BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

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File Number: T 0242/92 - 3.3.2

Application No.: 86 305 459.9

Publication No.: 0 211 543

Title of invention: Invasive microorganisms

Classification: C12N 15/00

D E C I S I O N
of 26 May 1993

Applicant: THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Headword: Invasive microorganisms/LELAND STANFORD JUNIOR UNIVERSITY

EPC Art. 83 and 84

Keyword: "Disclosure (yes); sufficiency (yes)" - "Claims; support by description"

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : T 0242/92 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 26 May 1993

Appellant : THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY
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Decision under appeal : Decision of the Examining Division of the European Patent Office dated 6 November 1991 refusing European patent application No. 86 305 459.9 pursuant to Article 97(1) EPC.

Composition of the Board :

Chairman : P.A.M. Lançon
Members : L. Galligani
E.M.C. Holtz

Summary of Facts and Submissions

I. European patent application No.86 305 459.9, published under No. 0 211 543, was refused by the Examining Division on 6 November 1991.

The decision was taken on the basis of a main request which comprised Claims 1 to 11 (all States except AT) and Claims 1 to 8 for Austria filed by letter of 16 January 1991. The first and second auxiliary requests filed on 22 October 1991 which comprised a modified Claim 1 (in the two versions for all States except AT and for Austria) were also rejected.

Claim 1 of the main request (all States except AT) read as follows:

" A unicellular microorganism having invasive phenotype attributable to a single membrane protein, the said protein being expressed as a result of the introduction of exogenous DNA into said microorganism or progenitor thereof ".

The claims for Austria were formulated as method claims.

II. The Examining Division refused the application under Article 97(1) EPC on the grounds that the it did not comply with the requirements of Article 83 EPC.

The decision is based on the following main reasons:

(a) the only example given in the application is one of a normally non-invasive bacterium (E.coli) into which exogenous DNA from Yersinia encoding a

single membrane protein that confers the invasive phenotype was introduced;

(b) no other suitable invasive organisms are known from common general knowledge or from postpublished literature which could be used to produce the same effect. The known Shigella flexneri, in which the invasive phenotype is encoded by at least two genes [see Infection and Immunity, 1985, Volume 49, pages 164 to 171 (1)], would not be suitable. As for the invasive organisms listed on page 9 of the description, no evidence has been provided that they could be used to put the invention into practice. To the skilled person testing of the listed organisms in order to find a suitable invasive organism would represent an undue burden of experimentation with no reasonable certainty of success;

(c) in view of the above, unlike in case T 292/85 (OJ EPO 1989, 275), there are good reasons to conclude that the process leading to the claimed product is not generally applicable and reproducible (reference is made to the Guidelines for Examination in the EPO, C-III, 6.4).

III. The Appellants appealed against this decision and paid the appeal fee.

A modified set of claims was filed together with the Statement of Grounds of Appeal by letter dated 16 March 1993.

The Appellants' arguments are essentially as follows:

(a) the application has shown for the first time that a single gene can be responsible for invasive phenotype and that it can be used for conferring the phenotype on a different, usually non-invasive, microorganism;

(b) a simple screening protocol has been provided for determining whether a single gene is present in an organism which allows for the transformation from a non-invasive host to an invasive host. This protocol has been shown in the examples to work in respect of Yersinia. There is no suggestion that it would not be effective in other organisms;

(c) the invention is restricted to a group of organisms known to invade mammalian cells which can be easily tested by the skilled person using the said screening protocol. The example of Shigella flexneri is not relevant, as prior to the invention, the problem of invasiveness was not understood;

(d) in the light of decisions T 292/85 and T 81/87 (OJ EPO, 1990, 250), it would be unfair to restrict the claims to the microorganism exemplified and exclude variants that might be used in the future and whose preparation can be considered undue only in the sense of excessive tedium.

IV. The Appellants request that a patent be granted on the basis of a modified Claim 1, followed by Claims 2 to 11 (all States except AT) amended accordingly, and the description as amended on page 9. This request corresponds to the first auxiliary request presented during the examination proceedings. Claim 1 reads as follows:

" A bacterium capable of invading mammalian cells having invasive phenotype attributable to a single membrane protein, the said protein being expressed as a result of the introduction of exogenous DNA into said bacterium or progenitor thereof".

The grant of a patent in respect of the corresponding claims for Austria is also requested.

Reasons for the Decision

1. The appeal is admissible.

2. *Amendments (Article 123(2) EPC)*

There are no objections under Article 123(2) EPC in respect of the amendments to the claims and to page 9 of the description. The restriction of the original term "unicellular microorganism" to "a bacterium" finds support in the application as originally filed (see page 9, lines 25 to 34).

3. *Clarity (Article 84 EPC) and sufficiency of disclosure (Article 83 EPC)*

The claimed bacterium is defined in the new Claim 1 on the basis of the following features:

(a) it is capable of invading mammalian cells (functional feature);

(b) feature (a) is attributable to a single membrane protein (functional feature);

(c) the protein of (b) is expressed as a result of the introduction into the bacterium of exogenous DNA (product-by-process feature).

