter "Mycogen"), a patentee of U.S. Patent No.5380831 (hereinafter "the '831 patent"), and its licensee, Agrigenetics, filed a suit against Monsanto Company (hereinafter "Monsanto") in the United States District Court for the Southern District of California, charging Monsanto with infringing the said patent.

For summary judgment, the district court ruled that: [1] the process claims of the '831 patent are invalid under Section 102(g), [2] Monsanto could not have infringed Section 271(g) based on any process Monsanto performed before the '831 patent issued, and [3] prosecution history estoppel barred application of the doctrine of equivalents to the product claims of the '831 patent. Mycogen filed an appeal against the summary judgment.

In the review by the appellate court on the appeal, the court's ruling on summary judgment that the '831 patent is invalid under Section 102(g) was reversed for the reason that there is a genuine issue of material fact as to judge whether Mycogen was diligent or not, whereas the appellate court affirmed that the district court's ruling that there was neither infringement under Section 271(g) nor patent infringement under the doctrine of equivalents for the scope of claims for patent.

(3) Details of legal decision

1) Infringement of process patent against a section imported (35 U.S.C. §271(g))

Section 271(g) defines that "Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States be liable as an infringer, if the importation, offer to sale, sale, or use of the product occurs during the term of such process patent".

The verbs "made" and "patented" in the phrase that "a product which is made by a process patented in the United States" are part of a parallel construction, which suggests that the process must have been patented at the time the product is made.

The principal purpose of the statute was to prevent a patent owner's competitions from avoiding the patent by producing products outside the United States and when importing them, and the purpose is evident from the legislative history. The statute was intended to grant patent holders the same protection against overseas infringers as well as against domestic entities. A domestic entities do not infringe a process patent if they practice the process before the beginning of the patent term, even if they sell the product of the process during the term of the

patent. Accordingly, the statute does not reach pre-issuance use of the later-patented process.

2) The doctrine of equivalents

Mycogen's filing was rejected for the grounds of obviousness and lack of enablement. Therefore, Mycogen canceled the widely defined claims on synthetic gene (claims of 1, 2, etc.) and replaced the claims by a narrow scope of claims on synthetic gene (claims 13 and 14 at the time of publication) defined by DNA sequence thereof.

In Festo, it was ruled that amendment that narrows the scope of a claim for any reason related to the statutory requirement of a patent will give rise to prosecution history estoppel to the amended claim element. There is no legally meaningful difference between revoking claims having broad scope to replace it with claims having narrow scope and amendment for narrowing the scope of claim. Accordingly, Mycogen's amendment constitutes prosecution history estoppel.

3) Section 102(g) (Omitted)

(4) Claims

1) Established claim (Abstract)

1. A method of designing a synthetic Bacillus thuringiensis gene to be more highly expressed in plants, comprising the steps of: analyzing the coding sequence of a gene derived from a Bacillus thuringiensis which encodes an insecticidal protein toxin, and modifying a portion of said coding sequence to yield a modified sequence which contains a greater number of codons preferred by the intended plant host than did said coding sequence.

13. A synthetic gene comprising the DNA sequence presented in Fig. 1, spanning nucleotides 1 through 1793.

14. A synthetic gene comprising the DNA sequence presented in Fig. 1, spanning nucleotides 1 through 1833.

2) Claims revoked during the process of examination (Abstract)

a1. A synthetic gene designed to be highly expressed in plants comprising a DNA sequence encoding an insecticidal protein which is functionally equivalent to a native insecticidal protein of Bt.

a2. A synthetic gene of claim 1 wherein said DNA sequence is at least about 85% homologous to a native insecticidal protein gene of Bt.

(5) References

1) File history

- Date of filing: Application of [US Patent Application No.57191] in May 3, 1993, as continued and partly continued application of [US Patent Application No. 535354] of September 26, 1983.
- Date of patent issue: January 10, 1995 [USP 5380831]

5. Decisions of the Boards of Appeal of the E.P.O. in Europe

5.1 Case Title: Novel Thrombolytic Protein

Case number:	T0743/97-3.3.4
Type of case:	Appeal against the ieterlocutory decision of opposition
Date of trial decision:	July 26, 2000
Name of country:	Europe
Parties concerned:	Genetics Institute, Inc. (Patentee), Boehringer Ingelheim GmbH (Opponent)
Document name:	The decision of the Technical Board of Appeal of EPO

(1) Main legal decision

1) Sufficiency of disclosure and support by the description of the patent specifications

A question that experimental data for supporting a claim to "having an improved fibrinolytic profile" are not described in the specification may be of relevance for issue of inventive step, if the achievement of an improvement is the decisive factor for non-obviousness, not for the issue of sufficient disclosure and support by the description because there are not doubts about the possibility of preparing and testing them with undue burden or application of inventive skill.

