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**Datasheet for the decision  
of 20 May 2021**

**Case Number:** T 1742/16 - 3.3.04

**Application Number:** 10726699.1

**Publication Number:** 2421550

**IPC:** A61K38/17

**Language of the proceedings:** EN

**Title of invention:**

Silk fibroin hydrogels and uses thereof

**Patent Proprietor:**

Allergan, Inc.

**Opponent:**

Tufts University

**Headword:**

Silk fibroin hydrogels/ALLERGAN

**Relevant legal provisions:**

EPC Art. 54, 56, 83, 123(2)

**Keyword:**

Amendments - allowable (no) - main request and auxiliary request 1

Novelty - auxiliary request 2 (yes)

Inventive step - auxiliary request 2 (yes)

Sufficiency of disclosure - auxiliary request 2 (yes)

**Decisions cited:**

**Catchword:**



**Beschwerdekammern**

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**Case Number: T 1742/16 - 3.3.04**

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 20 May 2021**

**Appellant:** Tufts University  
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**Decision under appeal:** **Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
13 May 2016 concerning maintenance of the  
European Patent No. 2421550 in amended form.**

**Composition of the Board:**

**Chairman** P. de Heij  
**Members:** A. Chakravarty  
O. Lechner

## **Summary of Facts and Submissions**

- I. European patent EP 2 421 550, entitled "*Silk Fibroin Hydrogels and uses thereof*" derives from European patent application No. 10 726 699.1. It was originally filed under the PCT and published as WO 2010/123945 ("the application as filed" or "the application").
- II. In an interlocutory decision, the opposition division decided that, account being taken of the amendments in the form of the main request (including the set of claims submitted on 11 February 2016), the patent and the invention to which it related met the requirements of the EPC (Article 101(3)(a) EPC).
- III. An appeal was filed by the opponent (appellant) against this interlocutory decision. The patent proprietor is respondent to this appeal.
- IV. In the decision under appeal, the opposition division dealt with objections raised by the opponent under Article 123(2) EPC, Article 83 EPC, Article 54 EPC and Article 56 EPC.
- V. With the statement of grounds of appeal, the appellant submitted documents D42 and D43 (see section IX., below).
- VI. The respondent replied to the statement of grounds of appeal and re-filed sets of claims of the main request (the set of claims considered allowable by the opposition division), the first and second auxiliary requests, first submitted on 11 February 2016, the third auxiliary request, first submitted on

20 October 2014 and the fourth and fifth auxiliary requests, first submitted on 29 February 2016.

VII. The board issued a summons to oral proceedings together with a communication pursuant to Article 15(1) RPBA 2007, setting out its preliminary and non-binding appreciation concerning the appeal. In that communication, the board set out its view that the subject-matter of claims 3 to 13 of the main request was not directly and unambiguously disclosed in the application as filed because for example, the dependencies of claim 4 as amended seem to result in added matter, as paragraphs [0013] and [0014] of the application as filed do not disclose an embodiment combining the features of a 23RGD motif with a hydrogel comprising 1 to 10% silk fibroin. This problem appeared to apply to all claim requests except auxiliary request 2.

VIII. Claims 1 to 3 of the main request read:

"1. A hydrogel comprising a substantially sericin-depleted silk fibroin and an amphiphilic peptide.

2. The hydrogel of Claim 1, wherein the hydrogel comprises 1% (w/v) to 10% (w/v) of silk fibroin.

3. The hydrogel of Claim 1 or 2, wherein the amphiphilic peptide comprises a RGD motif, preferably is a 23RGD."

Claims 1 to 3 of auxiliary request 1 are the same as claims 1 to 3 of the main request, except that in claim 3 "preferably is a 23RGD" is replaced by "for example a 23RGD".

IX. The following documents are mentioned in this decision.

D2: Gil E.S. *et al.*, "Effect of [beta]-sheet crystals on the thermal and rheological behavior of protein-based hydrogels derived from gelatin and silk fibroin", *Macromol. Biosci.*, 2005, 5(8), 702-709.

D3: Gil E.S. *et al.*, "Swelling behavior and morphological evolution of mixed gelatin/silk fibroin hydrogels", *Biomacromolecules*, 2005, 6(6), 3079-3087.

D6: Zuidam N.J. and Nedovic V.A. (eds), "Encapsulation Technologies for Active Food Ingredients and Food Processing", 2010, Chapter 3, Section 3.2.2.3 "Gelatin", pages 65-67; published online 1 November 2009.

