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File Number: T 772/89 - 3.3.2

Application No.: 83 306 655.8

Publication No.: 0 112 012

Title of invention: Genomic bovine growth hormone, its prevention, and hosts containing it

Classification: C12N 15/00

D E C I S I O N
of 18 October 1991

Applicant: Case Western Reserve University

Headword: Bovine growth hormone/C.W.R.U.

EPC Article 83

Keyword: "Sufficiency of disclosure - main and first auxiliary request (no)
- second auxiliary request (yes)"

Headnote



Case Number : T 772/89 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 18 October 1991

Appellant : Case Western Reserve University
Cleveland
Ohio 44106 (US)

Representative : Perry, Robert Edward
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Decision under appeal : Decision of Examining Division 023 of the
European Patent Office dated 29 June 1989
refusing European patent application
No. 83 306 655.8 pursuant to Article 97(1) EPC.

Composition of the Board :

Chairman : P. Lançon
Members : A. Nuss
R. Schulte

Summary of Facts and Submissions

- I. European patent application No. 83 306 655.8 was filed on 1 November 1983 and published under No. 0 112 012.
- II. The Examining Division refused this application under Article 97(1) EPC on the sole ground that the invention covered by Claims 2 to 4 lacked sufficiency of disclosure and thus the application did not meet the requirements of Article 83 EPC. The decision was based on 9 claims filed by the Appellant in a letter dated 8 September 1988.

Claim 1 is directed to a recombinant DNA molecule comprising the genomic nucleotide sequence encoding bovine growth hormone, the sequence being indicated in the claim.

Claims 2 to 4 read as follows:

"2. A host modified to contain a DNA molecule according to Claim 1.

3. A host according to Claim 2, which is a microorganism containing the DNA molecule as a replicatable DNA transfer vector.

4. A host according to Claim 3, in which the microorganism is Escherichia coli x 1776 or Escherichia coli HB101, and in which the plasmid is pBR322."

Claim 5 reads as follows:

"5. A process for preparing bovine growth hormone, which comprises culturing a host according to any of Claims 2 to 4."

III: In its decision, the Examining Division took the view that the Appellant did not show that the European patent application disclosed the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. As Claims 2 to 4 cover by implication hosts expressing the bovine growth hormone gene, it was up to the Appellant to show that such expressing hosts were well known to persons skilled in the art at the priority date. However, the Appellant neither did so in the documents as originally filed nor in the twelve additional documents filed with his letter dated 8 September 1988, among which document (1) Mol. Cell. Biol., 1982, 2, pages 233 to 240, the document the Appellant has mainly relied upon.

The Examining Division left undecided the question whether Claim 5 was also not allowable under Article 83 EPC.

IV. The Appellant lodged an appeal against the decision of the Examining Division.

V. In his written submissions, the Appellant argued essentially as follows:

(i) Among the documents submitted with his letter of 8 September 1988, there were some which disclosed the expression of DNA sequences having considerable homology with the BGH sequence of Claim 1 and others which disclosed that it was standard procedure in 1982 (i.e. at the priority date) to introduce recombinant genes into mammalian cells and obtain expression of these genes. In view of the fact that BGH was relatively small, had no post-translational processing beyond the ubiquitous signal sequence

cleavage and also no activity on standard mammalian cell lines, the skilled man would not have expected any difficulties in expressing the BGH gene by standard methods.

- (ii) An Affidavit signed by M. Post, one of the authors of document (1), was submitted in which M. Post affirmed that it was anticipated that the teaching of document (1) could be applied in a straightforward and predictable manner to the expression of BGH. The teaching of the Affidavit further tried to demonstrate that the procedure described in document (1) for the expression of ovalbumine, indeed with a slight modification, worked when applied to BGH. This straightforward success was a good basis for supposing that the exact procedure disclosed in document (1) would work for BGH.