2) Inventive step

The rationale of "improvement of fibri-

nolytic profile by modification of amino acid sequences in the specified regions", provided by the patent in suit, on which the claims at issue are based is not a mere intellectual exercise for designing compounds out of idle curiosity but a plan for achieving a technical result which was devised and developed starting from a series of prior art observation. The provision of this plan constitutes the further step contributed by the patent in suit to the art for which the question has to be asked whether it was inventive or not.

(2) Outline of the case

European Patent No.293394 is relevant to an invention of a modified protein having tissue plasminogen activator (t-PA)-type activity, wherein at least one of the consensus N-linked glycosylation sites is modified and wherein at least one or more amino acids in the specified regions at the N-terminal end of the molecule are deleted and/or substituted. The modified protein having t-PA-type activity has an improved fibrinolytic profile relative to native human t-PA. In opposition procedure, the present patent was decided to be maintained in subject matter of the auxiliary claim request lodged by the appellants (the proprietors). Expressing their dissatisfaction with the decision, however, the appellants filed a new main request and new documents with the statement of grounds of appeal. Then, the appellants submitted another main request at the oral proceedings. Disputes arouse on the following matters relevant to the main claim submitted at the oral proceedings; [1] the suitability of claim amendment, [2] the inventive step, [3] the issues of sufficiency of disclosure and support by the description. The boards of appeal disagreed to all the arguments submitted by respondents, set aside the decision of the opposition division and remitted the case to the first instance with the order to maintain the patent on the basis of the main request as submitted in the oral proceedings.

(3) Details of legal decision

1) Sufficiency of disclosure and support by the description of the patent specification (EPC 83, 84)

Respondents argued that the sufficiency of disclosure and support by the description were incomplete because actual experimental data relevant to "the improved fibrinolytic profile" were not disclosed in the specification. The boards of appeal, however, determined that the patent specifications provides sufficient details of technical information for preparing and testing the variants in the scope of claims, and disagreed to the respondents' arguments pertaining to the sufficiency of disclosure and support by the description for the reason that the arguments are matters relevant to inventive step as referred to the said paragraph (1) Main decision matters, subparagraph 1).

2) Inventive step (EPC 56)

The boards of appeal determined first that the problem to be solved in the present invention would be to provide variants having improved fibrinolytic profiles and that the claims at issue would propose the group of t-PA variants as well as the methods and means for making them and it also would actually provide a solution to the underlying technical problem. And then, they described their determination which was indicated in the said paragraph (1) main decision matters, subparagraph 2) against the arguments by respondents that 'no inventive step could be acknowledged to claims directed to a group of "contemplated" compounds for which no particular properties could be inferred from the patent specification other than, possibly, those already predictable from the prior art'. Then, the boards of appeal concretely investigated whether a skilled person could, readily achieve the claimed invention based on prior arts.

The boards of appeal decided that it was impossible to reach the subject-matter from any of the various prior arts including variants having modified N-terminal regions or modified consensus N-linked glycosylation sites cited by the respondents and that the prior arts are not sufficient for allowing skilled person to combine them with expecting realizing improved fibrinolytic profiles.

Respondents argued that the surprising effects argued by appellants could not be the ground of inventive steps because such effects were based on the post-published documents (document 26), whereas the boards of appeal took the document as expert opinions and affirmed the inventive step of the claim, confirming that the descriptions "uncertainties of the

relation between the structure and activity of t-PA" and "it was unexpected to find that removal of amino acids at the N-terminal end resulted in improved effects" are supporting the view of the said boards of appeal.