D8: WO 2005/012606

D15: Collette A.L. *et al.*, "Comparative In vivo Evaluation of a novel Silk hydrogel Injectable for Drug Delivery", page 719, corresponding to Abstract No. 719 of the 32nd annual meeting of the Society for Biomaterials 2007, mentioned in document D15a

D15a: Transactions of the 32nd annual meeting of the Society for Biomaterials, published 2012.

D17: Wang Y. *et al.*, "Stem cell-based tissue engineering with silk biomaterials", *Biomaterials*, 2006, 27(36), 6064-6082.

D18: Vepari C. and Kaplan D. "Silk as a biomaterial", *Progress in Polymer Science*, 32(8-9), 2007, 991-1007.

D20: Summary of the characteristics of collagen, taken from <http://www.chem.boun.edu.tr/webpages/courses/leathertechnology/deri4.htm> downloaded on 12 March 2014.

D26: US 5 120 829.

D32: Declaration by Dr. Daunch, February 2016.

D42: Declaration of Prof. David Kaplan, technical expert, dated 21 September 2016, and Appendix 1 thereto and Auweter *et al.*, referred to therein.

D43: Schaffner P. and Dard M., "Structure and function of RGD peptides involved in bone biology", CMLS, Cellular and Molecular Life Sciences, 60(2003), pages 119-132.

- X. The arguments presented by the appellant were directed to the claim request held allowable by the opposition division. However, the board has considered them in the context of all the claim requests on file at the oral proceedings before it (see section XVII., below). The arguments of the appellant relevant to the decision can be summarised as follows.

The appeal was directed against the decision of the opposition division to maintain the patent in amended form, on the grounds of Article 100(a) EPC (Article 54 EPC and Article 56 EPC), Article 100(b) EPC (cf. Article 83 EPC) and Article 100(c) EPC (cf. Article 123(2) EPC). No appeal was made on the grounds of Rule 80 EPC, Article 123(3) EPC, Article 84 EPC or Rule 116(1) EPC.

*Substantial procedural violation (Article 113(1) EPC)*

The decision under appeal was not sufficiently reasoned because it did not take all of the appellant's submissions into account. Instead, the opposition division substituted its own unproven suppositions in place of the evidence on file. This constituted a violation of the appellant's right to be heard pursuant to Article 113(1) EPC.

The requirement of sufficient reasoning had been violated in three ways. The first was the absence from the decision of evidence for the definition of "peptide" to mean "up to 100 amino acids". The second was the absence in the decision of a logical position on the narrow meaning of the term "amphiphilic", proposed by the respondent. This affected the sufficiency of disclosure of the claimed invention. The third was the lack of a decision on whether the silk fibroin of documents D2, D3 and D15 was "substantially sericin-depleted" and whether the "films" taught in documents D2 and D3 comprised a hydrogel.

For these reasons at least, the decision had to be set aside. In addition, the decision of the opposition division on compliance of the main request with the requirements of Article 123(2) EPC was not reasoned in the manner prescribed by Rule 111(2) EPC.

*Amendments (Article 123(2) EPC)*

*Claim 3*

Claim 3 had been amended to include subject-matter not disclosed in the application as filed. The statement that the RGD motif was preferably a 23RGD was not present in the original PCT application in the context



of the generic definition of a hydrogel according to claim 1 or claim 2 as maintained in the patent. Claim 3 of the application as filed merely gave 23RGD as an embodiment (not a preference) of an RGD motif in the context of a hydrogel according to claim 1 (not claim 2).

*Novelty (Article 54 EPC) in view of documents D2, D3, D17 and D18 - claim 1*

The subject-matter of claim 1 as maintained in the decision under appeal lacked novelty over the disclosure in documents D2 and D3 (and also in documents D17 and D18, which referred to them). The opposition division had accepted that documents D2 and D3 disclosed compositions which were hydrogels and which were made by using substantially sericin-depleted silk fibroin. Gelatin was a compound falling within the meaning of the feature "amphiphilic peptide". Indeed, all molecules of which gelatin was composed were peptides which retained the characteristic hydrophilic and hydrophobic groupings of collagen.

Gelatin was obtained by hydrolysing collagen, a naturally occurring full length protein (see document D6, pages 65 to 67, for the nature of gelatin). Gelatin was thus a peptide within the meaning of that term as understood by the person skilled in the art (see document D42, paragraph 3). The amphiphilic nature of the peptide was reported in document D6 (page 66, 4th full paragraph) and this was confirmed in document D42, Appendix 1 for the gelatin type used in documents D2 and D3 (see D2, page 703, second column, "Materials"; D3, page 3080, first column, "Materials").

Document D20 (page 1, numbered paragraph 6) reported that collagen was characterised by the occurrence of hydrophilic and hydrophobic space groupings in a chain, i.e it was amphiphilic. Since the largest of the molecules constituting gelatin was a peptide within the meaning of that term as understood by the person skilled in the art, it was clear that smaller of those molecules were also peptides. Since all the molecules of gelatin were peptides and the peptides of gelatins retained the characteristic hydrophilic and hydrophobic space groupings of collagens, gelatins were amphiphilic peptides within the meaning of the claim.

*Novelty and inventive step (Articles 54 and 56 EPC) in view of document D15 - claim 1*

Document D15 disclosed hydrogels that were relevant to both the novelty and inventive step of the subject-matter of claim 1 as maintained in the decision under appeal. Said subject-matter was anticipated by the disclosure in document D15 and/or lacked an inventive step in view of it alone or in combination with documents D8, D26 or D43.

*Inventive step (Article 56 EPC) in view of documents D8, D2, D3, D17 and D18.*

Document D8 represented prior art as close to the claimed invention as document D15. Starting from document D8, the analogous argument to that given starting from document D15, representing the closest prior art applied. The disclosure in document D8 was combined with that in one or more of documents D15, D43 and D26, teaching to use an amphiphilic peptide as the RGD peptide.

Documents D2, D3, D15, D17 and D18 had also been presented as closest prior art in the first instance proceedings and they were maintained in appeal.

*Disclosure of the invention (Article 83 EPC) - claim 1*

The invention was not disclosed in such a way as to enable the skilled person to carry it out. The claim referred to an "amphiphilic peptide". The skilled person could not determine which molecules were meant by said term without an undue burden with respect to the term "peptide", in view of the fact that the term included any peptide chain being shorter than the full protein. The declaration of Dr Daunch (document D32) exacerbated this problem because it stated that amphiphilic structures had to have "*molecular sizes that do not overwhelm the effect of the hydrophilic and hydrophobic residues*". However, the patent was silent both on the critical amino acid number and how to determine this non-overwhelming effect. There was no evidence that there was common general knowledge of these features in the published literature before the priority date or the filing date of the application.

- XI. The feature "substantially sericin depleted" did not describe the particular degree of sericin-depletion sufficiently clearly to be performed by the skilled person.
  
- XII. The arguments of the respondent relevant to the decision can be summarised as follows.

*Substantial procedural violation (Article 113(1) EPC)*

The appellant had raised three points where they considered that the opposition division had made a

substantial procedural violation. The first was the lack of evidence in the decision for the term "peptide" to mean amino acid chains of "up to 100 amino acids". The second was the absence of a logical position on the construction of the term "amphiphilic". Finally the appellant considered that there had been no discussion of the argumentation and evidence relating to "substantially sericin-depleted" and "films".

However, there had been no substantial procedural violation in any of these three points. In relation to the appellant's right to be heard, all disputed terms/features had either been discussed at great length during the written procedure or were addressed and discussed during the oral proceedings before the opposition division. The mere fact that the opposition division's position was different from the one of the proprietor did not amount to a substantial violation. The decision under appeal did not rely on grounds or evidence on which the parties had had no possibility to comment. Neither was the decision so unclear that the appellant would not understand how to respond. In relation to the argument that the decision was not reasoned in this respect, this was also incorrect. The opposition division mentioned the numerical cut-off in the definition of the term "peptide" merely to clarify that there was a distinction between the terms "peptide" and "protein". In relation to the term "amphiphilic", the opposition division explicitly referred to paragraphs [0013], [0079], [0083] and [0084] of the patent, which as such could therefore not come as a surprise.

A discussion of the argumentation and evidence relating to "substantially sericin-depleted" and "films" had not

been necessary for the opposition division to come to their decision.

*Main request*

*Amendments (Article 123(2) EPC) - Claim 3*

During the oral proceedings before the board it was argued that the skilled person, at the relevant date of the patent, reading the claims as originally filed in the context of the application as a whole, would understand that the RGD feature could be combined with the 1% (w/v) to 10% (w/v) of silk fibroin feature because both were disclosed as preferred embodiments. This was apparent directly from the claims as filed themselves, since the relevant subject-matter was present in claims 1 to 3 which reflected the importance given to the RGD motif and the particular proportion of silk fibroin in the hydrogel. The skilled person would not have placed undue emphasis on the claim dependency. Instead, turning to the description, the skilled person would have realised that the features in claims 2 and 3 were in preference present in combination, as both were mentioned as preferred in paragraphs [013] to [015], which related to the silk fibroin feature and the amphiphilic peptide features and in the description as a whole, where a hydrogel comprising 1% (w/v) to 10% (w/v) of silk fibroin and the definition of the amphiphilic peptide as comprising an RGD motif were mentioned as preferred throughout. It followed that claim 3 of the main request met the requirements of Article 123(2) EPC.

