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Datasheet for the decision of 21 July 2021

Case Number: T 2242/19 - 3.3.07

Application Number: 11724603.3

Publication Number: 2575770

IPC: A61K9/14, A61K9/16, A61L24/10, A61P7/04

Language of the proceedings: EN

Title of invention:
PROCESS FOR MAKING DRY AND STABLE HEMOSTATIC COMPOSITIONS

Patent Proprietor:
Baxter International Inc
Baxter Healthcare SA

Opponents:
Ferrosan Medical Devices A/S
Ethicon Inc.

Headword:
Hemostatic compositions / BAXTER

Relevant legal provisions:
RPBA Art. 12(4)
RPBA 2020 Art. 25(2), 11, 25(1)
EPC Art. 123(2), 83

Keyword:

Late-filed evidence - admitted (yes)
Amendments - allowable (yes)
Sufficiency of disclosure - (yes)
Remittal - special reasons for remittal

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Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 2242/19 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 21 July 2021

Appellant: (Patent Proprietor 1)	Baxter International Inc One Baxter Parkway Deerfield, IL 60015 (US)
Appellant: (Patent Proprietor 2)	Baxter Healthcare SA Thurgauerstrasse 130 8152 Glattpark (Opfikon) (CH)
Representative:	Alge, Daniel SONN Patentanwälte OG Riemergasse 14 1010 Wien (AT)
Respondent 1: (Opponent 1)	Ferrosan Medical Devices A/S Sydmarken 5 2860 Søborg (DK)
Representative:	Høiberg P/S Adelgade 12 1304 Copenhagen K (DK)
Respondent 2: (Opponent 2)	Ethicon Inc. U.S. Route 22 Somerville New Jersey 08876 (US)
Representative:	Kirsch, Susan Edith Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 6 June 2019**

revoking European patent No. 2575770 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Lécaillon
	Y. Podbielski

Summary of Facts and Submissions

I. European patent 2 575 770 (hereinafter "the patent") was granted on the basis of 14 claims. The independent claims of the patent as granted read as follows:

"1. A process for making a dry and stable hemostatic composition, said process comprising

a) providing a dry granular preparation of gelatin,
b) coating the granules in said dry granular preparation with a thrombin solution, thereby obtaining thrombin coated gelatin granules,
c) filling said thrombin coated gelatin granules into a final container,
d) finishing the final container to a storable pharmaceutical device containing said thrombin coated gelatin granules as a dry and stable hemostatic composition.

12. A finished final container obtained by the process of any one of claims 1 to 11.

13. Kit for administering a hemostatic composition comprising the finished container according to claim 12 and a container with a pharmaceutically acceptable diluent.

14. Thrombin coated granules of a biocompatible polymer suitable for use in hemostasis, wherein the polymer is gelatin."

II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and

it extended beyond the content of the application as originally filed.

III. The opposition division took the decision to revoke the patent. The decision was based on a main request and four auxiliary requests, all filed with the letter dated 13 March 2019.

IV. The opposition division decided in particular as follows:

(a) The subject-matter of the main request complied with Article 123(2) EPC because the limitation of the biocompatible polymer to gelatin amounted to the selection of one preferred embodiment of the application as published.

(b) The patent did not provide sufficient guidance as to how to obtain hemostatic compositions achieving the claimed stability criteria. Common general knowledge could not supplement this lack of information either. Performing the invention over the whole claimed range represented thus an undue burden for the skilled person. As a consequence neither the main request nor the auxiliary requests 1-4 fulfilled the requirements of Article 83 EPC.

V. The patent proprietor (appellant) lodged an appeal against the above decision of the opposition division and defended its case on the basis of a main request and twelve auxiliary requests filed with the statement setting out the grounds of appeal. The main request and auxiliary requests 1-4 corresponded in principle to the requests on which the first instance decision was based.

The claims of the main request, on which the present decision is based, corresponded to granted claims 1-8 and 10-14 (mere deletion of granted claim 9).

