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Datasheet for the decision of 28 June 2016

Case Number: T 0087/12 - 3.3.02

Application Number: 04721468.9

Publication Number: 1611236

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Language of the proceedings: EN

Title of invention:
Method for the production of Factor VII polypeptides

Applicant:
Novo Nordisk Health Care AG

Headword:
Purification of Factor VII/NOVO NORDISK HEALTH CARE AG

Relevant legal provisions:
EPC Art. 123(2)
RPBA Art. 13

Keyword:
Amendments - allowable (no)

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Catchword:

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Case Number: T 0087/12 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 28 June 2016

Appellant: (Applicant)	Novo Nordisk Health Care AG Thurgauerstrasse 36/38 8050 Zürich (CH)
Representative:	Nilsson, Karin Norvin Novo Nordisk A/S Corporate Patents Novo Allé 2880 Bagsværd (DK)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 26 August 2011 refusing European patent application No. 04721468.9 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	U. Oswald
Members:	K. Giebeler
	L. Bühler

Summary of Facts and Submissions

I. European patent application No. 04 721 468.9, entitled "Method for the production of GLA-residue containing serine proteases" and published as WO 2004/083421 (hereafter referred to as "the application as filed"), was filed with 83 claims.

II. Claims 24 to 33 and 40 of the application as filed read as follows:

"24. A method for the purification of a GLA-residue containing serine protease whereby a solution of a GLA-residue containing serine protease is subjected to a number of purification steps, wherein the pH at least in one of the purification steps has a value between 4.5 and 6.9 or has a value between 8.6 and 10."

"25. The method according to claim 24, wherein the free calcium ion concentration at least in one of the purification steps is higher than 1.2 mM."

"26. The method according to claim 25, wherein said free calcium ion concentration at least in one of the purification steps is higher than 1.3 mM, such as higher than 1.4 mM, such as higher than 1.5 mM, such as higher than 1.6 mM, such as higher than 1.7 mM, such as higher than 1.8 mM, such as higher than 1.9 mM, such as higher than 2.0 mM, such as higher than 2.1 mM, such as higher than 2.2 mM, such as higher than 2.3 mM, such as higher than 2.4 mM, such as higher than 2.5 mM, such as higher than 2.6 mM, such as higher than 3.0 mM, such as higher than 4.0 mM, such as higher than 5.0 mM, such as higher than 6.0 mM, such as higher than 7.0 mM, such as higher than 8.0 mM, such as higher than 9.0 mM, such as higher than 10.0 mM, such as higher than 20 mM, such as

higher than 40.0 mM, such as higher than 60.0 mM, such as higher than 80.0 mM, such as higher than 0.1 M, such as higher than 1 M, such as a free calcium ion concentration, where the solution is saturated."

"27. The method according to claim 24, wherein the free calcium ion concentration at least in one of the purification steps is lower than 0.10 mM."

"28. The method according claim 27, wherein the free calcium ion concentration at least in one of the purification steps is lower than 0.09, such as lower than 0.08, such as lower than 0.07, such as lower than 0.06, such as lower than 0.05, such as lower than 0.04, such as lower than 0.03, such as lower than 0.02, such as lower than 0.01, such as lower than 0.00."

"29. The method according to any one of the claims 24-28, wherein the free ion concentration of a divalent metal cation other than a zinc ion and a calcium ion at least in one of the purification steps is higher than 0.025 mM."

"30. The method according to claim 29, wherein said divalent metal cation is selected from the list consisting of Mg^{2+}, Cu^{2+}, Mn^{2+}, Co^{2+}, Fe^{2+}, Sm^{2+}, Ni^{2+}, Cd^{2+}, Hg^{2+}, Sm^{2+}, and Uo^{2+}."

"31. The method according to claim 30, wherein said divalent metal cation is selected from the list consisting of Mg^{2+}, Cu^{2+}, and Mn^{2+}."

"32. The method according to any one of the claims 29-31, wherein said free ion concentration of a divalent metal cation other than a zinc ion and a calcium ion at least in one of the purification steps

is higher than 0.025 mM, such as higher than 0.03 mM, such as higher than 0.035 mM, such as higher than 0.04 mM, such as higher than 0.045 mM, such as higher than 0.05 mM, such as higher than 0.055 mM, such as higher than 0.06 mM, such as higher than 0.1 mM, such as higher than 0.15 mM, such as higher than 0.2 mM, such as higher than 0.25 mM, such as higher than 0.3 mM, such as higher than 0.5 mM, such as higher than 1.0 mM."

"33. The method according to any one of the claims 24-32, wherein said GLA-residue containing serine protease is purified at least in one of the purification steps in the presence of a further divalent metal ion chelator."

"40. The method according to any one of the claims 24-38, wherein said GLA-residue containing serine protease is a Factor VII polypeptide."

III. The examining division refused the application under Article 97(2) EPC and held that neither the main request nor any of auxiliary requests 1 to 3 met the requirements of Articles 123(2) EPC.

IV. The applicant (appellant) filed an appeal against this decision. With the statement of grounds of appeal, the appellant filed a new main request and new auxiliary requests 1 to 4.

Claim 1 of the **main request** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide recovered from cell culture medium or milk is subjected to a number of purification steps,

wherein (a) at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration, or (b) at least one purification step is ion exchange chromatography, hydrophobic chromatography, chromatofocusing chromatography, size exclusion chromatography or affinity chromatography on an anti-factor VII antibody column,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA, the pH has a value between 4.5 and 6.9 and the free calcium ion concentration is lower than 0.10 mM."

Claim 1 of **auxiliary request 1** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein (a) at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration, or (b) the Factor VII polypeptide is recovered from cell culture medium or milk and at least one purification step is ion exchange chromatography, hydrophobic chromatography, chromatofocusing chromatography, size exclusion chromatography or affinity chromatography on an anti-factor VII antibody column,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA, the pH has a value between 4.5 and 6.9 and the free calcium ion concentration is lower than 0.10 mM."

Claim 1 of **auxiliary request 2** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein, the Factor VII polypeptide is recovered from cell culture medium or milk and at least one purification step is ion exchange chromatography, hydrophobic chromatography, chromatofocusing chromatography, size exclusion chromatography or affinity chromatography on an anti-factor VII antibody column,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA, the pH has a value between 4.5 and 6.9 and the free calcium ion concentration is lower than 0.10 mM."

Claim 1 of **auxiliary request 3** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA, the pH has a value between 4.5 and 6.9 and the free calcium ion concentration is lower than 0.10 mM."

V. Third party observations were filed on 5 November 2012.

VI. The appellant responded to the third party observations with letter of 18 January 2013.

VII. On 7 March 2016, the board summoned the appellant to oral proceedings. In an annex accompanying the summons pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) and expressing its preliminary opinion, the board explained in detail why neither of the sets of claims on file met the requirements of Article 123(2) EPC.

VIII. With letter of 27 May 2016, the appellant responded to the board's communication and filed auxiliary requests 3A, 3B and 3C.

Claim 1 of **auxiliary request 3A** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration,
wherein the pH in at least one of the purification steps has a value between 4.5 and 6.9, wherein the free calcium ion concentration at least in one of the purification steps is lower than 0.10 mM, and wherein said Factor VII polypeptide is purified in at least one of the purification steps in the presence of EDTA."

Claim 1 of **auxiliary request 3B** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of a further divalent metal ion chelator, which divalent metal ion chelator is EDTA, the pH has a value between 4.5 and 6.9 and the free calcium ion concentration is lower than 0.10 mM."

Claim 1 of **auxiliary request 3C** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration,
wherein the pH in at least one of the purification steps has a value between 4.5 and 6.9, wherein the free calcium ion concentration at least in one of the purification steps is lower than 0.10 mM, and wherein said Factor VII polypeptide is purified in at least one of the purification steps in the presence of a further divalent metal ion chelator, which divalent metal ion chelator is EDTA."

IX. During the oral proceedings before the board held on 28 June 2016, the appellant filed a new auxiliary request 4, replacing the previously filed auxiliary request 4, and a new auxiliary request 5.

Claim 1 of **auxiliary request 4** reads:

"A method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide is subjected to a number of purification steps,
wherein at least one purification step is anion exchange chromatography carried out at pH 6,
wherein, in said purification step, the Factor VII polypeptide is purified in the presence of EDTA and the free calcium ion concentration is lower than 0.10 mM."

Claim 1 of **auxiliary request 5** reads:

"A method for the purification of a Factor VIIa polypeptide whereby a solution of a Factor VII polypeptide recovered from cell culture medium or milk is subjected to a number of purification steps,
wherein (a) at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification or diafiltration, or (b) at least one purification step is ion exchange chromatography, hydrophobic chromatography, chromatofocusing chromatography, size exclusion chromatography or affinity chromatography on an anti-factor VII antibody column,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA and histidine, the pH has a value of 6 and the free calcium ion concentration is lower than 0.10 mM."

X. The appellant's arguments, as far as they are relevant for the present decision, can be summarised as follows:

Main request and auxiliary requests 1 to 3, 3A, 3B, 3C, and 4 - Article 123(2) EPC

The claims of all the requests met the requirements of Article 123(2) EPC, because the combination of features stated therein was directly and unambiguously derivable from the application as filed. In particular, the feature in claim 1 that the polypeptide is purified in the presence of EDTA was disclosed in the application as filed on page 13, lines 4-7, in claim 33 and throughout the examples.

Original claim 33 referred to the presence of a divalent metal ion chelator and page 13 disclosed only one short list of such chelators, which included EDTA. No new matter was created by deleting the other members of the list and thus arriving at EDTA.

Additionally, Examples 2, 5, 10 and 15, which described methods covered by claim 1, related to three different types of chromatography, and in each case EDTA was used. The skilled person, who knew that EDTA served to achieve low calcium ion concentrations by chelating the calcium ions, was thus taught by said examples that EDTA was the preferred divalent metal ion chelator and that a benefit with respect to the stability of Factor VII was achieved whenever it was used.

Furthermore, when looking at all examples as a whole, including those examples not covered by claim 1, the skilled person would realise that of the twelve instances in which a divalent metal ion chelator was

used in a purification step, nine (i.e. all but three) used EDTA. This demonstrated to the skilled reader of the application as filed a clear preference for EDTA in those cases in which a divalent metal ion chelator was used. The examples further showed that the use of EDTA was envisaged for both the high pH range and the low pH range originally disclosed. There was thus a basis for the combination of the use of EDTA as a divalent metal ion chelator with a low pH and a low calcium ion concentration.

Claim 1 of auxiliary request 4 was additionally based on page 7, lines 12-13 and Example 5 of the application as filed.

Auxiliary request 5 - Admission

Auxiliary request 5, although late-filed, should be admitted into the proceedings because it directly addressed the points raised by the board under Article 123(2) EPC.

XI. Final requests

The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with the statement of grounds of appeal, or, alternatively, on the basis of one of

- auxiliary requests 1 to 3 filed with the statement of grounds of appeal, or
- auxiliary requests 3A, 3B and 3C filed with letter of 27 May 2016, or
- auxiliary request 4 and 5 filed during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

Main request - Article 123(2) EPC

2. Article 123(2) EPC stipulates that a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

In accordance with the established case law of the boards of appeal, the relevant question to be decided in assessing Article 123(2) EPC is whether the skilled person would derive the subject-matter as amended directly and unambiguously from the application as filed, meaning that the amendments must not result in the introduction of technical information which a skilled person would not have objectively derived from the application as filed. Moreover, the content of a document as originally filed may not be seen as a reservoir of features from which features pertaining to separate embodiments can be combined in order to artificially create a particular embodiment.

3. Claim 1 of the application as filed concerns a "method for the purification of a Factor VII polypeptide whereby a solution of a Factor VII polypeptide (...) is subjected to a number of purification steps, wherein (a) at least one purification step is hydrophobic interaction chromatography, size exclusion chromatography, anion exchange chromatography, ultrafiltration, immunoaffinity purification, or diafiltration, or (b) at least one purification step is ion exchange chromatography, hydrophobic interaction chromatography, chromatofocusing chromatography, size

exclusion chromatography or affinity chromatography on an anti-factor VII antibody column,
wherein, in at least one of said steps, the Factor VII polypeptide is purified in the presence of EDTA, the pH has a value between 4.5 and 6.9, and the free calcium ion concentration is lower than 0.10 mM."

4. The appellant submitted that the features of the claimed method found a basis in the following parts of the application as filed:

- Original claim 24, which was directed generally to methods for purifying a GLA-residue containing serine protease by subjecting it to a number of steps, wherein the pH in at least one of the steps was between 4.5 and 6.9 or between 8.6 and 10; the optional higher pH range had been dropped,

- original claim 27, which was dependent on original claim 24 and referred to a free calcium ion concentration of lower than 0.10 mM,

- original claim 40, which was dependent on original claims 24-38 and specified that the GLA-residue containing serine protease was a Factor VII polypeptide,

- original claim 33, which was dependent on original claims 24-32 and specified the presence of a divalent metal chelator at least in one of the purification steps,

- page 13, lines 4-7 referred to a list of divalent metal ion chelators which included EDTA, and most of the examples described the use of EDTA,

- page 11, lines 27-36 and page 33, lines 10-23 disclosed the specified purification steps for parts (a) and (b) of claim 1, respectively.

5. With respect to the disclosure in the application as filed of the combination of features in claim 1, notably the combination of the feature concerning the presence of EDTA with the remaining features of the claim, the following is to be noted.

5.1 Page 13, lines 4-7 refers to EDTA and states that "The divalent metal ion chelator may be a polycarboxylic acid cheating agent, citrate, bathocuproine, bathophenanthroline, DTPA, ethylenediaminetetraacetic acid (EDTA), EGTA, penicillamine, TETA, TPEN, and derivatives thereof". Any preference for EDTA over the other divalent metal ion chelators in the list is not derivable from this passage.

5.2 The appellant submitted that the selection of EDTA from the list at page 13, lines 4-7 could be considered to be the result of the deletion of the other members of one single list and was therefore allowable under Article 123(2) EPC.

The board cannot follow this argument, because in order to arrive at the combination of features of the method of claim 1, additional selections have to be made, i.e. the pH value (between 4.5 and 6.9 or between 8.6 and 10), the free calcium concentration (see original claims 25-28 for possible concentration ranges), the free ion concentration of a divalent metal cation other than zinc and calcium (see original claims 29-32), the GLA-residue containing serine protease (see original claims 24 and 40), and the nature of the at least one purification step (see page 11, lines 27-36 and page

33, lines 10-23). The claimed combination of features is thus the result of selections from more than one list.

5.3 The question thus arises whether a preference for EDTA as divalent metal ion chelator in the context of the remaining features of claim 1 is directly and unambiguously derivable from other parts of the application as filed. The board notes that apart from the passage on page 13, lines 4-7 discussed above, reference to EDTA is made only in the examples section of the application as filed.

5.4 According to the appellant, a basis for EDTA as being the preferred divalent metal ion chelator was provided by Examples 2, 5, 10 and 15 of the application as filed. The appellant submitted that the words "in at least one of said steps" in the context of claim 1 had to be read as meaning that the specified conditions had to be present during a part of the purification step only, and not necessarily throughout it, and that, therefore, said examples described embodiments covered by claim 1.

5.5 Example 2 describes the purification of Factor VIIa by hydrophobic interaction chromatography on a column packed with Toyopearl MD-G Butyl resin. The column was equilibrated with a buffer having a pH of 7.5 and containing calcium and copper ions, then loaded with the Factor VIIa solution and washed with the same buffer. None of the chromatographic stages of equilibration, loading or washing of the column was carried out in the presence of EDTA. The bound Factor VIIa was then eluted using 20 mM EDTA, 50 mM histidine and pH 6.0.

Both Examples 10 and 15 describe the purification of Factor VIIa by immunoaffinity chromatography on a column packed with a Ca^{2+}-dependent anti-Factor VIIa monoclonal antibody. In both examples, the column was equilibrated with a solution containing calcium, loaded with a culture supernatant previously stabilised by the addition of calcium, washed in the presence of calcium, and finally eluted in the presence of 30 mM EDTA, 50 mM histidine, at pH 6.0.

Each of Examples 2, 10 and 15 thus describes that a solution of Factor VIIa was subjected to a specified type of chromatography, i.e. either hydrophobic interaction chromatography or immunoaffinity chromatography. The chromatography included the commonly known stages of chromatographic processes, namely equilibration, loading, washing and elution. In each of said examples, only the final stage, i.e. the elution of Factor VIIa from the column, was performed in the presence of EDTA, at a concentration of 20 mM in the case of the hydrophobic interaction chromatography and 30 mM in the case of the immunoaffinity chromatography.

5.6 The board considers that the skilled person cannot directly and unambiguously derive from said examples of the application as filed that EDTA would be generally preferable over the other divalent cation ion chelators referred to on page 13, lines 4-7 of the application as filed. In particular, a skilled person would not directly and unambiguously derive from said examples that EDTA should preferably be used as chelator independently of the specific circumstances of said examples, e.g. in any of the other types of chromatography listed in claim 1, in any of the chromatographic stages other than elution, at any

concentration, at any pH within the claimed range and at any free calcium concentration lower than 0.10 mM.

Therefore, Examples 2, 10 and 15 do not constitute an adequate basis for the generalisation adopted in claim 1.

5.7 Example 5 describes that an anion exchange chromatography was performed on a column packed with Pharmacia Q-Sepharose Fast Flow. The column was equilibrated with a solution containing 5 mM EDTA, 10 mM histidine, at pH 6.0. The subsequent loading of the column with a solution containing a Factor VIIa analog, the washing of the column, and finally the elution of the Factor VIIa analog from the column were carried out in the absence of EDTA.

The board considers that this disclosure does not provide a basis for the generalisation adopted in claim 1 either, because it cannot be directly and unambiguously derived from said example that EDTA should preferably be used as chelator independently of the specific circumstances of said examples, e.g. in any of the other types of chromatography listed in claim 1, in any of the chromatographic stages other than equilibration, at any concentration, at any pH within the claimed range and at any free calcium concentration lower than 0.10 mM.

5.8 The board thus takes the position that the combination of features in claim 1, and in particular the selection of EDTA and its combination with (i) the different kinds of chromatography specified in the claim, (ii) the pH range between 4.5 and 6.9, and (iii) a free calcium ion concentration lower than 0.10 mM, provides

the skilled person with additional technical information not disclosed in the application as filed.

5.9 The appellant further submitted that when looking at all examples of the application as filed as a whole, including those examples not covered by claim 1, the skilled person would realise that, of the twelve instances of a metal ion chelator being used in a purification step, nine (i.e. all but three) used EDTA. He/she would therefore conclude that EDTA was the preferred metal ion chelator.

5.10 The board cannot follow this line of argument, either. Firstly, those examples of the application as filed which are not covered by the amended claims cannot provide an adequate basis for the subject-matter claimed. Secondly, the mere fact that more examples of the application as filed describe the use of EDTA than the use of another divalent metal ion chelator, namely citrate, could be merely incidental and does not provide the skilled person with a direct and unambiguous disclosure of EDTA as being preferred. It has to be borne in mind that the question to be considered in the context of Article 123(2) EPC is not what may be rendered obvious by the disclosure of the application as filed, but what is directly and unambiguously derivable therefrom.

In the present case, the board is convinced that the claimed combination of features from separate embodiments of the application as filed is not directly and unambiguously derivable therefrom.

6. The board concludes that claim 1 of the main request does not meet the requirements of Article 123(2) EPC.

Auxiliary requests 1 to 3, 3A, 3B and 3C - Article 123(2) EPC

7. Each of claims 1 of auxiliary requests 1 to 3, 3A, 3B and 3C is directed to a method for the purification of a Factor VII polypeptide, which is characterised *inter alia* by the use of at least one of various types of chromatographic purification steps, the presence of EDTA, a pH value between 4.5 and 6.9 and a free calcium ion concentration of lower than 0.10 mM.

As set out in detail for claim 1 of the main request above, it is not directly and unambiguously derivable from the application as filed that EDTA should generally be used as the preferred divalent metal ion chelator. Therefore, the selection of EDTA and its combination with the remaining features of the claimed methods creates added subject-matter.

Consequently, auxiliary requests 1 to 3, 3A, 3B and 3C do not meet the requirements of Article 123(2) EPC.

Auxiliary request 4 - Article 123(2) EPC

8. Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 1 in that the at least one purification step is defined as anion exchange chromatography carried out at pH 6. The claim still refers to the features that the Factor VII polypeptide is purified in the presence of EDTA and that the free calcium ion concentration is lower than 0.10 mM.

9. This request replaced former auxiliary request 4 filed with the statement of grounds of appeal and was, pursuant to Article 13 RPBA, admitted into the proceedings because it was seen as an attempt to overcome an objection under Article 123(2) EPC raised

in the board's communication accompanying the summons to oral proceedings.

10. Page 7, lines 12-14 of the application as filed, to which the appellant referred as a basis under Article 123(2) EPC for claim 1, states that "Stabilisation of culture supernatant, immunoaffinity capture and purification by anion exchange chromatography carried out at pH 6 have by the inventors of the present invention been shown to have an enormous advantage over the known FVII purification processes." However, said passage does not mention EDTA and thus provides no direct and unambiguous disclosure of the claimed method.

11. The appellant further submitted that claim 1 was based on Example 5 of the application as filed.

As set out in detail in point 5.7 above, Example 5 describes the purification of a Factor VIIa analog by anion chromatography, whereby only the equilibration of the column, but not any of the subsequent stages of loading, washing and elution, was performed in the presence of 5 mM EDTA. The board considers that the generalisation in claim 1 to the presence of EDTA at any stage of the anion exchange chromatography and at any concentration cannot be directly and unambiguously derived from the application as filed.

Additionally, the specific range of a free calcium concentration of lower than 0.10 mM is not mentioned in the context of Example 5. There is no disclosure in Example 5 or in any other part of the application as filed of combining the presence of EDTA with the specific range of a free calcium concentration of lower than 0.10 mM.

12. Therefore, the method of claim 1 extends beyond the contents of the application as filed.

13. Consequently, auxiliary request 4 does not meet the requirements of Article 123(2) EPC.

Auxiliary request 5 - Admission

14. Claim 1 of auxiliary request 5 differs from claim 1 of the main request in that it refers (i) to Factor VIIa (instead of Factor VII) in line 1, (ii) to the presence of EDTA and histidine (instead of EDTA only) and (iii) to a pH of the value of 6 (instead of a value between 4.5 and 6.9).

15. Auxiliary request 5 was filed at the oral proceedings before the board and its admission is at the board's discretion (Article 13(1) RPBA).

16. According to the appellant, this request should be admitted into the proceedings because it addressed objections raised by the board under Article 123(2) EPC with respect to claim 1 of the main request.

17. The board acknowledges that claim 1 of auxiliary request 5 attempts to address the issues relating to the presence of histidine in Examples 2, 5, 10 and 15 and the purification of Factor VIIa in Examples 2, 10 and 15 of the application as filed. However, the claim does not address (let alone overcome) the principal objection relating to the lack of a disclosure in the application as filed of a preference for EDTA in the general context of claim 1, e.g. in any of the types of chromatography listed in the claim, in any of the

chromatographic stages, at any concentration and at any free calcium concentration lower than 0.10 mM.

Therefore, the board made use of its discretionary power under Article 13 RPBA and decided not to admit auxiliary request 5 into the proceedings.

18. It follows from the above that none of the claim requests is both admissible and allowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin U. Oswald

Decision electronically authenticated