VI. The Appellant submitted two auxiliary requests. Auxiliary request (I) is identical to the main request, with the exception of Claim 2 in which the term "host" has been amended to read: "microorganism or cell line host". In auxiliary request (II), Claims 2 to 5 of the main request have been deleted and Claims 6 to 9 accordingly renumbered.

VII. The Appellant requested that the decision under appeal be set aside and a patent be granted on the basis of the claims of the main request or of any of auxiliary request (I) or (II).

Reasons for the decision

1. The appeal is admissible.
2. Amendments (Article 123(2) EPC)

The Board endorses the finding of the Examining Division that the claims of the main request comply with Article 123(2) EPC.

The amendment proposed for Claim 2 in auxiliary request (I) finds support on page 5, lines 4 to 5 of the original description, where one can read: "They (the BGH genomic clones of the invention) can be used to direct the synthesis of BGH in a suitable eukaryotic host, e.g. cell lines and organisms". Moreover, it is clear from original Claim 4 that the host may be a microorganism. In the Board's view, therefore, the fact that the term "microorganism" is used in the amended claim, whereas the description as originally filed refers to "organism", cannot lead to the conclusion that the European patent application as amended contains subject-matter which extends beyond the content of the application as filed.

The amendments proposed in auxiliary request (II) only amount to the deletion of Claims 2 to 5 of the main request.

No objection with regard to Article 123(2) thus arises in relation with any of the auxiliary requests.

3. Sufficiency of the disclosure (Article 83 EPC)

Main Request

- 3.1 Claim 2 of the main request is directed to a host containing the DNA molecule defined in Claim 1. It thus

covers hosts suitable for both cloning and expressing the genomic BGH nucleotide sequence and the description must accordingly contain a disclosure enabling the man skilled in the art to prepare both types of hosts. As regards the cloning, the Examining Division has never objected to the sufficiency of disclosure and the Board does not see any reason to content this point. As regards the expression the description does not contain any example of a suitable host but the Appellant sustains that the common general knowledge of the man skilled in the art enabled him to prepare such a host without undue burden.

3.2 In his Statement of Grounds of Appeal, the Appellant has mainly relied on document (1) (and the corresponding Affidavit from M. Post), selected out of the twelve documents all submitted with his letter dated 8 September 1988. The Board accordingly will base its decision mainly on this document.

3.3 The first question which arises is whether document (1), which is a scientific paper published in March 1982, can be considered as common general knowledge of the man skilled in the art. The Boards of Appeal have already addressed the question of what constitutes common general knowledge within the meaning of the EPC. In decision T 580/88 of 25 January 1990 (unpublished in OJ EPO), the Board considered that as a general principle, the disclosure cannot be made sufficient by means of a document not cited in the application as filed (see points 2.2 and 2.3 of the Reasons). The Board also reaffirmed the need to draw a distinction between general technical literature or standard textbooks, which are clearly within common general knowledge, and patent specifications, which as a general rule, are not. This principle was first affirmed in decision T 171/84 (OJ EPO 1986, 95) and an exception was introduced by decision T 51/87 (OJ EPO 1991, 177) which decided that when the

invention is in a field of research which is so new that technical knowledge is not yet available from textbooks, special considerations prevail on whether or not the common general knowledge of the man skilled in the art may include a patent specification.

In the present case, it remains questionable whether in 1982, the field of recombinant DNA technology was still so new that the man skilled in the art would have derived his knowledge from sources such as scientific papers not yet available from textbooks but available only from scientific publications. In view of the remaining doubt and the outcome of the subsequent question to be answered, the Board is ready to accept in this case, in favour of the Appellant, the view that document (1) can be considered as part of the common general knowledge of the man skilled in the art of producing a mature protein via a recombinant host.

- 3.4 The second question which arises is whether the man skilled in the art as above defined would, without undue burden, arrive at the invention covered by Claim 2 having at his disposal the content of document (1).

Document (1) discloses the expression of the chicken ovalbumin gene with an expression system consisting of the Herpes Simplex Virus 1 (HSV-1) tk gene covalently linked to an HSV-1 alpha promoter directed away from the tk gene. The tk gene allows for efficient and unambiguous selection of cells which carry the ovalbumin gene, the transformed cells being TK- (see page 233, column 2, lines 4 to 17). The paper ends up by saying that it seemed likely that the HSV alpha protein promoter was a general tool that could be used to obtain efficient expression of spliced and unspliced genes in mammalian cells (see page 239, last sentence). Being aware of this teaching, a straightforward

procedure for the man skilled in the art aiming at expressing another gene (BGH gene instead of chicken ovalbumin gene) would therefore have been to use the promoter disclosed in document (1).

3.5 By contrast, the Applicant's evidence, as provided for in the Affidavit submitted by M. Post, according to which the skilled man could produce BGH in view of document (1), tends only to demonstrate that, in the present case, a procedure different from that disclosed in document (1) was in fact used for the production of BGH. In particular, the promoter used was an immediate early promoter from human cytomegalovirus. Consequently, another human herpes virus is used, instead of the HSV-1 alpha promoter disclosed in document (1). The selection gene is also different since the procedure disclosed in the Affidavit uses the mouse dhfr gene - instead of the tk gene disclosed in document (1). The Applicant thus does not provide any evidence that at the priority date of the present application, (i.e. 8 November 1982), document (1) contained sufficient information on a specific expression system that would enable the man skilled in the art to find hosts suitable to perform the alleged invention.

3.6 As regards all the other documents (2) to (12), the Appellant has refrained from developing a complete argumentation, but has only indicated in general terms that these documents disclosed standard procedures, directly applicable to the expression of the BGH gene, for the expression of recombinant DNA by mammalian cells. It is up to the Appellant to develop a complete and convincing argumentation to support his submissions and, when citing documents, to clearly point out which parts of the documents are particularly relevant in relation with these submissions. In the present case, the Board has no reason to believe, contrary to the Appellant's

assertion, that these documents contain a disclosure of standard methods to introduce recombinant DNA into mammalian cells and obtain expression of those genes. A standard method in the field of recombinant DNA technology is, by definition, a method which can be applied as such, in a straightforward manner, for the expression of genes other than those exemplified in the description of the method. The Board has nevertheless examined documents (2) to (12) of its own motion, but has found in these documents neither a disclosure of the specific expression system used by M. Post for the expression of the BGH gene (which tends to prove that the method used by M. Post was not a standard method in 1982), not an indication that any of the disclosed methods was of a general applicability (which tends to prove that none of the disclosed method was a standard method in 1982). And the Applicant has never himself provided any evidence that any of the methods disclosed in documents (2) to (12) for the expression of a determined gene actually worked in a straightforward manner for the expression of the BGH gene. Under these circumstances, the question of the exact date of publication (before or after the priority date of the present application) of some of the cited documents could be ignored.

It follows from the above that the Board has no reasons to believe that a host according to Claim 2, insofar as it is an expression host, was available to the main skilled in the art on the basis of the common general knowledge in this field.

- 3.7 In these circumstances, the patent application in suit does not provide a sufficient disclosure within the meaning of Article 83 EPC.

For this reason, the Appellant's main request must fail.

4. First auxiliary request (auxiliary request (I))

The claims of the first auxiliary request do not differ from those of the main request in a way which could provide a basis for a different evaluation of the sufficiency of the disclosure of the subject-matter of Claim 2. The above reasoning, therefore, applies.

5. Second auxiliary request (auxiliary request (II))

5.1 By deleting the refused Claims 2 to 4 as well as former Claim 5, the second auxiliary request is restricted to unamended Claim 1 and to four renumbered claims directed to the plasmids and cloning strains as deposited.

5.2 Accordingly, their subject-matter meets the requirements of sufficiency of disclosure within the meaning of Article 83 EPC.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the Examining Division for further prosecution on the basis of Claims 1 to 5 of the second auxiliary request.

The Registrar:

The Chairman:

P. Martorana

P.A.M. Lançon