VI. The following items of evidence relevant for the present decision were filed by the appellant with its statement setting out the grounds of appeal:

D31 and D31a-D31d: Affidavit by Heinz Gulle and attachments a)-d)
D32: Yields in Fluid Bed Processes

VII. Oral proceedings were held before the Board on 21 July 2021.

VIII. The appellant requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request or one of auxiliary requests 1-12, all filed with the statement setting out the grounds of appeal. They also requested that the case be remitted to the opposition division for examination of the grounds of opposition under Article 100(a) EPC in the event that the grounds of opposition under Articles 100(b) and 100(c) EPC do not prejudice the maintenance of the patent.

IX. The respondents requested that the appeal be dismissed. They further requested that auxiliary requests 5-12 not be admitted into the appeal proceedings. Respondent 1 additionally requested that documents D31-D32 not be admitted into the appeal proceedings.

X. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

(a) D31, D31a-D31d and D32 were filed in reaction to the surprising decision of the opposition division considering the main request as being not sufficiently disclosed and were therefore to be admitted into the appeal proceedings.

(b) Claim 1 of the main request found basis in the original application as stated in the first instance decision. The main request fulfilled the requirements of Article 123(2) EPC.

(c) The patent provided sufficient information to perform the claimed process in a reproducible manner so as to obtain storage stable hemostatic compositions. This was further confirmed by the supplementary experimental data provided in D31 and its annexes and D32. Moreover, the respondents did not provide any evidence of the contrary. Hence, the main request fulfilled the requirements of Article 83 EPC.

XI. The arguments of the respondents, as far as relevant for the present decision, can be summarised as follows:

(a) D31, D31a-D31d and D32 should have been filed already in the first instance proceedings in reply to the objections of lack of sufficiency of disclosure raised in the notices of opposition. Furthermore these documents were not *prima facie* relevant. They were thus not to be admitted into the appeal proceedings.

(b) The amendments performed in claim 1 of the main request infringed Article 123(2) EPC, for the following reasons:

- the limitation of the claimed polymer to gelatin constituted an unallowable intermediate generalisation,
- the combination of gelatin as biocompatible polymer coated with thrombin as coagulation inducing agent was not originally disclosed, and
- the original application did not provide any basis for a polymer exclusively consisting of gelatin.

(c) The patent did not provide sufficient guidance (i) to obtain stable compositions and (ii) to carry out the claimed process over the whole scope. Regarding point (i), the results provided in the patent (see paragraph [0071]) as well as in D31 (and annexes) revealed that the parameter defining a stable composition according to the patent (see paragraph [0012]) was not fulfilled when performing the claimed process. There was no other information on how to achieve said parameter. With respect to point (ii), no information was provided as to how to avoid thorough wetting of any type of gelatin. A high number of non-working embodiments would actually be covered by the claims *e.g.* when using non-cross-linked or porous gelatin, without providing any alternatives to enable performing the invention. The main request did thus not fulfill the requirements of Article 83 EPC.

Reasons for the Decision

1. Admittance of new items of evidence

1.1 Documents D31, D31a-D31d and D32 were submitted with the statement setting out the grounds of appeal, filed before 1 January 2020. Following the transitional

provisions set out in Article 25(2) of the Rules of Procedure of the Boards of Appeal (RPBA) 2020, their admittance must be decided on the basis of Article 12(4) RPBA 2007.

1.2 Documents D31, D31a-D31d and D32 were filed by the appellant in reaction to the decision of the opposition division considering that the patent in suit did not enable the skilled person to prepare stable hemostatic compositions. These items of evidence are meant to support the fact that
- compositions according to the examples of the patent in suit actually fulfill the requirement of stability as defined in paragraph [0012] thereof (D31 and annexes), and
- a loss of thrombin activity occurs during coating (D31 and annexes) as known from common general knowledge (D32).

1.3 The respondents argued that the lack of sufficiency of disclosure including the issue of achievement of the claimed stability was already raised in the notices of opposition. According to the respondents, the appellant had consequently the obligation to file all the possible evidence already in response to said notices, including the present items of evidence. In particular, the items D31a-D31d were reports of experiments performed by the appellant and as such were available to the appellant when filing the reply to said notices of opposition.

1.4 The Board however notes that the question of the achievement of the stability criteria was merely one of several issues raised in the notices of opposition. Said notices included in particular further reasons in support of insufficiency of disclosure. Furthermore,

according to the preliminary opinion of the opposition division the invention was sufficiently disclosed. Contrary to the opinion of respondent 1, said preliminary opinion did actually tackle the issue of achievement of the claimed stability but considered that it related to Article 84 EPC (see annex to the summons to oral proceedings of the opposition division, page 7). Hence, the Board considers that there were therefore no compelling reasons for the appellant to file in the written proceedings before the opposition division any further experimental results or documents in addition to its arguments provided in the reply to the notices of opposition regarding the achievement of the stability criteria. This issue became crucial only during the oral proceedings before the opposition division, at which point in time the gathering and filing of the present items of evidence was not reasonably possible.

1.5 Finally the Board observes that the *prima facie* relevance of the present documents, which was contested by the respondent 1, is not a criterion required for assessing their admittance under Article 12(4) RPBA 2007.

1.6 Hence, the Board does not exercise its discretion pursuant to Article 12(4) RPBA 2007 to exclude these documents from the appeal proceedings. D31, D31a-D31d and D32 are accordingly admitted into the appeal proceedings.

Main request

2. Amendments

2.1 Claim 1 of the main request is based on original claim 1 wherein:
(i) the "biocompatible polymer suitable for use in hemostasis" was replaced by "gelatin", and
(ii) the "(preparation of) coagulation inducing agent" was replaced by "thrombin (solution)".

2.2 The Board notes that the modification (ii) is individually disclosed in original claim 3. Furthermore, as explained by the opposition division gelatin is one of the possible "biocompatible polymer suitable for use in hemostasis" listed in original claim 12 which inter alia depends on original claim 3 (modification (i)). The limitation of said feature to one alternative originally disclosed amongst one list does not infringe *per se* Article 123(2) EPC. This is further confirmed by the fact that, as underlined by the opposition division, gelatin is one of the preferred alternatives thereof as revealed from the examples.

2.3 In this context the respondents brought forward the following arguments:

(a) The amendment (i) would constitute an unallowable intermediate generalisation because only more specific types of gelatin granules where originally individually disclosed, namely cross-linked gelatin (see original claim 17) or specific type of gelatin granules having specific physico-chemical properties (see page 9, 3rd paragraph and example 1).

(b) The combination of gelatin as biocompatible polymer coated with thrombin as coagulation inducing agent would not be originally disclosed.

(c) Original claim 12 as well as original page 8, 3rd paragraph refer to a polymer which "contains" or "may be formed from" gelatin. These passages cannot provide a basis for a polymer which "is", *i.e.* consists of, gelatin as claimed in claim 1 of the main request.

2.4 Concerning point (a), the Board notes that, as explained under point 2.2, gelatin in general is disclosed as one possible biocompatible polymer to be used in the claimed process. The fact that more specific embodiments are further described, and may be most suited for the claimed process, does not limit the original disclosure to said specific embodiments. Instead, the original disclosure has to be considered in its entirety.

2.5 Regarding point (b), the Board notes that original claim 12 is depending on original claim 3, so that original claim 12 discloses a list of combinations, each one of them containing thrombin with one of the listed polymers. On that reading original claim 12 discloses the claimed combination. The Board also notes that original product claim 25 is specifically directed to thrombin coated gelatin granules.

2.6 As far as point (c) is concerned, the Board is satisfied that the original disclosure directly and unambiguously discloses that the biocompatible polymer not only "contains" but "is" gelatin (see for example original claim 25 or original page 9 line 11).

2.7 Hence, claim 1 of the main request is supported by the original application. The respondents did not raise any objection regarding the compliance with Article 123(2) EPC of the remaining claims of the main request. Claims 2-13 of the main request find basis in the original claims. The Board thus considers that the claims of the main request fulfill the requirements of Article 123(2) EPC.

3. Sufficiency of disclosure

3.1 The respondents contested that the claimed invention was sufficiently disclosed for the following reasons:

(a) The patent did not provide sufficient guidance to the skilled person to obtain compositions which are indeed "stable" as required by claim 1.

(b) The skilled person could not perform the claimed process over its entire scope.

3.2 Preparation of a stable composition

3.2.1 The Board observes that the claims do indeed not provide any definition of the feature "stable". It was however undisputed amongst the parties that, in view of the overall teaching of the patent, storage stability is meant.

3.2.2 The respondents argued that the sole definition of said storage stability was to be found in the paragraph [0012] of the patent and provided that "no less than 400 I.U./ml (for a 500 I.U./ml product) after reconstitution after 24 months storage in dry form at room temperature (25°C) are still present (i.e. 80%

thrombin activity or more remaining compared to the initial activity before lyophilization)". The respondents then explained that, according to the results reported in paragraph [0071] of the patent (72%-75% thrombin recovery after 3, 6 and 12 months *i.e.* below the 80% defined in paragraph [0012]), the examples of the patent did not achieve said level of storage stability. The patent would not provide any other guidance allowing to prepare compositions fulfilling the criteria of paragraph [0012].

3.2.3 The Board notes that paragraph [0012] represents one isolated passage of the patent and the parameter mentioned therein is presented as one way of determining storage stability, *i.e.* it does not constitute an absolute definition thereof (see in paragraph [0012] the expression "can be determined"). Its definition is furthermore ambiguous since the reference value taken for thrombin initial activity is not clearly specified. It is on the one hand mentioned as a "500 I.U./ml product", which would seem to refer to the thrombin solution initially used for the coating, and on the other hand as the "initial activity before lyophilization", which would rather seem to refer to the step following coating. In this regard it is also observed that a step of lyophilization is not mentioned anywhere else in the patent.

3.2.4 Conversely the examples represent an independent passage of the patent. In said section, it is mentioned that, based on the thrombin recovery measurements made, the prepared coated granules satisfy the criteria of being "stable" (see paragraphs [0071] and [0072]). This statement is in line with the fact that the thrombin recovery values for storage over 3, 6 and 12 months are constant (72%-75% thrombin recovery, see paragraph

[0071]), which would be understood by any skilled person as representing stability upon storage. Contrary to paragraph [0012], this passage is *per se* unambiguous.

3.2.5 Moreover, the statement regarding the obtaining of stable compositions in paragraph [0071] may not even be in contradiction with the parameter defined in paragraph [0012]. The reference value for the initial thrombin activity used for the calculation of the thrombin recovery in paragraph [0071] appears to be the one of the thrombin solution used to perform the coating (see paragraphs [0042], [0067], [0070]). As explained above (see point 3.2.3), the reference value used to determine the parameter of paragraph [0012] may, on the other hand, correspond to the thrombin activity of the already coated particles at t=0 of the storage ("initial activity before lyophilization"). As argued by the appellant, a loss of thrombin activity upon coating would be expected by the skilled person. If this interpretation of paragraph [0012] would be followed, it would appear justified that the values of paragraph [0071] are lower than the percentage defined in paragraph [0012].

3.2.6 When assessing sufficiency of disclosure, in particular in the present case in which the claims do not define the feature "stable", the entire disclosure has to be taken into account. Hence, the data and the resulting statement regarding stability of the final granules provided in paragraphs [0071]-[0072] cannot be disregarded or questioned because of one isolated and ambiguous passage of the patent.

3.2.7 The respondents further argued that paragraph [0071] of the patent did not indicate the value of thrombin

activity at t=0 of the storage. This implied that a loss of thrombin activity may have occurred during the three first months. The Board notes that the results provided in table 2 of D31 seem to confirm that the thrombin activity is stable during the three first months of storage. In any case, the absence of data at t=0 in paragraph [0071] cannot lead to the conclusion that the coated granules would not be stable within said period of time. The Board finally notes that the respondents did not provide any evidence substantiating such a lack of stability during this storage period.

3.2.8 The respondents also contested that the data provided in D31 revealed a reduction of thrombin activity at 24 months storage for the sample #0289 (see table on page 2), so that storage stability over 24 months was not substantiated. Independently of any consideration regarding the relevance of this individual result, the Board observes that the claims are not in any way limited to a particular minimal time period regarding the storage stability. The mention of a 24 months time period in the definition of the parameter in paragraph [0012] is not considered relevant, as said parameter is not considered to be an absolute criterion defining a stable composition according to the claims (see above point 3.2.3). Similarly the absence of detailed results at t=0 and t=24 months in the patent despite the statement that these measurements were made (see paragraph [0055] of the patent), cannot lead to the conclusion that stable compositions cannot be prepared.

3.2.9 The respondent additionally referred to paragraph [0051] of the patent, which mentions the obtaining of "high yields above 95%". According to the respondent this would be an indication of the thrombin coating yield, thus implying that a high initial (at t=0)

thrombin activity was obtained. This would be inconsistent with a loss of thrombin activity upon coating. The Board observes that, as pointed out by the appellant, the yield referred to in paragraph [0051] is said to indicate "the deposition of the solids from the thrombin solution on the solid starting material". As the thrombin solution contains, in addition to thrombin, sodium chloride and mannitol (see paragraph [0042] of the patent), it cannot be concluded that the yield of deposition of all the solids coming from the thrombin solution necessarily and directly correlates with the thrombin recovery upon coating.

3.2.10 In conclusion, the Board understands the feature "stable" in the claims as the storage stability of the final hemostatic composition *i.e.* maintenance of the thrombin activity of the final thrombin coated gelatin granules upon storage, independently of the initial activity level and without any specific storage time period. In this context, the Board notes that a successful objection of lack of sufficiency of disclosure presupposes that there are serious doubts substantiated by verifiable facts (Case Law of the Boards of Appeal, 9th Edition II.C.9). In the absence of experimental data on the side of the respondents substantiating a lack of stability upon storage, the information provided by the patent, in particular the data of paragraph [0071], render a stability upon storage credible.

3.3 Performing the invention over the whole claimed scope

3.3.1 The respondents argue that the process of claim 1 of the main request encompasses a large number of non-working embodiments (in steps a) and b)) and that the patent would not provide alternatives enabling to

perform the invention. In particular non-cross-linked gelatin would dissolve in a thrombin solution so that thrombin coated non-cross-linked gelatin granules could not be prepared. Moreover the patent would not provide sufficient detail on the coating process, in particular on how to avoid "thorough wetting", especially when using porous gelatin granules or gelatin powder.

3.3.2 The Board notes that the respondents have not provided experimental data substantiating the presence of non-working embodiments. Furthermore the skilled person would be aware of the solubility issues of non-cross-linked gelatin in thrombin solutions and would find in paragraphs [0028]-[0032] of the patent sufficient information to perform cross-linking of the gelatin and overcome such issues. Similarly the skilled person would be aware of the issues linked to porous gelatin granules in the context of coating and would additionally find in paragraph [0010] guidance regarding the choice of suitable particles. The reference to a powder in said paragraph relates unambiguously to a sub-class of granular materials having the finer grain size and would not be understood as any gelatin powder. Finally the patent provides detailed information regarding suitable processes, apparatus and conditions to perform the coating step (see paragraphs [0014]-[0019] and [0042]). The skilled person would thus be able to perform a coating while avoiding thorough wetting of the granules as described in the patent without undue burden.

3.4 Accordingly, the Board comes to the conclusion that the invention claimed in the main request is sufficiently disclosed.

4. Remittal

4.1 Under Article 11 RPBA 2020, which applies in the present case according to Article 25(1) RPBA 2020, the board may remit the case to the department whose decision was appealed if there are special reasons for doing so.

4.2 In the present case, the appealed decision does not address the grounds for opposition under Article 100(a) EPC. As recalled in Article 12(2) RPBA 2020, the primary object of the appeal proceedings is to review the decision under appeal in a judicial manner. This principle would not be respected if the Board were to conduct a complete examination of the all the opposition's grounds. Consequently, under these circumstances, the Board considers that special reasons for remitting the case to the opposition division exist. The respondents had no objections against a remittal. Therefore, the Board considers it appropriate to accede to the appellant's request for a remittal.

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 for further prosecution.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated