BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS | BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE | CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Publication in the Official Journal ~~Yes~~ / No

File Number: T 109/91 - 3.3.2

Application No.: 83 302 478.9

Publication No.: 0 093 611

Title of invention: Composite plasmid

Classification: C12N 15/00

D E C I S I O N
of 15 January 1992

Proprietor of the patent: AJINOMOTO CO., INC.

Opponent: DEGUSSA AG, Frankfurt
- Zweigniederlassung Wolfgang -

Headword: Composite plasmid/AJINOMOTO

EPC Articles 54(3) and (4), 111

Keyword: "Novelty - burden of proof - Weight of evidence in opposition proceedings - Remittal to Opposition Division for further examination of novelty"

Headnote follows.

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Headnote

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Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : T 109/91 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 15 January 1992

Appellant : (Opponent)
Degussa AG, Frankfurt
- Zweigniederlassung Wolfgang-
Rodenbacher Chaussee 4
Postfach 1345
W - 6450 Hanau 1 (DE)

Respondent : (Proprietor of the patent)
AJINOMOTO CO., INC.
5-8, Kyobashi 1-chome, Chuo-ku
Tokyo 104 (JP)

Representative :
Bond, Bentley George
Haseltine Lake & Co
28 Southampton Buildings
Chancery Lane
London WC2A 1AT (GB)

Decision under appeal :
Interlocutory decision of the Opposition Division of the European Patent Office dated 7 December 1990 concerning maintenance of European patent No. 0 093 611 in amended form.

Composition of the Board :

Chairman : P.A.M. Lançon
Members : U.M. Kinkeldey
R.L.J. Schulte

Summary of Facts and Submissions

I. European patent application No. 83 302 478.9 was granted as European patent No. 0 093 611 with thirteen claims.

II. Notice of opposition against the European patent was filed and revocation of the patent was requested on the grounds of Article 100(a), in particular of Article 54(3) EPC.

The Respondents submitted during the opposition proceedings several requests. Claims 1 and 4 of the second auxiliary request read as follows:

"1. A composite plasmid which comprises (A) a DNA replication region derived from a plasmid (a) chosen from pAM 330 (ATCC 13869), pAM 286 (FERM-P 5485) or pHM 1519 (ATCC 13058), and (B) a gene fragment derived from a plasmid (b) capable of propagating in Escherichia coli and having at least a region expressing drug resistance.

4. A composite plasmid which comprises (A) a DNA replication region derived from a plasmid (a) chosen from pAM 330 (ATCC 13869), pAM 286 (FERM-P 5485) or pHM 1519 (ATCC 13058), and (B) a gene fragment derived from a plasmid (b) capable of propagating in Bacillus subtilis and having at least a region expressing drug resistance."

III. The Opposition Division maintained the patent on the basis of these claims for the following reasons:

In EP-A-0 082 485 (document (1)) which had to be considered as prior art within the meaning of Article 54(3) EPC indeed the subject-matter of Claims 1 and 4 was disclosed as far as the more general features were concerned of (A) a DNA replication region derived from a plasmid (a) capable of propagating in a Coryneform

glutamic acid-producing bacterium and (B) a gene fragment derived from a plasmid (b) capable of propagating in E. coli or B. subtilis and having at least a region expressing a drug resistance. Document (1) disclosed furthermore certain examples of such plasmids.

Since, however, in the claims of the patent in suit reference was made to certain distinguished deposited plasmids, lack of novelty of the claims in question could only be proved by showing that the complete DNA sequence of the specific plasmid as mentioned in document (1) was identically the same as the one of the deposited claimed plasmids. This comparison could be carried out by DNA sequencing techniques developed nowadays. Through the deposition of the plasmids in question not only some properties of said plasmids were disclosed but also the whole molecule was made available to the public and consequently all its properties were potentially disclosed. Therefore, although the Opponent had shown that the submitted parameters are comparable for both plasmids, these parameters were considered as not being sufficient either in quantity or in quality to allow a clear conclusion about the identity between said two plasmids.

The Opposition Division hence considered that the Opponent had not demonstrated the identity between two plasmids in question and that, therefore, the objection under Article 54(3) EPC was not founded.

IV. The Appellants lodged an appeal against the decision and submitted a Statement of Grounds.

During the appeal proceedings the Appellants argued essentially as follows:

Sufficient evidence was provided by the experiments submitted during the opposition proceedings. These experiments and results already provided an analysis of many more features as were contained in the description of the plasmid in question in the patent itself. It was thus a requirement going far beyond the burden of proof of an Opponent to provide evidence that the entire DNA sequence of the plasmids to be compared was identical. To consider the deposition of living material as a de facto description as it did the Opposition Division was not derivable from the law.

The results of the experiments provided by the Respondents here thus were considered to be sufficient to show that one of the starting plasmids mentioned in Claims 1 and 4 was not novel.

