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Datasheet for the decision of 9 August 2021

Case Number: T 0139/18 - 3.3.01

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Language of the proceedings: EN

Title of invention:
High viscosity macromolecluar compositions for treating ocular conditions

Patent Proprietor:
ALLERGAN, INC.

Opponent:
STRAWMAN LIMITED

Headword:
Pre-filled syringe/ALLERGAN

Relevant legal provisions:

EPC Art. 54(3)
EPC R. 139
RPBA 2020 Art. 13(2)

Keyword:

Main request and auxiliary request 2- admittance (yes)
Main request and auxiliary requests 1-3 - novelty (no)
Auxiliary request 4 - admittance (no)

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Case Number: T 0139/18 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 9 August 2021

Appellant: (Patent Proprietor)	ALLERGAN, INC. 2525 Dupont Drive Irvine, CA 92612 (US)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Respondent: (Opponent)	STRAWMAN LIMITED Orchard Lea Horns Lane Combe Witney, Oxfordshire OX29 8NH (GB)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 15 November 2017 revoking European patent No. 2606899 pursuant to Article 101(2) and Article 101(3)(b) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	J. Molina de Alba
	M. Blasi

Summary of Facts and Submissions

I. The decision under appeal is the opposition division's decision revoking European patent No. 2 606 899.

The decision was based on the patent as granted and the claims of six auxiliary requests.

II. The following document is cited in this decision:

D4: WO 2008/121665

III. The patent had been opposed on the grounds of Article 100(c), (b) and (a) EPC, for lack of novelty and of inventive step.

In the appealed decision, the opposition division concluded, among other things, that:

- claim 1 as granted and claim 1 of auxiliary requests 1 and 2 added subject-matter (Article 76(1) and Article 123(2) EPC), and
- the subject-matter of claim 1 of auxiliary requests 3 to 6 lacked novelty over document D4 (Article 54(3) EPC).

IV. The patent proprietor (appellant) filed notice of appeal against the decision. With the statement of grounds of appeal, it filed four sets of claims as its main request and auxiliary requests 1 to 3.

The main request and auxiliary request 2 were identical to claim requests that had been withdrawn at the oral proceedings before the opposition division. The claims

of auxiliary requests 1 and 3 were identical to those of auxiliary requests 4 and 6 on which the appealed decision was based, respectively.

Claim 1 of auxiliary request 1 reads as follows:

"*1. A pre-filled syringe containing a gel composition comprising:*

a therapeutically effective amount of a macromolecular anti-angiogenic component (MAAC) wherein: the MAAC comprises (i) a direct or indirect inhibitor of a vascular endothelial growth factor (VEGF) activity, or (ii) a direct or indirect inhibitor of a vascular endothelial growth factor (VEGF) activity which is an agent selected from the group consisting of a nucleic acid and a polypeptide; and

a viscosity enhancing component which comprises hyaluronic acid in an amount of 1-4 % (w/v) based on the gel composition; and

wherein the gel composition has a viscosity of 70,000 mPa·s (cps) or more at a shear rate of 0.1/second at 25°C."

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 1 in that the MAAC has been limited to option (ii).

V. In its reply to the statement of grounds of appeal, the opponent (respondent) requested that the appeal be dismissed.

VI. In a communication dated 18 November 2020, sent as an annex to the summons to oral proceedings which were

scheduled in view of the corresponding requests by the parties, the board gave its preliminary opinion on the case. It considered that the main request and auxiliary request 2 filed with the statement of grounds of appeal were inadmissible pursuant to Article 12(4) RPBA 2007 because they had been withdrawn in the opposition proceedings. In addition, the board raised doubts as to the novelty of the subject-matter of each of the requests on file over D4.

VII. With a letter dated 24 June 2021, the appellant filed two sets of claims as its main request and auxiliary request 2 to replace the requests of the same designation filed with the statement of grounds of appeal. The new claim requests were identical to those of auxiliary requests 3 and 5 on which the decision was based. The appellant submitted that they were the requests originally intended, and requested their admission as a correction under Rule 139 EPC.

Claim 1 of the main request reads as follows:

"*1. A pre-filled syringe containing a gel composition comprising:*

a therapeutically effective amount of a macromolecular anti-angiogenic component (MAAC) wherein:
the MAAC comprises (i) a direct or indirect inhibitor of a vascular endothelial growth factor (VEGF) activity, or (ii) a direct or indirect inhibitor of a vascular endothelial growth factor (VEGF) activity which is an agent selected from the group consisting of a nucleic acid and a polypeptide; and

a viscosity inducing component which is a polymeric hyaluronate component, wherein the hyaluronate

component is present in an amount of 1-4 % (w/v) based on the gel composition; and

wherein the gel composition has a viscosity of 70,000 mPa·s (cps) or more at a shear rate of 0.1/second at 25°C."

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the MAAC has been limited to option (ii).

VIII. In a letter dated 28 July 2021, the respondent objected to the admission of the claim requests filed by the appellant on 24 June 2021.

IX. Oral proceedings were held before the board on 9 August 2021. As agreed by the parties, the oral proceedings took the form of a mixed-mode hearing in which the respondent attended by videoconference. In the course of the oral proceedings, the appellant filed the claims of auxiliary request 4.

Claim 1 of auxiliary request 4 differs from claim 1 of the main request in that it requires the MAAC to comprise a protein selected from the group consisting of an antibody and an antibody mimic.

X. At the end of the oral proceedings, the board's decision was announced.

XI. The appellant's arguments, where relevant to the present decision, can be summarised as follows:

The subject-matter of claim 1 of the main request was novel. D4 disclosed a plurality of components and delivery vehicles. To arrive at the subject-matter of

claim 1 it was necessary to make at least two selections: a macromolecular compound as the active ingredient and a gel containing 1-4 %(w/v) of hyaluronate component as the delivery vehicle.

Regarding the active ingredient, D4 strongly focused on small molecules (pages 29-51 and examples), so the choice of a macromolecule constituted a selection that went against the general preference of D4.

As to the delivery vehicle, the passage on page 22, lines 16-22 disclosed two alternative embodiments in relation to the concentration of the hyaluronate component, namely 0.05-0.5 %(w/v) and 1-4 %(w/v). D4 did not disclose any preference for a composition containing a hyaluronate component within the second concentration range: the examples illustrated compositions within both ranges and claim 2 showed that there was not even a general preference for viscous (gel) compositions, since gels, solutions and suspensions were claimed at the same level. Hence the choice of the range 1-4 %(w/v) constituted a second selection.

The respondent's argument that the passages on page 11, lines 26-29 and page 20, lines 26-29 of D4 taught a general preference for compositions with a hyaluronate component content of 1-4 %(w/v) was flawed. The passages indicated some preference for compositions having a viscosity of at least 70 000 cps, but this preference was not a general one, and moreover a viscosity of at least 70 000 cps could not be correlated with a content of 1-4 %(w/v) hyaluronate component. D4 stated on page 21, lines 15-20 that the amount of viscosity enhancing component depended on various factors, e.g. its molecular weight. Thus the

viscosity of at least 70 000 cps was not univocally linked to a hyaluronate component concentration of 1-4 %(w/v). For instance, the same viscosity could be obtained with lower amounts of a hyaluronate component having a higher molecular weight. The fact that none of the claims in D4 related to that concentration range supported the conclusion that the range was not generally preferred.

Auxiliary request 4 should be admitted into the proceedings. It was a reaction to the development of the arguments in the appeal proceedings and, in particular, to the board's preliminary opinion (point 9.2.1). The latter referred for the first time to the passage on page 20, lines 26-29 of D4, which disclosed a preference for compositions having a viscosity of at least 70 000 cps. The amendment in claim 1 of auxiliary request 4 *prima facie* overcame the objection of lack of novelty over D4 and was based on one of the granted claims.

XII. The respondent's arguments, where relevant to the present decision, can be summarised as follows:

Document D4 anticipated the subject-matter of claim 1 of the main request because only one selection was required to arrive at it. Like the patent, D4 concerned compositions for intra-ocular injection comprising a VEGF inhibitor as anti-angiogenic agent, namely a tyrosine kinase inhibitor (TKI), and a viscosity inducing component. Preferably the compositions had a viscosity of at least 70 000 cps at a shear rate of 0.1/second at 25°C (page 11, lines 25-27).

The choice of the TKI to be a macromolecule was the only selection required. Contrary to the appellant's

contention, this choice was not less preferred: the paragraph bridging pages 10 and 11 presented macromolecules as equivalent to small molecules.