(4) References

1) File history
- Date of filing: January 30, 1987 [EP Application No.87902884.3] (Date of priority claim: January 31, 1986 [USP Application No.825104], and other 3 applications)
- Date of patent issue: April 20, 1994 [EP 293394B]
- Date of decision for opposition: April 15, 1997

2) Patent family
- Japan: Patent No.2527454, Patent No. 2568382 and Patent No.2679915

3) References
- Document (26): WO-A-89/00197

5.2 Case Title: Astaxanthin Producing Yeast

Case number:	T 0737/96-3.3.4
Type of case:	Administrative review against the decision of opposition
Date of trial decision:	March 9, 2000
Name of country:	Europe
Parties concerned:	DSM N. V. [Respondents (patentees)], [hereinafter "appellant (opponents)"] Burns Philp & Co. Ltd., Arher-Daniels-Midland Company, KI Chemical Industry Co. Ltd., Kyowa Hakko Kogyo, Igene Biotechnology, Inc.
Document name:	The decision of the Technical Board of Appeal of EPO

(1) Main legal decision

1) Inventive step (EPC 56)

It was obvious for the skilled person to enter the route of treating a naturally occurring Phaffia rhodozyma strain with a mutagen for making more astaxanthin. This involved nothing out of the ordinary, but only the persistent application of routine mutation techniques. The boards of appeal found nothing in the available prior art which would have dissuaded the skilled person from using this widely used approach on Phaffia and considered that the incomplete knowledge about Phaffia would not have deterred the skilled person therefrom as mutagenesis is well suited in such technical circumstances.

(2) Outline of the case

Claim 1 proposes essentially a method of preparation of a Phaffia rhodozyma yeast cell which, under defined conditions, produces astaxanthin in an amount of at least 600 μg per g of yeast dry matter. The method comprises treating a naturally occurring Phaffia rhodozyma yeast cell with a mutagen.

The patentees and three out of the four opponents lodged an appeal against the interlocutory decision of the opposition division by which 'the European patent No.0367 765 was maintained in amended form on the basis of the auxiliary request then on file (method claims 1 to 10)'.

Oral proceedings took place thereafter, and patentees filed a new main request (claims 1-14) and an auxiliary request (claims 1-14) in replacement of all previous requests.

(3) Details of decision matters [Inventive step, EPC 56]

The boards of appeal stated that the relevant question in relation to inventive step is what measures the skilled person faced with the stated technical problem would have considered adopting, in the light of the quoted prior art and common general knowledge, and whether these would have included a method covered by claim 1.

As for this question, the patentees argued that "In view of the peculiarities of Phaffia rhodozyma, which had been shown to be strikingly different from other yeasts, and which was still unknown in many aspects, the skilled person would not have readily considered applying mutagenesis thereto in order to improve the yields of astaxanthin and knew that random mutagenesis was not straightforward and by no means always successful. Even if he or she

had come to the idea of applying it to Phaffia, this would not have been done with a reasonable expectation to isolate mutants displaying the yields actually achieved by the patent in suit".

Contrary to patentee's position, the boards of appeal considered that the skilled person would have considered applying mutagenesis technique precisely for the reasons that; [1] Document (2) explicitly invited the skilled person to improve the astaxanthin yields by way of genetic manipulation and, by reference to document(8), pointed to mutagenesis as this was the only technique, [2] Mutagenesis techniques were well known in the art and the application of these techniques did not presuppose much knowledge of the properties of the target organism, and [3] As not much was known about Phaffia, genetic engineering and protoplast fusion were not readily practicable. For these reasons, the boards of appeal considered that it was obvious for the skilled person to enter the route of treating the known Phaffia rhodozyma strains with a mutagen in order to improve yields of astaxanthin.

For the reasons given above, the boards of appeal considered that the measures adopted by a skilled person faced with the underlying technical problem would have included a method as covered by claim 1.

Claims of the auxiliary request were limited to the specifically deposited strains of Phaffia or mutants or derivatives thereof. One of the appellants, however, objected that the patent proprietors were not entitled to claims covering their mutants or derivatives producing open-ended amounts of astaxanthin because these were not sufficiently disclosed.

As for the above claims, the boards of appeal found that the mutants or derivatives, albeit achieved by conventional mutagenesis techniques, constituted a contribution to the art which deserved patent protection because it contained elements of surprise which justified the recognition of an inventive step.

As regards the "mutants or derivatives" of the deposited strains, the boards of appeal did not share the appellants' view for the reasons that it would be contrary to the principle of granting a fair protection for the patentee if mutants or derivatives of the deposited strains were not covered by the claims and that none of the claims at issue was specifically directed to mutants or derivatives producing eg 2000 or 3000 µg per g of yeast dry matter for which questions of enablement would have to be discussed.