*Auxiliary request 1*

The same arguments applied to claim 3 of auxiliary request 1.

*Auxiliary request 2*

*Status of document D15 as comprised in the state of the art according to Article 54(2) EPC*

Document D15 was not pre-published. The opposition division's statement that there was no valid reason to assume that this document had not been made available at the meeting in April 2007 was not suitable to prove the availability to the public of the document. No proof of this public availability had in fact been provided. Document D15 did not contain any publication date. Document D15a merely disclosed 2007 and 2012 as copyright dates. Neither of these were proof of the publication date of document D15 and its content.

*Novelty (Article 54 EPC) - claims 1 and 2*

*Over documents D2, D3, D17 and D18*

Neither document D2 nor D3 disclosed a hydrogel comprising a substantially sericin-depleted silk fibroin or an amphiphilic peptide.

Concerning the latter, the appellant's view that gelatin, a constituent of the hydrogels disclosed in documents D2 and D3 was an amphiphilic peptide was incorrect. Document D6 for instance stated that gelatin was a protein, not a peptide. Furthermore, no single citation had been provided in which gelatin was

referred to as a "peptide". In his declaration (document D32), Dr Daunch confirmed this view.

The experimental report, document D42 had been provided by the appellant and purported to prove that gelatin was or comprised an amphiphilic peptide. However, it did not achieve this. Firstly, it did not show conclusively that the gelatin used was identical to the gelatin used by the authors of documents D2/D3, 11 or 12 years earlier.

Secondly, the data present in document D42 were inconclusive. There was no indication that any of the peptides having a length of less than 100 amino acids actually was an amphiphilic peptide. The hydrodynamic diameters of the micelles found (i.e. of those proteins or peptides supposed to be amphiphilic) could not be directly linked to the existence of a single amphiphilic peptide in the gelatin mixture. Moreover, the actual gel shown in the document did not comprise a single visible band corresponding to the marker for that size.

Thus, documents D2 and D3 did not disclose a hydrogel comprising an amphiphilic peptide as claimed. Since documents D17 and D18 were only relevant due to reference to documents D2 and D3, these did not anticipate the claimed subject-matter either.

*Inventive step (Article 56 EPC) in view of document D8*

The claimed subject-matter was inventive starting from document D8 as the closest prior art.

*Disclosure of the invention (Article 83 EPC)*

The argument that the term "amphiphilic peptide" was not sufficiently disclosed in the patent was an objection introduced only during oral proceedings before the opposition division, allegedly in reaction to declaration, document D32. Thus, the argument was late filed during the opposition proceedings and should be excluded from the appeal proceedings. The objection regarding "substantially sericin depleted" was also not to be admitted into the appeal proceedings as it could have been submitted in the first instance proceedings.

On the issue of whether or not the expression "amphiphilic peptide" was the cause of the claimed invention not meeting the requirements of Article 83 EPC, it was noted that a person of skill in the art understood that a peptide was a much smaller molecule than a protein and would also easily be able to provide such a molecule. Indeed, this latter point was not contested by the appellant (see point 5.6.10 of the statement of grounds of appeal).

The term "amphiphilic" would also not have presented an undue hurdle in working the invention because the person of skill in the art knew that an amphiphilic peptide should have both hydrophobic and hydrophilic properties and could carry out the invention by choosing the amino acids accordingly. Should the resultant molecule be very large, it could have a three-dimensional configuration in which the effect of the hydrophobic and hydrophilic residues was overwhelmed, leading to a non-amphiphilic molecule. However, the person of skill in the art would recognise that this was the case and knew that such a molecule did not fall within the expression "amphiphilic



peptide". Furthermore, the objection made by the appellant was, at least in part, an objection of lack of clarity. However, lack of clarity was not a ground for opposition.