Regarding the viscosity inducing component, the embodiment on page 22, lines 16-19 of D4 relating to compositions containing 1-4 %(w/v) polymeric hyaluronate component was preferred. Therefore its choice did not involve a selection. This was derivable from the general preference in D4 for viscosities in the higher range (page 11, lines 26-29 and page 20, lines 26-29) and from the clause introducing the embodiment as "a further useful embodiment" rather than just as "one embodiment". The embodiment was also taught as having very high polymer viscosity and forming a gel that was to be marketed in a pre-filled syringe. The preference for the embodiment of 1-4 %(w/v) hyaluronate content was further supported by the paragraph bridging pages 13 and 14, which linked a preferred viscosity of 80 000-300 000 cps with a hyaluronate concentration of 2-3 %(w/v). Although viscosity was not determined only by the concentration of the hyaluronate component, D4 disclosed a correlation between the preferred viscosity values and the higher hyaluronate concentration range. Even though the claims of D4 did not mention specific viscosities, independent claim 13 referred explicitly to a high-viscosity hyaluronic acid carrier.

Auxiliary request 4 should not be admitted pursuant to Article 13(2) RPBA 2020 because there had been no change in the respondent's case. Even if there had been a development of arguments in the proceedings, this would not have constituted exceptional circumstances justifying the filing of new claims. In any case, a new claim request which clearly overcame the objection of

lack of novelty over D4, i.e. the reason for revocation of the patent, should have been filed at the outset of the appeal proceedings. At the latest, the claims should have been filed immediately after receipt of the board's preliminary opinion rather than at the end of the oral proceedings. Furthermore, claim 1 raised new issues, such as lack of clarity.

XIII. The parties' final requests were as follows:

- The appellant requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the claims of the main request as filed with the letter dated 24 June 2021 or, alternatively, the claims of:
  auxiliary request 1 as filed with the statement of grounds of appeal,
  auxiliary request 2 as filed with the letter dated 24 June 2021,
  auxiliary request 3 as filed with the statement of grounds of appeal, or
  auxiliary request 4 as filed during the oral proceedings before the board.

- The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible. It meets the requirements of Articles 106 to 108 and Rule 99(2) EPC.

2. *Admittance of the main request - Rule 139 EPC and Article 13(2) RPBA 2020*

The appellant filed the claims of the main request with its letter dated 24 June 2021 to replace the claims of a previous main request filed with the statement of grounds of appeal. The replacement of the claim request was requested as a correction under Rule 139 EPC.

The board decided to admit the new main request into the appeal proceedings because the replacement of the previous main request can be allowed under Rule 139 EPC and is not precluded by Article 13(2) RPBA 2020. Considering the board's judgment on the issue of novelty in relation to the main request (see point 4), the board does not need to give details of the decision to admit the main request.

3. *Admittance of auxiliary request 2 - Rule 139 EPC and Article 13(2) RPBA 2020*

The appellant filed the claims of auxiliary request 2 with its letter dated 24 June 2021 to replace the claims of a previous auxiliary request 2 which had been filed with the statement of grounds of appeal. The circumstances and considerations in relation to

auxiliary request 2 are identical to those of the main request.

In view of the board's judgment on the issue of novelty (see point 5), the board does not need to give further details on its decision to admit auxiliary request 2.

4. Novelty over D4 - claim 1 of the main request (Article 54(1) and (3) EPC)

4.1 Document D4 is an international patent application which validly entered the regional phase before the EPO. It was published after the filing date of the contested patent, but its filing and priority dates are earlier than the respective dates of the contested patent.

In the decision under appeal (section 5.3.2), the opposition division held that D4 was prior art under Article 54(3) EPC. This aspect of the decision was not contested by the appellant (see statement of grounds of appeal, page 2, penultimate paragraph), therefore it is not part of these appeal proceedings.

4.2 D4 discloses (page 5, paragraph 2) anti-angiogenic compositions for intra-ocular injection comprising a TKI and a hyaluronic acid component. The TKI is a VEGF inhibitor and constitutes the anti-angiogenic component (page 7, line 25 and following paragraphs). The hyaluronic acid component is the viscosity inducing component (page 11, lines 12-14). As in the contested patent, the viscosity values in D4 are in relation to a shear rate of 0.1/second at 25°C (page 6, lines 25-26). These values range from 10 to 300 000 cps, but viscosities of at least 70 000 cps are particularly

preferred (page 11, lines 26-29 and page 20, lines 26-29).

Having regard to the above, the question of whether the subject-matter of claim 1 of the main request is anticipated by D4 boils down to assessing whether D4 discloses a composition in which the anti-angiogenic component is a macromolecule and the polymeric hyaluronate component is present in an amount of 1-4 %(w/v). In D4, the compositions containing 1-4 %(w/v) of polymeric hyaluronate component are associated with the formation of high-viscosity gels that are advantageously marketed in pre-filled syringes (page 22, lines 21-24; page 61, lines 15-20; page 62, lines 10-14).