For these reasons, the boards of appeal set aside the decision under appeal, and remitted the case to the first instance with the order to maintain the patent on the basis of the auxiliary request submitted in the oral proceedings.

(4) Claims (Abstracts)

(The main request)

1. A method of preparation of Phaffia rhodozyma yeast cell which, when grown under conditions comprising an oxygen transfer rate of at least 30 mmoles/l/hour on Difco YM medium at 20-22°C for 5 days in 500 ml shake flasks with two baffles containing 50 ml of the medium and subjected to orbital shaking at 150 rpm, the inoculum being 100 µl of a four days old YM culture, produces astaxanthin in an amount of at least 600µg per g of yeast dry matter, determined by HPLC analysis using pure astaxanthin as a standard on a methanol extract of the yeast prepared by subjecting a suspension of 0.2 g of yeast dry matter in 20 ml of methanol to 5 x 1 minutes of disintegration at intervals of half a minute, the disintegration being performed at a temperature of at the most 20°C in a glass ball mill containing 15 g of glass balls having a diameter of 0.4 mm, the glass ball mill being provided with a cooling jacket with ice water, said method comprising treating a naturally occurring Phaffia rhodozyma yeast cell with a mutagen which is ethylmethan sulphonate or N-methyl-N'-nitro-N-nitrosoguanid.

(The auxiliary request)

1. A Phaffia rhodozyma yeast cell which is yeast cell belonging to the yeast strain deposited under the accession No. 225-87 CBS, or the yeast strain deposited under the accession No. 215-88 CBS, or the yeast strain deposited under the accession No. 224-87 CBS, which has retained its astaxanthin-producing capability, and when grown under conditions comprising an oxygen transfer rate of at least 30 mmoles/l/hour on Difco YM medium at 20-22°C for 5 days in 500 ml shake flasks with two baffles containing 50 ml of the medium and subjected to orbital shaking at 150 rpm, the inoculum being 100 µl of a four days old YM culture, produces asta-

xanthin in an amount of at least 600μg per g of yeast dry matter, determined by HPLC analysis using pure astaxanthin as a standard on a methanol extract of the yeast prepared by subjecting a suspension of 0.2 g of yeast dry matter in 20 ml of methanol to 5 x 1 minutes of disintegration at intervals of half a minute, the disintegration being performed at a temperature of at the most 20°C in a glass ball mill containing 15 g of glass balls having a diameter of 0.4 mm, the glass ball mill being provided with a cooling jacket with ice water.

(5) References

1) File history
- Date of filing: April 15, 1988 [EP Application No.88903778.4]
  (Date of priority claim: April 15, 1987 [Danish Application No.871998])
- Date of patent issue: August 25, 1993 [EP 367765B]
- Date of decision for opposition: June 27, 1996

2) Patent family
- Japan: Examined patent application publication No.14340/1995, Unexamined patent application publication No.69969/1999
- USA: USP 5599711 etc

3) References
- Document (8): Murillo F. J. et al., Appl. Environ. Microbiol., Vol. 36, pp.639-642 (1978)

6. Closing

Biotechnology Committee has been publishing the decisions of the judiciaries for biotechnology in Japan, Europe, and the US for the past 10 years. In this paper, focusing attention mainly on the validity of patents or the patentability of an invention, we selected 6 decisions from the Tokyo High Court, the CAFC, and the Boards of Appeal of the EPO made over the past 3 years.

Comparative studies on patentability in the field of advanced new technologies, including biotechnology, have been performed in the Tripartite Patent Offices. It is difficult to say, however, that the patent practices of examination as to the patentability of biotechnological invention have been fully harmonized in the Tripartite Patent Offices. Under these circumstances, judging from the findings of the Board of Appeal, the Patent Office, and the Court introduced here in, it is obvious that there are significant differences in the patent examination practices in the Trilateral Offices and the legal standards of patentability among the Trilateral. Concerning common understandings based upon the above Trilateral circumstances in the field of biotechnology, we can say that it is required for the patent applicant to provide more complete specifications in the application, in order to claim the valid patent rights for an invention. Our role, as patent practitioners, working for the acceptance of patent applications, is becoming more and more important, from the stage of preparation of patent specifications for preparing complete specification.

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