The quoted features are comprehensible from a technical point of view. Their combination defines clearly the object of the invention.

The requirement of clarity is therefore satisfied by the claims of the three requests.

The Examining Division refused the application on the grounds of insufficient disclosure under Article 83 EPC. However, in the Board's view, an objection, if at all, to the scope of main Claim 1 would primarily arise under Article 84 EPC.

Thus the question at issue here is whether or not the extent of generalisation from the description to the claims is permissible.

The example given in the application relates specifically to the introduction into E.coli of an exogenous gene from Yersinia which encodes a single membrane protein responsible for the invasive capability (inv gene). E.coli is shown to acquire thereby the invasive phenotype. Thus the desired effect is obtained.

The application describes a general selection protocol for identifying the genetic capability of invasiveness and provides a non-exhaustive list of organisms from which inv genes can be obtained. It is generally stated that preferred organisms are those which provide a single gene resulting in invasive capability and that the affinity for the mammalian host receptor should be

at least about 0.1. Yersinia is said to be paradigmatic of such organisms.

Admittedly, the possibility of transferring the invasive phenotype from pathogenic bacteria to non-invasive bacteria was known in the art (see the introductory part of the present description, which refers inter alia, to document (1)). However, as is apparent from the introduction to the application and from (1), this property was thought to be plasmid-linked and to be associated with the expression of more than one gene product. The present applicant has shown that in Yersinia, at least, the invasiveness phenotype is linked to a chromosomal gene (designated as inv) encoding a single membrane protein. This finding constitutes the basis for the claimed subject-matter.

According to the Examining Division, the fact that in Shigella flexneri the invasive phenotype is encoded by at least two genes (at least four major peptides appear to be involved) raises serious doubts about the existence of any other invasive microorganisms, apart from Yersinia, which could be used to carry out the invention. In the Examining Division's opinion, the existence of this unsuitable variant and the consequent uncertainty about the starting materials represent an undue burden to the skilled person.

The Board concedes that no evidence is available to show that the invasiveness phenotype is associated with the expression of a single membrane protein in any of the organisms other than Yersinia listed on page 9 of the description. However, there seem to be no serious doubts, sustained by verifiable facts, about the possibility of extending the teaching of the present application in an analogous way to other organisms.

The arguments based on Shigella are not tenable because:

(i) Shigella is not listed as a donor of the inv gene in the present application (N.B. Shigella is merely mentioned on page 8, line 27 as a possible source of antigens to be expressed in the resulting bacterium) and

(ii) Shigella is automatically excluded as a donor of the inv gene based on the wording of the main claim which **explicitly** requires the invasiveness phenotype to be attributable to **a single membrane protein.**

The application instructs the skilled person to use, as a source of the inv gene, microorganisms which can provide a single gene resulting in invasive capability (see description page 9, lines 35 to 36; main claim). Consequently, the skilled person would not be inclined to use Shigella flexneri in which, according to (1), the inv capability is linked to **more than one** gene.

On the other hand, no well-founded reasons have been put forward to show that the approach successfully exemplified in respect of Yersinia could not be applied, in an analogous way, to other organisms for which - now or in the future - the above requirement is satisfied.

According to EPO case law, the function of Article 84 EPC is to safeguard the interest of applicants and the public alike, in that the claims, while ensuring fair protection, may not cover subject- matter which in the light of the description would not be readily available to the skilled person (see, for example, T 26/81, OJ EPO 1982, 211; T 133/85, OJ EPO 1988, 441).

In the present case it is not disputed that the information in the application is sufficient to carry out the invention in respect of the Yersinia inv gene. The mere fact that only one way of carrying out the invention is indicated does not in itself offer grounds for considering that the application is not entitled to broader claims. At the present stage no concrete evidence is available that the skilled person would be unable to extend the particular teaching of the description to a broader field by using routine methods. In view of the contribution to the art by the present applicant it would be unjustified, in the absence of well-founded reasons, to restrict the claims to the specifically exemplified embodiment.

The same approach has been followed by this Board in other cases (see, for example, T 292/85 OJ EPO 1989, 275; T 19/90 OJ EPO 1990, 476 and T 81/87 OJ EPO 1990, 244), and there are no reasons in the present case to depart from previous practice.

To sum up, the Board finds that the claims are supported by the description, in accordance with Article 84 EPC, the invention being sufficiently disclosed within the meaning of Article 83. The extent of generalisation adopted in the claims is therefore considered permissible.

4. During the examination proceedings, the Examining Division conceded novelty and inventiveness of the specific embodiment relating to Yersinia (see official communication dated 6 September 1990, in particular item 2.5). However, since the Board considers that a broader claim is allowable under Article 84 EPC, the novelty and inventive step issues will have to be examined in respect to said broader claim. The case is

therefore remitted to said first instance for further prosecution under Article 111 EPC.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution on the basis of the modified Claim 1 with the consequent amendments to Claims 2 to 11 in the two versions for all States except AT and for AT and of the amended page 9 as filed by letter dated 16 March 1992.

The Registrar: The Chairman:

P. Martorana P.A.M. Lançon