- XIII. Oral proceedings before the board took place on 20 May 2021. The appellant had informed the board in writing that they would not attend. The proceedings were continued in their absence (Rule 115(2) EPC and Article 15(3) RPBA).
- XIV. During the oral proceedings, the respondent filed a replacement set of claims as auxiliary request 2. The claims of this request read as follows:
- "1. An hydrogel comprising a substantially sericin-depleted silk fibroin, and an amphiphilic peptide.
2. The hydrogel of Claim 1, wherein the hydrogel comprises about 1% (w/v) to about 10%(w/v) of silk fibroin".
- XV. At the end of the oral proceedings, the chairman announced the board's decision.
- XVI. The appellant requested that the decision under appeal be set aside and that the patent be revoked. Alternatively, the decision under appeal should be set aside due to a substantial procedural violation (breach of the right to be heard and lack of a reasoned decision) and the case should be remitted to the opposition division for further prosecution. In this case, reimbursement of the appeal fee was requested.
- XVII. The respondent's final requests were that the patent be maintained on the basis of the main request (i.e. the

set of claims as maintained by the opposition division) or alternatively on the basis of auxiliary request 1 as filed on 11 February 2016 or on the basis of auxiliary request 2, as filed during the oral proceedings before the board.

### **Reasons for the Decision**

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

#### *Substantial procedural violation (Article 113(1) EPC)*

2. The appellant submitted that the opposition division had violated the requirement that a decision be reasoned in three ways; i) the decision did not provide any evidence for the definition of "peptide" to mean "up to 100 amino acids"; ii) the decision did not provide a logical position on the narrow meaning of the term "amphiphilic", proposed by the respondent, which in turn, affected the sufficiency of disclosure of the invention. Finally, iii) the decision did not address whether the silk fibroin of documents D2, D3 and D15 was "substantially sericin-depleted" or whether the "films" taught in documents D2 and D3 comprised a hydrogel.
3. Addressing the first issue, the board notes that the opposition division stated: "*The opposition division is of the opinion that indeed no exact number of amino acids can be said to define the distinction between a protein and a peptide. However, it seems generally recognized that "peptides" consist of no more than 100 amino acids, whereas proteins are structures composed of a higher number of amino acids. Even though no unambiguous amino acid number can be said to define the*

*limit between a protein and a peptide, it is considered that the skilled man would be able to select many compounds falling within the term amphiphilic peptide, because the term is explained in the patent, and because various examples of hydrophilic and hydrophobic domains are described.*" (see decision under appeal, point 16.3). Thus, the appellant is not correct that the opposition division relied on an unproven definition of the term "peptide". On the contrary, the opposition division concurred with the appellant that the term is ambiguous, but considered why the skilled person, in spite of this ambiguity, was able to select several amphiphilic peptides.

4. In relation to the meaning of "*amphiphilic*" within the feature "*amphiphilic peptide*", the board notes that, also in this context, the opposition division in their assessment of sufficiency of disclosure decided that the description explains what is considered to be an amphiphilic peptide, giving examples of hydrophilic and hydrophobic domains and that the declaration document D32 of Dr Daunch did not contradict that explanation (*ibid*). It therefore cannot be concluded that the opposition division failed to decide on the alleged narrow interpretation of "*amphiphilic*" by the respondent, as this interpretation is clearly not endorsed.
  
5. In deciding that documents D2, D3 and D15 did not anticipate the subject-matter of the independent claims, the opposition division held that none of these documents disclosed "*an amphiphilic peptide*" (see decision under appeal, points 17.2 and 17.6). Thus, it was not necessary for the opposition division to decide whether the silk fibroin of these documents was "*substantially sericin depleted*". For the same reason,

it was irrelevant to discuss and decide whether the films disclosed in document D2 and D3 comprised a hydrogel.

6. In the allegation that the decision under appeal lacked reasoning concerning the compliance of the main request with the requirements of Article 123(2), the appellant refers to "the above reasons", which are, the board assumes, those stated in point 5.5 of the statement of grounds of appeal. In this section, the appellant alleges that several aspects of the reasoning of the opposition division were incorrect. However, the board cannot identify any objection of lack of reasoning, except where the appellant argues that the opposition division did not address the question whether the newly introduced subject-matter of the dependent claims which resulted from amended dependencies, was directly and unambiguously derivable from the application as filed (*ibid*, point 5.5.8).
7. This allegation is not correct because this issue is clearly addressed in point 12.2, third paragraph, of the decision under appeal, where it is explained why the opposition division considered that the combination of features resulting from multiple dependencies in the main request is disclosed in paragraphs [012] to [027] of the application as filed.
8. In view of the foregoing, the board cannot identify any insufficient reasoning or other procedural violation by the opposition division.

*Amendments (Article 123(2) EPC) - Main request - claim 3*

9. The subject-matter of claim 3 is not directly and unambiguously disclosed in the application as filed. In particular, the dependency on claim 2 results in subject-matter relating to a hydrogel comprising 1% (w/v) to 10% (w/v) of silk fibroin and wherein the amphiphilic peptide comprises an RGD motif. This combination is not derivable from the application because original claim 3, which defines the amphiphilic peptide as comprising an RGD motif, is dependent on claim 1 only. Moreover, original claim 2 which defines the hydrogel as comprising 1% (w/v) to 10% (w/v) of silk fibroin, is separately dependent on claim 1. Thus, the original claims do not disclose a hydrogel having a combination of the subject-matter of original claim 3 with that of original claim 2.
  
10. Furthermore, this subject-matter is not derivable from the description of the application as filed. Paragraphs [013] and [014] respectively describe the silk fibroin and the amphiphilic peptide components of the hydrogel of certain embodiments. Paragraph [013] reads "*In another embodiment [...] The gel phase may comprise about 0.5% to about 20% silk fibroin protein by mass, for example about 1 % to about 10% [...]*". Paragraph [014] reads "*In a particular embodiment, the peptide is an amphiphilic peptide consisting of a tail region, followed by a spacer region and finally the sequence arginine-glycine-aspartic acid, known as the RGD motif [---]*".
  
11. The disclosure in the above-mentioned paragraphs does not include a combination of the RGD feature with the particular claimed percentage range for the silk fibroin. Moreover, paragraph [013] relates to an

embodiment of the invention having a gel phase and a carrier phase and not to the more generally defined hydrogel presently claimed.

12. The respondent argued that the skilled person reading the claims as originally filed, in the context of the application as a whole, would understand that the RGD feature could be combined with the 1% (w/v) to 10% (w/v) of silk fibroin feature because both were disclosed as preferred embodiments.
13. However, while it is true that the skilled person would have understood that a hydrogel according to claim 3 as filed had to have a certain percentage of silk fibroin, the board is not persuaded that the skilled person would have understood that 1% (w/v) to 10% (w/v) of silk fibroin was preferred. Indeed, it appears from the description that "*about 4% to about 6% silk fibroin*" is the preferred amount, as this is mentioned multiple times, for instance in paragraphs [015], [016], [020], [0151], [179], [0231], [0232], [0245] and [0250]. Thus, the board cannot agree with respondent's argument that the application as filed when read as a whole directly and unambiguously discloses a hydrogel comprising 1% (w/v) to 10% (w/v) of silk fibroin, wherein the amphiphilic peptide comprises an RGD motif.
14. In conclusion, claims 1 to 3 as originally filed read on their own or in combination with the application as a whole do not disclose the subject matter of claim 3 of the main request. Claim 3 and dependent claims therefore do not meet the requirements of Article 123(2) EPC.

*Auxiliary request 1 - claim 3*

*Amendments (Article 123(2) EPC)*

15. The same issues under Article 123(2) EPC that led to the negative decision for claim 3 of the main request are present for claim 3 of auxiliary request 1. This claim therefore does not meet the requirements of Article 123(2) EPC for the reasons given for claim 3 of the main request.

*Auxiliary request 2*

16. The board decided to admit this claim request in view of exceptional circumstances, as mentioned in Article 13(2) RPBA. The respondent could have been taken by surprise by the change of opinion of the board regarding the issue of compliance of auxiliary request 2 with the requirements of Article 123(2) EPC, from the positive view expressed in the communication pursuant to Article 15(1) RPBA, to a negative view expressed during the oral proceedings.

*Amendments (Article 123(2) EPC)*

17. The objections that led to the board's negative decision on the main request and auxiliary request 1 do not apply to this claim request because the corresponding claims have been deleted.

*Status of document D15 as comprised in the state of the art according to Article 54(2) EPC*

18. Document D15 was cited as prior art by the appellant in relation to both novelty and inventive step of the claimed subject-matter. The respondent argued that it

had not been demonstrated that it or its contents had been available to the public at the the relevant date of the patent.

19. Document D15, as supplied by the appellant, is a single-sided document with an abstract carrying the title "Comparative In Vivo Evaluation of a Novel Silk Hydrogel Injectable for Drug Delivery". The only bibliographic information given on the document itself are the authors' names, their institutional affiliations and "Abstract number - 719" is printed in the footer of the document. No publication date is given.
20. In the absence of a publication date, the board must conclude that document D15 on its own is not sufficient proof that it or its contents were available to the public at the relevant date of the patent (20 April 2009). It remains to be assessed whether it can be proven by other means that document D15 or its contents had been made available to the public.
21. Document D15a, filed by the appellant during the opposition proceedings, has a cover page with the title "*32nd Annual Meeting of the Society for Biomaterials 2007*", and "*Transactions of the 32nd Annual Meeting Volume XXX*". This cover page also mentions the date of the meeting, 18 to 21 April 2007. There are two copyright dates on the document, one being 2007 and the other being 2012. Document D15a contains a reference to an abstract having the same number and title as document D15, as well as a page having the contents of document D15, i.e. the abstract with its title, with the number 719 in the footer.



22. The board considers that document D15a establishes that a document, essentially identical to document D15, was published in 2012.
23. In point 17.3 of the decision under appeal, the opposition division took the view that "*there seems to be no valid reason to assume that the poster 719 was not made available at the meeting in 2007*". While it can be accepted that a poster with the title was indeed presented at the meeting, in the board's view, it has not been established that the contents of the poster presented at the meeting were identical to those disclosed in document D15 or to the abstract published in the conference proceedings document D15a.
24. In view of this, the board cannot conclude that document D15 or the contents of document D15 or the abstract in document D15a were available to the public before the priority date of the patent.

*Novelty - Article 54 EPC*

*Over documents D2, D3, D17 and D18*

25. Claim 1 is for a hydrogel comprising a substantially sericin-depleted silk fibroin and an amphiphilic peptide.
26. Documents D2 and D3 disclose the production of mixed gelatin/silk fibroin hydrogels. The appellant had submitted that these hydrogels anticipate the subject-matter of claim 1, *inter alia* because gelatin is an amphiphilic peptide. However, in the decision under appeal, the opposition division held that documents D2 and D3 did not disclose hydrogels comprising an amphiphilic peptide because, although gelatin might be

amphiphilic, the term gelatin referred mainly to larger molecules than normally understood by the expression "peptide". Moreover, there was no definite proof that it was the smaller chains, i.e. the peptides, which provided for the amphiphilicity.

27. On appeal, the appellant submitted that in view of the disclosure in document D6 that gelatin was obtained by hydrolysing collagen, a naturally occurring full length protein (see document D6), gelatin was a peptide within the meaning of that term as understood by the person skilled in the art. The amphiphilic nature of gelatin was also reported in document D6 (page 66, fourth full paragraph) and had been confirmed in document D42.
28. The board is not persuaded by these submissions. Document D6, while recognising that "Gelatins do not occur naturally but are manufactured from collagens by processes that destroy the secondary and higher structures of collagen" (*supra*) and also recognising that gelatins are amphiphilic (page 66, penultimate paragraph) also states that "*Gelatin is a heterogeneous mixture of single- or multi-stranded polypeptides, each with extended left-handed proline helix conformations and containing between 300 and 4,000 amino acids (Chaplin 2007)*" (see page 66, second paragraph). Thus, as noted by the examining division, document D6 does not categorise gelatins as a peptide.
29. Document D42 (declaration of Dr Kaplan) was cited by the appellant as demonstrating that gelatin was an amphiphilic peptide. Several considerations speak against accepting this on the basis of document D42 alone. The first is that although it has been argued that, due to the indefinite definition of "peptide" in the art, the skilled person could interpret an amino

acid sequence of 300 amino acids as a peptide, no evidence has been provided of any skilled person actually considering an amino acid sequence of such length (or longer) to be a peptide. Secondly, Figure 1 of the appendix, an SDS-Page gel of gelatin type A 175 g Bloom and gelatin peptide fraction, which purports to show the presence of a peptide fraction, in fact shows no bands at all of the relevant 300 amino acids size or shorter. Thus, no conclusions can be drawn from these data. Thirdly, document D42 being a document produced on behalf of a party, carries a lower evidential weight than an independently authored document. As considered above, no such independent evidence has been provided. Thus, document D42 is not convincing evidence that the skilled person at the relevant date regarded gelatin as peptide, let alone an amphiphilic one.

30. In view of the above, the board maintains the opposition division's decision that the disclosure in documents D2 and D3 (and documents D17 and D18 which refer to the former documents) does not anticipate the subject-matter of claim 1.

*Over document D15*

31. Since this document is not comprised in the state of the art it cannot anticipate the claimed subject-matter.
32. In view of the above considerations the board concludes that the subject-matter of claims 1 and 2 is novel.

*Inventive step (Article 56 EPC) - claims 1 and 2*

33. In the statement of grounds of appeal, the appellant provided substantiated arguments as to why the subject-matter of the main request lacked an inventive step starting from document D15 representing the closest prior art.
34. However, in point 24. above, the board decided that document D15 was not comprised in the state of the art for the patent in suit, thus it cannot serve as closest prior art.
35. Point 5.8.8 of the statement of grounds of appeal contains the following passage: "*D2, D3, D15, D17, D18 and D21 are maintained in the present appeal as candidate closest prior art publications, without prejudice to the potential role of any prior art in these proceedings as additional prior art to render the claimed subject-matter obvious*". No further reasons were provided as to why it had to be concluded that the claimed subject-matter lacked an inventive step.
36. In point 5.8.28 of the statement of grounds of appeal it is stated "*alternatively, it may be considered that D8 is as close as D15. In that event, the analogous argument is proposed starting from D8 and applying one or more of D15, D43 and D26 as secondary prior art teaching to use an amphiphilic peptide as the RGD peptide*". However, no particular disclosure in document D8 was identified as representing the closest prior art. Thus, the board and the respondent would on their own have to identify a relevant passage in that document and determine the difference between this and the claimed subject-matter.
37. The board therefore takes the view that a line of argument starting from any of documents D2, D3, D8, D17

and D18 was not substantiated and therefore cannot be considered by the board (Article 12(2) and (4) RPBA 2007).

38. In view of the above considerations, the subject-matter of claims 1 and 2 meets the requirements of Article 56 EPC.

*Disclosure of the invention - Article 83 EPC*

39. The appellant's objection to the term "amphiphilic peptide" is based on the allegation that the skilled person could not without an undue burden provide suitable amphiphilic peptides in view of the fact that the unclear term "amphiphilic peptide" had to be interpreted broadly, i.e. it included any long peptide chains being shorter than the full protein, which, even if they contained hydrophobic and hydrophilic regions, might fold in such a way that they were not amphiphilic overall.
40. In the written proceedings the respondent requested to not admit this objection into the appeal proceedings. This request was not maintained during the oral proceedings (see the respondent's final requests). The board therefore sees no reason to hold the objection inadmissible. However, the objection cannot be endorsed.
41. The requirements of Article 83 EPC are complied with if the patent discloses the claimed invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.
42. It is established case law that an "*objection of lack of sufficient disclosure presupposes that there are*

*serious doubts, substantiated by verifiable facts" and that "[i]n order to establish insufficiency, the burden of proof is upon an opponent to establish on the balance of probabilities that a skilled reader of the patent, using his common general knowledge, would be unable to carry out the invention" (Case Law of the Boards of Appeal of the European Patent Office, 9th edition, II.C.9; references omitted).*

43. In the present case, the appellant relies on the unknown molecular size of the peptide referred to in claim 1 and the statement in declaration D32 that "*the term 'amphiphilic' is used throughout scientific literature for structures of molecular sizes that do not overwhelm the effect of the hydrophilic and hydrophobic residues*" (see section IV) to support the case that the skilled person faced an undue burden in identifying such "amphiphilic peptides".
44. The board accepts that the definition in declaration, document D32, is essentially correct and was known by the skilled person. However, it does not see this statement as establishing that the skilled person could not have made or identified amphiphilic peptides based on the disclosure of the patent in combination with common general knowledge.
45. In the case of those longer peptides where folding could be an issue, the board has seen no evidence that the skilled person could not make those long peptides and identify those that were amphiphilic, based on the disclosure of the patent in combination with common general knowledge. The fact that the patent does not teach the skilled person the maximum size of the peptide does not alter the conclusion.

46. The appellant furthermore made a conditional objection that if the proprietor took a position to the effect that "substantially sericin-depleted" provided or contributed to novelty or inventive step, then an objection was made that the particular degree of sericin-depletion to be regarded as "substantial" was not disclosed sufficiently for the invention to be performed by a person skilled in the art, contrary to Article 83 EPC.
  
47. The board is not persuaded by this argument for several reasons. Firstly, although brought under Article 83 EPC, the objection is one of an alleged lack of clarity of the expression "substantially sericin-depleted" and should properly have been made under Article 84 EPC. However, Article 84 EPC is not a ground of opposition. Secondly, the board has seen no evidence that the skilled person could not make sericin-depleted silk fibroin and indeed this has not been argued.
  
48. In view of the above considerations, the board is of the view that the disclosure of the claimed invention meets the requirements of Article 83 EPC.
  
49. Thus, auxiliary request 2 meets the requirements of the EPC.

## 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 with the order to maintain the patent on the basis of auxiliary request 2 as filed during oral proceedings before the board on 20 May 2021 (Annex II to the minutes) and a description to be adapted thereto.

The Registrar:

The Chairman:



B. ter Heijden

P. de Heij

Decision electronically authenticated