The Respondents argued essentially as follows:

Plasmid pCG1 was described and claimed in document (1) by certain restriction sites and other data. There was further disclosed a composite plasmid constructed in part from plasmid pCG1. The territory covered by the claims of the patent in suit included a composite plasmid which, in part, was constructed from a plasmid pHM1519. Whether the prior art extended into the area of the claim depended upon whether pHM1519 and pCG1 were identical. This was a matter of fact. The burden of proof was upon the Appellants to show that the prior art did contain subject-matter which extended into the claimed territory. The only way in which the Appellants could achieve this was to provide full DNA sequence data for the two plasmids. Not to require an analysis of identity to that degree would mean shifting the burden of proof onto the Patentee.

As to the experiments and the values for the length of certain restriction fragments, provided during the opposition proceedings with a letter of 17 January 1990 it was pointed out that in the case of the restriction enzymes BglII and ScaI the lengths differed by the value of 0.02 respectively. Therefore, although it was agreed that all other restriction fragments were identical, the mentioned differences were by no way negligible. In view of this both plasmids had to be considered as not being identical and thus Claims 1 and 4 were novel over document (1).

V. Oral proceedings took place on 15 January 1992.

During the oral proceedings the Respondents filed an auxiliary request based on claims which differed from those of the main request such that the plasmid pHM1519 as one of the starting materials was cancelled in Claims 1 and 4.

VI. The Appellants requested that the decision under appeal be set aside and that the European patent No. 0 093 611 according to the main request be revoked.

The Respondents requested that the appeal be dismissed; auxiliary request: to maintain the patent on the basis of Claims 1 to 11 filed during oral proceedings.

The Appellants did not submit any request with respect to the auxiliary request of the Respondents.

Reasons for the Decision

1. The appeal is admissible.

2. Novelty (Article 54(3) and (4) EPC)

2.1 Only the question of novelty is at issue.

2.2 Document (1) is considered as the closest state of the art. It relates broadly to novel vector plasmids. In particular there are disclosed novel vector plasmids and processes for producing the same by inserting DNA fragments containing a gene expressible in a microorganism belonging to the genus Corynebacterium or Brevibacterium into a plasmid derived from a microorganism belonging to the genus Corynebacterium or Brevibacterium. On page 7, lines 3 to 25, of document (1) certain plasmids being able to autonomously replicate in cells of the genus Corynebacterium or Brevibacterium are disclosed, one of them being the plasmid in question pCG1. It is described that this plasmid and further plasmids have been deposited with two acknowledged depositories namely the American-type Culture Collection and the Fermentation Research Institute, Agency of Industrial Science and Technology. In the case of plasmid pCG1 the deposition number is mentioned on page 10, line 11. From the written disclosure on page 10, line 10 in connection with Figure 4 of document (1) a further feature of plasmid pCG1 is apparent, namely that it contains a unique BglII recognition site and that this plasmid was isolated from Corynebacterium glutamicum 225-57 (ATCC 31808 and FERM P-5865). By reference to the deposition number the availability of plasmid pCG1 as starting material for further recombinant DNA techniques in the construction of derivative plasmids is given.

2.3 In the patent in suit the plasmid pHM1519 is disclosed in the specification in written form. In Figure 3 the restriction map of this plasmid is shown, wherein a

molecular weight of 1.8 Md is given and further the location and identification of certain restriction enzyme sites. Inter alia it is apparent from this Figure that the plasmid contains a unique BglII restriction site. In Table 3 on page 7 again the sensitivity to restriction enzymes and the restriction site map is shown. Furthermore, it is disclosed that the plasmid in question pHM1519 had been separated from Corynebacterium glutamicum (ATCC 13058). This plasmid was deposited to supplement the written description of this plasmid, to ensure its availability and disclosure within the meaning of Rule 28 EPC.

2.4 A comparison of the features of the two plasmids in question as disclosed in written form shows that both plasmids had been isolated from bacteria of the same species, namely Corynebacterium glutamicum and that both of them have the same BglII restriction site. These common features provide a first indication that the claimed plasmid may well be the same as that described in document (1).

2.5 The Board agrees with the argument of the Respondents that in opposition proceedings the burden of proof is on the Opponent to show that a technical disclosure in a prior art document is the same as the one in a patent attacked by an Opponent (cf. T 270/90 of 21 March 1991, point 2.1). In the present proceedings the Appellants were aware of this situation and therefore made use of the possibility to provide further comparative data of the plasmids in question by investigating further technical features of the plasmids as deposited. They requested samples of both plasmids from the depositories and carried out an analysis of altogether 27 restriction sites and the length of the respective restriction fragments (see letters of 18 October 1989 and 17 January 1990). The restriction

sites are identical for both plasmids as shown in the experiments provided by the Appellants and also are in accordance with the restriction sites shown in Table 3 and Figure 4 of the patent in suit. From a table submitted during the opposition proceedings by the Appellants with letter of 18 October 1989, it is further evident which restriction enzymes do not cut at all the plasmids to be compared. Also these results are identical for both plasmids.

2.6 The Respondents put emphasis on the fact that the results provided by the Appellants show in two cases differences in the length of the restriction fragments, namely for the fragment BglII, where a length of 3.15 is given for plasmid pHM1519 and a length of 3.13 for the plasmid pCG1. Further a length of 3.06 in the case of the fragment ScaI for the plasmid pHM1519 was found whereas a length of 3.08 in the case of plasmid pCG1 was given. In the Board's view these differences are not decisive and cannot lead to the judgment that the plasmids must be considered as not being identical. Rather, the Board considers the quality and quantity of the features which correspond to each other in both plasmids as sufficient and convincing proof in view of which the mentioned tiny differences are negligible.

2.7 The Opposition Division raised during the proceedings the argument that showing the identity of the restriction sites as has been done by the Appellants provides less than 5% identity of the DNA of the complete plasmids to be compared. This was considered not to be sufficient to convince the Opposition Division of the identity of the two plasmids. However, in view of those data provided by the Appellants, which show full comparability for those restriction enzymes which do not cut at all the plasmids, being features which to the skilled person also provide information about typical characteristics of a certain DNA

- entity, does not at the same time giving any evidence about the exact base pair sequence of the plasmids. This shows that the evaluation of less than 5% identity of the DNA sequence apparent from the evidence provided by the Appellants is not the only conclusion which can be drawn for answering the question of identify. Rather this feature must be weighed in the light of the fact that restriction characteristics as such have their own force of expression. In other words, considerably more information was actually available.

2.8 It is true that a comparison of the complete nucleotide sequence of both plasmids, as requested by the Opposition Division as the only sufficient evidence of identity or non-identity of the plasmids to be compared, would provide more information about the molecular identity of the two plasmids. It is, however, the question whether in the cases of deposited plasmids the Opponent - to fulfil its burden of proof - has to provide an analysis of each and every technical detail of the deposited material. The Opposition Division based its request in this respect on the assumption that by the deposition of living material the depositor de facto not only disclosed some properties of this living material, but indeed made the whole molecule available to the public and consequentially potentially disclosed the entirety of its properties.

2.9 In the Board's opinion, the position of the Opposition Division confuses the requirements of Article 54, Article 83 and Rule 28 EPC and the quantity and quality of the burden of proof of an Opponent in opposition proceedings. Rule 28 states the requirement of a sufficient disclosure within the meaning of Article 83 EPC as far as microorganisms are concerned which cannot be described in words such that the invention can be carried out by a skilled person. A such disclosed plasmid, as is

the case here, can be used by a skilled person without the necessity of the knowledge of the molecular structure of this plasmid. A connection of the requirements of a deposition of living material to the implicit knowledge of the molecular structure for the purposes of the judgment of novelty is not self-evident.

2.10 The standard burden of proof in opposition cases is generally expressed as proof on the balance of probabilities, absolute certainty is not required but a degree of probability which in human experience verges on certainty (D 5/86, OJ EPO 1989, 210). If the evidence is such that the Division or the Board can conclude "we think it more probable than not", the burden is discharged. The burden of proof may shift constantly as a function of the weight of the evidence. In this case the Appellants provided enough evidence to demonstrate to the conviction of the Board that the plasmids in question are identical. The mere allegation of the Respondents that the plasmids are not identical is for the Board not convincing. After the shift of burden of proof it would have been the obligation of the Respondents to substantiate their allegation of non-identity by facts.

2.11 When now weighing the evidence now on file, it becomes apparent that the Opponents already went far beyond what had been disclosed in words to describe the plasmids to be compared by requesting the deposited microorganisms from the depository, isolating the respective plasmids and analysing as much as 27 restriction sites, the respective length of the restriction fragments and defining eight restriction enzymes which do not cut the plasmids at all. Although one can accept the Respondent's argument that even an identity of that amount of restriction characteristics does not exclude the possibility that there may be other differences of the plasmids, it is

nevertheless also the case that an identity of that degree of restriction characteristics provide evidence of convincing weight. In this context it is important that there is nowhere any hint in the documents or in the submissions on file that the plasmids to be compared may differ in any respect, for example in containing certain different genes coding for different proteins.

2.12 The Board thus concludes that the evidence provided by the Appellants that plasmid pCG1 is the same as the claimed plasmid pHM1519 is convincing and there was no necessity for the Appellants to go further in its analysis of the complete DNA-molecules of both plasmids.

3. During the opposition proceedings it was requested that the Opponents provide as convincing evidence of the identity of the plasmids in question a complete nucleotide sequence analysis. The patent was maintained because the Opponents did not do so. The Board now comes to the conclusion that these reasons cannot be followed and accordingly a new position arises in which the Respondents should be allowed the opportunity to provide evidence to the contrary. The Board therefore considers it to be in the interest of fairness that the parties be given, the opportunity to react to the new position before two instances and thus the case is remitted in accordance with Article 111(1) EPC.

4. The question of novelty of the claims of the main request being not finally decided yet leaves no room for examination of the auxiliary request.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Opposition Division for further prosecution.

The Registrar: The Chairman:

P. Martorana P.A.M. Lançon