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Datasheet for the decision of 14 January 2009

Case Number: T 1331/07 - 3.3.08

Application Number: 92924278.2

Publication Number: 0670848

IPC: C12N 1/21

Language of the proceedings: EN

Title of invention:
High molecular weight collagen-like protein polymers

Patentee:
PROTEIN POLYMER TECHNOLOGIES, INC.

Opponent:
STEINECKE, Dr. Peter

Headword:
Collagen-like polymers/PROTEIN POLYMER

Relevant legal provisions:
EPC Art. 123(2)

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main request - added subject-matter (yes)"
"Auxiliary requests 1 to 4 - added subject-matter (yes)"

Decisions cited:
-

Catchword:
-

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Case Number: T 1331/07 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 14 January 2009

Appellant: (Patent Proprietor)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 31 May 2007 revoking European patent No. 0670848 pursuant to Article 102(1) EPC 1973.

Composition of the Board:

Chairman: L. Galligani
Members: P. Julià
C. Heath

Summary of Facts and Submissions

I. European patent No. 0 670 848, based on the International application PCT/US92/09485 and published under the PCT as WO 93/10154 with the title "High molecular weight collagen-like protein polymers" (referred to in this decision as "the application as originally filed"), was granted with 12 claims.

II. The patent was opposed on the grounds as set forth in Articles 100(a),(b) and (c) EPC and revoked because the opposition division considered that the main request (claims as granted) did not fulfil the requirements of Article 123(2) EPC and that claim 1 of a first auxiliary request filed at the oral proceedings of 19 March 2007 contravened Article 54 EPC.

III. The patentee (appellant) filed a notice of appeal, paid the appeal fee and, in a letter dated 5 October 2007, submitted a statement setting out its grounds of appeal. The appellant maintained the same requests as before the opposition division, namely the claims as granted as main request and the first auxiliary request filed on 19 March 2007. This latter request was filed again with the grounds of appeal together with new auxiliary requests 2 to 4.

IV. In a letter dated 22 February 2008, the opponent (respondent) replied to appellant's grounds of appeal.

V. With the summons to oral proceedings, the board sent a communication dated 2 September 2008 pursuant to Article 15(1) of the Rules of the Boards of Appeal

(RPBA), indicating its preliminary, non-binding opinion to the parties, in particular on Article 123(2) EPC.

VI. In letters dated, respectively, 12 December 2008 and 7 January 2009, both the appellant and the respondent informed the board of their intention not to attend the oral proceedings while maintaining all their requests on file.

VII. Oral proceedings took place on 14 January 2009 in the absence of both parties.

VIII. Claim 1 of the appellant's **main request** (claims as granted) read as follows:

"1. A collagen-like polymer of at least 30kD as determined by SDS-PAGE, obtainable by expression in a unicellular organism from a construct prepared in vitro,

comprising at least 60 weight % of triads having glycine as the first amino acid and at least 40 number % said triads comprising at least one proline wherein the overall proline content between said glycines of said triads is less than 60 number %,

having as a motif present at least twice, either contiguous or non-contiguous, a sequence having the following formula:

$$\{(GXO)_nZ\}_m$$

wherein:

X and O are selected such that the motif has a proline content of less than or equal to 40 number %;

Z has from 0 to 50 amino acids and is other than repetitive GXO;
m is at least 1;
n is in the range 4 to 100;
the total number of different triads in the $(GXO)_n$ motif is at least three;
and said polymer has a collagen-like property selected from the group consisting of helix formation, reversible denaturation and gel formation."

Claims 2 to 6 were directed to particular embodiments of claim 1. Claims 7 to 8 related to DNA sequences encoding a collagen-like polymer according to claims 1 to 6 and claim 9 to a unicellular microorganism comprising those DNA sequences. Claim 10 was directed to a method for producing these collagen-like polymers using the microorganism of claim 9. Claims 11 and 12 concerned a formed object (gel, film, fiber) comprising the collagen-like polymers.

IX. The subject-matter of claim 1 of all the **auxiliary requests 1 to 4** was directed to "a collagen-like polymer" sharing the same first features as the "collagen-like polymer" of claim 1 of the main request, namely being "of at least 30kD as determined by SDS-PAGE, obtainable by expression in a unicellular organism from a construct prepared in vitro, comprising at least 60 weight % of triads having glycine as the first amino acid and at least 40 number % said triads comprising at least one proline wherein the overall proline content between said glycines of said triads is less than 60 number %".

X. The arguments of the appellant, insofar as relevant to the present decision, may be summarised as follows:

Main request
Article 123(2) EPC

The feature "said polymer has a collagen-like property selected from the group consisting of helix formation, reversible denaturation and gel formation"

This feature had a basis in the description on page 4, lines 21 to 24. The presence of the term "etc." at the end of the list of properties indicated to the skilled person that any one or more of these properties could be chosen to define a "collagen-like" polymer so the presence of all three of these properties at the same time was neither necessary nor required by this section of the description.

The feature "at least 30 kD as determined by SDS-PAGE"

No arguments were presented by the appellant in the appeal proceedings regarding this feature, even though it was explicitly objected by the respondent in its reply to the grounds of appeal. In its communication pursuant to Article 15(1) of the RBPA, the board also questioned the interpretation made by the opposition division of this feature in its decision. The appellant did not, however, reply thereto.

XI. The arguments of the respondent, insofar as relevant to the present decision, may be summarised as follows:

Main request
Article 123(2) EPC

The feature "said polymer has a collagen-like property selected from the group consisting of helix formation, reversible denaturation and gel formation"

Singling out and defining any one of the properties referred to in the description as filed to mean "being like collagen" neither was supported nor made sense since the individual properties could be found in other proteins as well.

The feature "at least 30 kD as determined by SDS-PAGE"

The person skilled in the art knew that 1 Da was a unit of mass that equalled the weight of one hydrogen atom. This was the meaning of "kD" (kilodaltons, 1000 Da) in original claim 1. Nowhere in the description was there a statement that the term "Dalton" or "kD" had to be defined otherwise. This common use of the terms "Dalton" and "kD" was even a prerequisite when willing to understand the instructions in original claim 1 and the teaching of the application as filed since the presence of the repetitive sequence (triad) was given in weight % and % per weight, respectively. Thus, the skilled person in order to conceive a collagen-like polymer had to calculate the number of triads on a reliable basis and thus refer to the calculated molecular weight of the polymer. Otherwise, it was not possible to follow the instructions because: i) the apparent molecular weight for a given polymer could be obtained only after it had been conceived and produced; and ii) the value would have varied and be dependent on

the host expression system employed to produce the polymer and the SDS-PAGE conditions used to determine the molecular weight. Therefore, the actual molecular weight was always indicated for the selected polymers simply in kD on the basis of the calculated molecular weight of the intended polymer.

The kD values observed in SDS-PAGE/Western blots related to the apparent molecular weight, thus experimental mass, which was sufficient in order to determine whether any novel protein had been expressed. The disclosure relied on by the appellant for defining kD by SDS-PAGE determination in the application as filed merely related to the detection of novel protein bands, i.e. to prove that the predefined polymer had been expressed. For this purpose, the indication of the apparent molecular weight in relation to a marker protein ladder was certainly appropriate and the actual experimental conditions were not essential. However, there was no mentioning whatsoever that for the purpose of the definition and construction of the claimed polymer, its molecular weight had to be determined experimentally.

XII. The appellant (patentee) requested in writing that the decision under appeal be set aside and the patent be maintained on the basis of the main request (claims as granted) or, in the alternative, any of auxiliary requests 1 to 4 filed with the grounds of appeal on 5 October 2007.

XIII. The respondent (opponent) requested in writing that the appeal be dismissed.

Reasons for the Decision

Main request
Article 123(2) EPC

1. In the communication dated 2 September 2008 pursuant to Rule 15(1) of the RPBA (cf. point V *supra*), the board expressed its preliminary opinion that the opposition division's conclusions in respect of the feature "*said polymer has a collagen-like property selected from the group consisting of helix formation, reversible denaturation and gel formation*" could be followed. In line with the decision under appeal, the board was of the preliminary opinion that this feature constituted added subject-matter (cf. page 4, point 9(ii) of the board's communication). The interpretation made by the opposition division of the feature "*at least 30 kD as determined by SDS-PAGE*" was also questioned by the board (cf. page 6, point 10(v) of the board's communication).

2. Whereas the first feature is only present in the main request, the second feature is found in all requests on file, namely in the main request (claims as granted) and in auxiliary requests 1 to 4 (cf. point IX *supra*). Thus, the conclusion reached for this second feature in the main request will apply to all these auxiliary requests as well. It is noted that no substantive reply to the board's communication have been made by any of the parties, both of which decided not to use the opportunity to present their case at oral proceedings while maintaining their respective requests (cf. points VI and VII *supra*).

The feature "said polymer has a collagen-like property selected from the group consisting of helix formation, reversible denaturation and gel formation"

3. According to the appellant, this feature has a basis on page 4, lines 21 to 24 of the application as filed which reads "*the polymers will be further characterized in, being like collagen, providing helices, capable of denaturation and renaturation, forming gels, etc.*" and, wherein particular emphasis has been put on the term "*etc.*" as indicating that any one or more of these properties could be chosen to define a "collagen-like" polymer (cf. point X *supra*). However, the board cannot share the appellant's argument, since the interpretation made of the term "*etc.*" is considered to be inappropriate and not to be in line with the natural interpretation of this term.

4. The appellant's reference found in the application as filed characterizes the designed, synthetic polymers disclosed in the application as "*being like collagen*" or, as the case may be in the claimed subject-matter, being "*collagen-like*" and therefore, having the properties known to characterize natural collagen. A list of some of those properties known to characterize natural collagen, as that given in the reference relied upon by the appellant, does not suggest in any manner that a single one of these properties or, of other undefined (non-listed) properties that might fall within the general term "*etc.*", is sufficient for a polymer to be defined as being a "*collagen-like*" polymer, i.e. for defining the intended "*likeness*" to natural collagen. Appellant's reference does not

support a selection of each and every one of the natural collagen's properties for defining the likeness of a designed, synthetic polymer to natural collagen. Hence, this feature is considered to constitute added subject-matter within the meaning of Article 123(2) EPC.

The feature "at least 30 kD as determined by SDS-PAGE"

5. In the application as filed, both "the summary of the invention" and "the description of the specific embodiments" constantly and consistently refer to "*synthetic*" genes encoding the compositions of the invention, i.e. the "*collagen-like polymers*" disclosed in the application (cf. *inter alia* page 3, lines 15 to 24, page 4, lines 11 to 14) and, accordingly, as stated in the application as filed, the compositions of the invention are described by specific "*formuli*" [sic!] (cf. page 5, lines 18 to 19). Similarly, reference is also made in the claims as originally filed to a "*construct prepared in vitro*" (cf. claim 1 of the application as filed). As synthetic constructs, they will be designed by the skilled person following the disclosed "*formuli*" and they will have therefore specific molecular weights that may easily be calculated on the basis of these constructs' specific "*formuli*". This all the more so, since particular components of those constructs are defined by specific weight percent (cf. *inter alia* page 5, lines 7 to 12, page 6, lines 24 to 25, claim 1).

6. It is also in this context that reference is made in the application as filed to the molecular weight of the "*collagen-like polymers*", namely "*the polymers of this invention will be characterized by having a molecular*

weight of at least about 30 kD ..." (cf. page 4, lines 16 to 18), which is the reference relied upon by the appellant. However, there is no mention to SDS-PAGE in this reference nor is any found in "the summary of invention" or in "the description of the specific embodiments". What is more, there is no reference at all to any experimental method for determining the specific molecular weight of the designed polymers in the general description of the application as filed, although this feature is well understood by the skilled person to be an essential feature for characterizing those collagen-like polymers and absolutely necessary for establishing the correct - precise and exact - amount of some of their components (weight %).

7. It is only in Example 1 of the application as filed that polyacrylamide gel electrophoresis of proteins is described (cf. page 25, lines 4 to 17). Example 1 describes first DNA preparation methods, mRNA methods and bacterial transformation methods. The reference to the SDS-PAGE is found in the section concerned with "Antibody production, Protein Chemistry and Electrophoresis of Proteins" just before the subsection "Protein expression analysis". Example 2 relates to "DNA design" and discloses several specific polymer gene constructions which are expressed in E. coli strains. It is in the context of protein expression analysis that reference is made to an "apparent molecular weight" determined by SDS-PAGE (cf. page 40, lines 13 to 15 and page 70, lines 5 to 7). Although the apparent molecular weight of the SDS-PAGE protein bands of different constructs is indicated in the Tables given in Example 2 (cf. Tables 5, 8, 11 and 14), there is always and consistently a reference to the specific

molecular weight of all those constructs as well (cf. *inter alia* page 40, line 26, page 42, line 18, page 48, line 13). In line with the general description of the invention, and in contrast to the experimental SDS-PAGE molecular weights, these specific molecular weights are understood to be those molecular weights calculated from the "*formuli*" of the designed synthetic constructs.

8. In the application as filed, the determination of molecular weights by SDS-PAGE is always disclosed as an "apparent molecular weight" of a SDS-PAGE band and used - only and exclusively - to identify whether or not an expressed protein has the desired size (cf. page 13, lines 3 to 6). This size derives, however, from a specific synthetic polymer gene construct previously designed and thereby, having a specific (calculated) molecular weight. It is only this specific molecular weight which allows for a correct calculation of the exact amount or (weight) percentage of some components of those constructs. There is no formal support in the application as filed linking or combining (weight) percentages and (apparent) molecular weights as determined by SDS-PAGE. Such a combination can only be derived from separate parts of the application, namely the general description of the invention and particular disclosures present only in the examples of the application. There is, however, no hint or suggestion in the application leading the skilled person to such a combination and therefore, in line with the established case law of the boards of appeal which rules out to combine features pertaining to separate embodiments in order to artificially create new embodiments (cf. "Case Law of the Boards of Appeal of the EPO", 5th edition 2006, III.A.1.1, page 235), this combination represents

added subject-matter within the meaning of Article 123(2) EPC.

9. Thus, the main request does not fulfil the requirements of Article 123(2) EPC.

Auxiliary requests 1 to 4
Article 123(2) EPC

10. Although all auxiliary requests have been amended to overcome the objection raised under Article 123(2) EPC as regards the feature in relation to the collagen-like property by requiring the polymer to have the three properties of helix formation, reversible denaturation and gel formation, claim 1 of all auxiliary requests still comprises the feature "*of at least 30 kD as determined by SDS-PAGE*" (cf. point IX *supra*). Hence, the reasons given above in points 5 to 9 *supra* for the main request also apply to all auxiliary requests, which therefore contravene Article 123(2) EPC as well.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski L. Galligani