4.3 Regarding the anti-angiogenic component, the respondent referred to the passage bridging pages 10 and 11 of D4. The passage discloses that the TKI component includes a macromolecule, such as a protein, peptide, nucleic acid, modified nucleic acid or a peptide nucleic acid. Therein, it is stated that "*[a]dditionally, or alternative, the TKI component may comprise an organic molecule other than a macromolecule*". Non-macromolecular TKI components are also referred to as "small molecules".

Thus the passage bridging pages 10 and 11 of D4 presents a choice between macromolecular and small anti-angiogenic components (or their combination); choosing the macromolecular component involves one selection.

4.3.1 On this point, the appellant noted that D4 extensively discloses small molecules (pages 29-51) and that the compositions in the examples contain only small

molecules. Therefore macromolecular components had to be considered as being less preferred than small molecules, and their selection went against the general teaching of D4.

4.3.2 The board disagrees. The paragraph bridging pages 10 and 11 discloses macromolecules and small molecules at the same level of preference, and there is no specific disclosure in D4 giving greater preference to small molecules. The fact that D4 describes more examples of small molecules does not necessarily mean that they are generally more preferred. In fact, the passage on page 10, lines 10-34 also recites several examples of macromolecules, including proteins and nucleic acids. Therefore the board does not see that the selection of a macromolecule from the choices presented in the paragraph bridging pages 10 and 11 is precluded.

4.4 With respect to the concentration of the polymeric hyaluronate component, the parties referred to the two embodiments disclosed on page 22, lines 16-24 of D4. The passage reads as follows (emphasis added by the board).

"***In one embodiment,*** *the present compositions include a polymeric hyaluronate component in an amount in a range about 0.05% to about 0.5%(w/v).* ***In a further useful embodiment,*** *the hyaluronate component is present in an amount in a range of about 1% to about 4%(w/v) of the composition.* ***In this latter case, the very high polymer viscosity*** *forms a gel that slows particle sedimentation and diffusion of dissolved solutes upon injection in the eye. Such a composition may be marketed in pre-filled syringes since the gel cannot be easily removed by a needle and syringe from a bulk container.*"

Considering that the choice of a macromolecule as the active component already involved one selection, the issue of novelty hinges on whether the choice of the second embodiment on page 22, lines 16-24 constitutes an additional selection. For the reasons explained below, the board concurs with the respondent that, in view of the general teaching of D4, the embodiment relating to 1-4 %(w/v) hyaluronate component was preferred and did not require a selection to be made.

4.4.1 First of all, the board notes that the language of the text introducing the embodiments is not the same in both cases. The composition with the lower hyaluronate content is referred to as "an embodiment" while the composition with the higher hyaluronate content is "a further useful embodiment". Although the board does not necessarily concur with the respondent that this automatically means that the second embodiment is preferred, it certainly points towards a difference of appreciation between the two embodiments.

4.4.2 As indicated above (point 4.2), D4 describes compositions with viscosities in the range 10-300 000 cps, but viscosities of at least 70 000 cps are particularly preferred (page 11, lines 26-29 and page 20, lines 26-29). It is generally known that higher concentrations of viscosity inducing agent produce higher viscosities. Hence it is reasonable to assume that the embodiment containing higher concentrations of hyaluronate component would provide compositions within the higher (i.e. preferred) range of viscosities.

4.4.3 In that respect, the appellant argued that D4 does not disclose a correlation between viscosities above 70 000 cps and hyaluronate concentrations in the range

of 1-4 %(w/v). It then referred to the passage on page 21, lines 15-20, which states that the specific amount of viscosity inducing component employed depends on several factors, e.g. the molecular weight of the viscosity inducing component. This means that, in theory, hyaluronate components of high molecular weight could provide viscosities beyond 70 000 cps at concentrations within the range of 0.05-0.5 %(w/v) and, conversely, hyaluronate components of low molecular weight might not achieve a viscosity of 70 000 cps at concentrations within the range of 1-4 %(w/v).

The board accepts that molecular weight and other factors have an influence on the amount of hyaluronate component that needs to be added to the composition to achieve a given viscosity. However, the board concurs with the respondent that the appellant's argument cannot counter the clear teaching in D4 that viscosities above 70 000 cps are preferred and that these are achieved by hyaluronate concentrations within the range of 1-4 %(w/v) rather than 0.05-0.5 %(w/v). This teaching may be derived from the following sections of D4:

Examples 2-8 show that compositions comprising 0.05-0.5 %(w/v) of a sodium hyaluronate with an average molecular weight of 0.6 million daltons have a viscosity of 20-500 cps. However, the same sodium hyaluronate used in examples 9-13 at concentrations of 2.0-3.0 %(w/v) produces viscosities of 100 000-300 000 cps. These results are in line with the teaching in the paragraph bridging pages 13 and 14, which associates viscosities of 80 000-300 000 cps with hyaluronate concentrations of 2-3 %(w/v). In addition, the passage on page 22, lines 16-24 states that the

compositions containing 1-4 %(w/v) hyaluronate exhibit very high polymer viscosity.

4.4.4 Consequently, the board holds that the second embodiment on page 22, lines 16-24 of D4 is preferred and that its choice does not constitute a selection.

4.5 In summary, D4 discloses a preferred embodiment which is a gel composition for intra-ocular injection having a viscosity of at least 70 000 cps at a shear rate of 0.1/second at 25°C and comprising 1-4% (w/v) of a polymeric hyaluronate component. It also discloses that, due to its high viscosity, this preferred composition is to be marketed as a pre-filled syringe.

In addition, as a result of a single selection, the therapeutically active ingredient is a macromolecular TKI, i.e. a macromolecular anti-angiogenic component which is a VEGF inhibitor.

Hence D4 discloses the combination of features in claim 1 of the main request. The claim therefore does not meet the requirements of Article 54(1) and (3) EPC.

5. *Novelty over D4 - claim 1 of auxiliary requests 1 to 3 (Article 54(1) and (3) EPC)*

As conceded by the appellant in the discussion of the admission of the main request, claim 1 of auxiliary request 1 defines essentially the same subject-matter as claim 1 of the main request. Therefore it too lacks novelty over D4.

Claims 1 of auxiliary requests 2 and 3 correspond to claim 1 of the main request and auxiliary request 1, respectively, with the additional limitation that the

MAAC has been restricted to option (ii), i.e. the VEGF inhibitor is a nucleic acid or a polypeptide. As noted by the respondent, the paragraph bridging pages 10 and 11 of D4 discloses nucleic acids, proteins and peptides as examples of macromolecular TKIs. Hence the choice of the MAAC to be a nucleic acid or a polypeptide still represents a single selection and cannot confer novelty on the subject-matter of claim 1 of auxiliary requests 2 and 3.

6. *Admittance of auxiliary request 4 - Article 13(2) RPBA 2020*

The appellant filed the claims of auxiliary request 4 at the oral proceedings once the board had come to the conclusion that the subject-matter of all the claim requests then on file lacked novelty over D4.

According to Article 13(2) RPBA 2020, any amendment to a party's case at such a late stage of the proceedings is, in principle, not taken into account unless there are exceptional circumstances which have been justified with cogent reasons by the party concerned.

The appellant justified the filing of new claims by a development of the arguments on file occasioned by the citing of the passage on page 20, lines 26-29 of D4 in the board's preliminary opinion.

This passage was cited by the board in the context of the argument that higher-viscosity compositions were generally preferred in D4, so the choice of the compositions with a higher hyaluronate content did not constitute a selection from a list of equivalent items.

The passage cited by the board conveys essentially the same information as the one on page 11, lines 26-29 cited in the decision under appeal (page 24, paragraph 3) in support of exactly this argument. That passage on page 11 of D4 had also been cited by the respondent in its reply to the statement of grounds of appeal (page 4, paragraph 4) in the context of novelty over D4, although the respondent did not explicitly outline the argument that higher-viscosity compositions were generally preferred; the argument came to the fore with the board's preliminary opinion.

The board considers that this shift of the focus of the respondent's argument to align with the reasons in the appealed decision underlined in the board's preliminary opinion is part of the normal development of a case. Therefore it does not amount to exceptional circumstances within the meaning of Article 13(2) RPBA 2020.

Furthermore, the respondent is right in that, considering that the patent had been revoked for lack of novelty over D4, a claim request clearly overcoming the opposition division's finding of lack of novelty could have been filed at the outset of the appeal proceedings. However, when lodging the appeal, the appellant confined itself to defending claim requests that had been considered in the decision under appeal. Furthermore, auxiliary request 4 could also still have been submitted in written proceedings as a direct response to the board's preliminary opinion, which had been issued more than eight months before the date of the oral proceedings. Instead, the appellant chose to submit this claim request only at the end of the oral proceedings, i.e. at the latest stage of the appeal proceedings. Therefore the development of the case

referred to by the appellant does not constitute cogent reasons which might justify this late filing.

In conclusion, the board decided not to admit auxiliary request 4 into the proceedings pursuant to Article 13(2) RPBA 2020.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated