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Datasheet for the decision of 18 October 2011

Case Number: T 2006/08 - 3.3.08

Application Number: 02013607.3

Publication Number: 1260582

IPC: C12N 9/64

Language of the proceedings: EN

Title of invention:
Conjugates of factor IX and a biocompatible polymer

Patentee:
BIOVITRUM AB

Opponent:
Baxter Aktiengesellschaft

Headword:
Conjugated factor IX/BIOVITRUM

Relevant legal provisions:
EPC Art. 83, 54, 56, 113(1)
EPC R. 103(1)(a)

Keyword:
"Main request, claims as granted - sufficiency of disclosure (yes); novelty (yes), inventive step (yes)"
"Refund of the appeal fee (no) - substantial procedural violation (no)"

Decisions cited:
G 0002/98, T 0026/85, T 0019/90, T 0558/95

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 2006/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 18 October 2011

Appellant: (Patent Proprietor)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted on 30 June 2008 revoking European patent No. 1260582 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
J. Geschwind

Summary of Facts and Submissions

I. European patent no. 1 260 582 is based on European patent application no. 02 013 607 which was a divisional application of the earlier European patent application no. 96 932 915 filed on 27 September 1996. The patent, which was revoked by the opposition division under Article 100(b) EPC for lack of sufficiency of disclosure (Article 83 EPC), had been granted with 5 claims and claim 1 read as follows:

"*1. A process for improving the in vivo function of a factor IX by shielding exposed targets of factor IX, comprising:*

(a) immobilizing factor IX by interaction with a group-specific adsorbent carrying anionic-exchange ligands;
(b) activating a biocompatible polymer;
(c) conjugating the activated biocompatible polymer to external sites of the immobilized factor IX; and
(d) eluting the conjugate from the adsorbent."

Claims 2 to 5 were directed to various embodiments of the method of claim 1.

II. The patentee (appellant) filed a notice of appeal and a statement setting out its grounds of appeal together with an auxiliary request and further documentary evidence (document D10).

III. The opponent (respondent) replied to the appellant's grounds of appeal and submitted further experimental evidence (Annex II).

IV. With the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) informing the parties of the board's preliminary, non-binding opinion on substantive matters.

V. No further substantive submissions were made by the parties in reply to the board's communication.

VI. After several requests to postpone oral proceedings, which were not granted by the board (with reference to the "Notice of the Vice-presidents of DG2 and DG3", OJ EPO, 2000, 456), the respondent's representative informed the board of its intention not to attend the upcoming oral proceedings.

VII. Oral proceedings took place on 18 October 2011 in the absence of the respondent. At the end of the oral proceedings the appellant withdrew its auxiliary request.

VIII. The following documents are cited in this decision:

D4: WO 93/15189 (publication date: 5 August 1993);

D5: WO 94/13322 (publication date: 23 June 1994);

D6: WO 94/29370 (publication date: 22 December 1994);

D8: S.B. Yan, J. Mol. Recognition, May/June 1996, Vol. 9, pages 211 to 218;

D10: M. Jacobs et al., J. Biol. Chem., 1994, Vol. 269, No. 41, pages 25494 to 25501.

IX. The appellant's arguments, insofar as they are relevant to the present decision, may be summarized as follows:

Article 100(b) EPC

According to the case law, an objection for lack of sufficiency of disclosure had to be based on serious doubts substantiated by verifiable facts (T 19/90, OJ EPO 1990, 476). The patent contained a detailed description, including several working examples, of how to perform the claimed method. While the working examples related to factor VIII, there was no indication whatsoever that the same method could not be carried out for factor IX. The structural and functional differences between factors VIII and IX were irrelevant for the claimed method which did not rely on the structure of the active site of the protein but rather on the immobilization of the protein through negatively charged residues present on its surface. The existence of negatively charged residues on the surface of factor IX were known in the art, as shown *inter alia* by document D10. Prior art on file also showed that factor IX could be immobilized on group-specific anion exchange materials. Respondent's allegations were not supported by any relevant documentary or experimental evidence and therefore, the respondent had not discharged its burden of proof. The improvement in the *in vivo* function of factor IX, as required in claim 1, was in relation to native, non-conjugated factor IX.

Article 100(a) EPC in connection with Article 56 EPC

Document D6, the closest prior art, disclosed the PEGylation of factor IX with the aim of improving its *in vivo* function. Thus, the technical problem to be solved was the provision of an alternative method for the PEGylation of factor IX. The solution provided by the patent involved the use of "*a group-specific adsorbent carrying anionic-exchange ligands*" which targeted negatively charged amino acids on the surface of factor IX. Although the skilled person was aware of the impaired biological function of factor IX upon PEGylation and eventually would have come across document D4 which taught to specifically shield the active site of enzymatic proteins (serine proteases) prior to their PEGylation, there was no hint in the prior art towards this solution which was based on a different concept from that disclosed in document D4. While it could be argued that benzamidine - a specific inhibitor blocking the catalytic site of the serine proteases exemplified in document D4 - could also function as an anion exchanger, its very basic pK of around 11 did not render it suitable for use in the claimed method.

Substantial procedural violation and reimbursement of the appeal fee

The decision of the opposition division went against the established case law and resulted from a wrong application of the legal basis underlying the issue of sufficiency of disclosure. Despite the lack of evidence supporting opponent's allegations, the opposition division considered that the burden of proof had

shifted from the opponent to the patentee and that the alleged deficiencies of the patent could not be redressed in any manner, thus depriving the patentee of the possibility of referring further experimental data. This conclusion, expressed at oral proceedings for the first time, was in contradiction to the previous two preliminary opinions of the opposition division which were based on the same facts and evidence as regards Article 83 EPC and which concluded that the opponent's arguments on the alleged lack of sufficiency were not convincing. An appeal would not have been necessary if the opposition division had not disregarded the established principles of burden of proof.

X. The respondent's arguments, insofar as they are relevant to the present decision, can be summarized as follows:

Article 100(b) EPC

The purpose of the claimed method, namely to improve the *in vivo* function of factor IX, was a limiting feature of claim 1 and thus, highly relevant for the claimed method. The patent did not disclose the claimed method in an enabling manner because the entire experimental data disclosed in the patent related to factor VIII but not to factor IX, and the prior art showed the two proteins to be completely different both structurally and functionally. There was a clear indication in the prior art that the method disclosed in the patent could not be extrapolated to factor IX without undue burden. The experiments reported in Annex II showed the resulting specific activities of factor IX to be significantly lower than those of factor VIII

when both proteins were treated according to the method of claim 1 and when compared to the respective untreated proteins. According to the case law, the patent had to describe at least one way to carry out the claimed subject-matter. The patent failed to disclose how to carry out a process for improving the *in vivo* function of factor IX. Because of this deficiency, it was not even necessary to file experimental evidence to support the objection of lack of enablement. The burden of proof to show that the patent disclosed the claimed subject-matter in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art laid thus on the patentee.

Entitlement to the claimed priority

The priority document disclosed a process for chemical modification of a polypeptide (claim 1), which could be factor IX (claim 3), but it did not disclose a process for improving the *in vivo* function of factor IX. There was only a reference to a process for improving the *in vivo* function of factor VIII (*inter alia* paragraph bridging pages 7 and 8). Accordingly, the method of claim 1 was novel over the disclosure of the priority document and hence, in view of decision G 2/98 (OJ EPO 2001, 413), the priority could not be acknowledged.

Article 100(a) EPC in connection with Article 54(2) EPC

Document D5 disclosed a process for improving the *in vivo* half-life and the immunogenicity of therapeutically or diagnostically useful molecules. This process had the same features as the method of

claim 1, in particular the specific binder disclosed therein was a "*group-specific adsorbent carrying anionic-exchange ligand*" as defined in claim 1. Document D5 further stated that any molecule having a desired activity, typically a protein, could be used in the disclosed process and thus, factor IX was also included. The use of factor IX in the claimed method could not be considered as a selection invention because the pre-requisite for a selection invention, namely that a person skilled in the art would not have seriously contemplated applying the teaching of document D5 to factor IX, was not met. According to decision T 26/85 (OJ EPO 1990, 22), anything comprised in the state of the art could be regarded as having been made available to the public in so far as the information given was sufficient to enable the skilled person to practice the invention.

Article 100(a) EPC in connection with Article 56 EPC

Document D5 disclosed a process for improving the *in vivo* function of a protein comprising the steps of binding a protective substance to its active site, conjugating an activated polymer to said protein, and separating the protein from the protective substance afterwards. This process was used for binding PEG to proteins - and thus, also to factor IX - while protecting their active site with a specific binding substance immobilized on a column. The alleged inventive contribution of the patent was to use an anion-exchange resin as a selective - and therefore specific - binder of reactive lysine groups of factor IX. According to the patent, by specifically binding the reactive sites of factor IX during the conjugation

process, the active sites of factor IX were protected and thus, the *in vivo* function of factor IX was allegedly improved. The fact that the group-specific anion-exchange resin could also bind to sites of factor IX different from its reactive sites, did not alter the fact that the resin was used for specifically binding the reactive sites of factor IX in the method of claim 1. Thus, claim 1 lacked inventive step in view of document D5 alone.

As shown by document D6, it was known in the art to improve the *in vivo* function of factor IX by binding it to biocompatible polymers (PEG). A person skilled in the art would combine the teachings of documents D5 and D6 when looking for a process for improving the *in vivo* function of factor IX and would arrive at the method of claim 1. Likewise, document D4 disclosed the protection of the active sites of proteins during PEGylation by binding the active sites to immobilized substances. Thus, it was known in the art that PEGylation of the active sites of a protein could be avoided in order to improve the *in vivo* function of the PEGylated proteins. Accordingly, the method of claim 1 lacked inventive step in view of the combination of documents D5 with D4.

Prior art on file showed the selective, and reversible, immobilization of factor IX on anionic-exchange ligands, i.e. the use of a group-specific adsorbent carrying anion-exchange ligands for immobilizing factor IX. Document D8 showed that vitamin K-dependent proteins, including factor IX, had an amino-terminal Gla-domain important for the calcium ion binding properties of these proteins and thus contributing to their activity. From this prior art, it was derivable that factor IX

could also be immobilized by interaction with a group-specific adsorbent carrying anionic exchange ligands. The combination of document D5 with this prior art rendered the method of claim 1 not inventive.

Substantial procedural violation and reimbursement of the appeal fee

The objection for lack of sufficiency of disclosure had been on file since the beginning of the opposition and thus, the patentee had had ample time and opportunity to react to it in an appropriate manner. The patentee should have known that provisional opinions of the opposition division were not binding for further proceedings (T 558/95 of 10 February 1997).

XI. The appellant (patentee) requested that the decision under appeal be set aside, that the patent be maintained as granted and that the appeal fee be reimbursed.

XII. The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

Main and sole request - Claims as granted

Article 100(b) EPC

1. In the decision under appeal, the opposition division came to the conclusion that the claims as granted did not fulfil the requirements of Article 83 EPC, because

all examples of the patent concerned factor VIII and not factor IX, being that factor IX was only briefly mentioned in the general part of the description. In view of the large structural and functional differences between these two factors, it could not be expected that the conclusions reached for factor VIII could be *prima facie* applied to factor IX without undue experimentation.

2. Claim 1 as granted is directed to "*a process for improving the in vivo function of a factor IX by shielding exposed targets of factor IX*", the process then being defined by the method steps (a) to (d) (cf. Section I *supra*). According to the established case law, an objection for lack of sufficiency of disclosure should be based on serious doubts - substantiated by verifiable facts - that the process itself, as defined by the method steps, could not be successfully applied to factor IX without undue burden. Moreover, the claimed process implies that an improved *in vivo* function of factor IX is achieved, since this is the purpose of the claimed process and thus, a limiting feature of the claimed subject-matter. From the argumentation put forward by the opposition division as well as by the respondent, it is however not apparent to the board to what extent the undisputedly existing structural and functional differences between factors VIII and IX may have an impact in the extrapolation of the method disclosed in the patent-in-suit for factor VIII to factor IX.

2.1 *As for the method*, the board considers that, although no experimental details are provided for factor IX in the patent-in-suit, no undue experimentation would be

required to carry out the method steps (a) to (d) with factor IX. The patent-in-suit provides sufficient information (cf. paragraph [0020] *et seq*., Examples 3 to 5 of the patent-in-suit) and there is also prior art on file which demonstrates that no special contribution from a skilled person would be required for immobilizing factor IX on (group-specific) adsorbent anionic-exchange materials. The PEGylation of factor IX was also well-known in the art (cf. document D6 and paragraphs [0004] and [0008] of the patent-in-suit).

2.2 *As for the effect* or the presence of an improved *in vivo* function of factor IX, it was known from the prior art that, while the specific activity of a PEGylated protein usually decreases, a PEGylated protein also has a longer half-life and a decreased immunogenicity compared to the non-PEGylated protein. This is specifically disclosed in document D6 in relation to factor IX (cf. page 4 lines 10 to 16 of document D6). These properties provide an overall improvement in the *in vivo* function of the protein. The degree of modification allows a trade off between advantages (longer half-life and lower immunogenicity) and disadvantages (decreased activity) (cf. *inter alia* paragraphs [0002] to [0004] of the patent-in-suit). Accordingly, it is plausible that the claimed process does achieve an improvement of the *in vivo* function of factor IX. It is worth noting here that the improvement defined in claim 1 has to be achieved over the *in vivo* function of a native, non-conjugated factor IX.

Respondent's experimental evidence (Annex II)

3. In reply to the appellant's grounds of appeal, the respondent submitted an experimental report (Annex II) to support its argumentation (cf. Section III *supra*). According to the respondent this report shows that the resulting specific activities for factor IX are significantly lower than those obtained for factor VIII when both are PEGylated using NHS-chemistry (sic) and when compared to the respective untreated proteins. As regards this experimental evidence, the board has the following observations:

3.1 Indeed, it is shown in Annex II that, after PEGylation of recombinant factor VIII and factor IX, the specific activities are 49.9% and 55% for factor VIII and 13.5% and 21.8% for factor IX - all in comparison to the corresponding un-conjugated starting material. However, the experiments performed in Annex II have not been performed in accordance with the process of claim 1. In particular, the critical first step of this process, namely the immobilization of the protein by interaction with a group-specific adsorbent carrying anionic-exchange ligands, i.e. step (a) of claim 1 (cf. paragraphs [0011] and [0018] of the patent-in-suit), has not taken place.

3.2 While in Annex II it is shown that the decrease of specific activity upon PEGylation is larger for factor IX than for factor VIII, this result cannot serve as evidence that the performance of step (a) of the process of claim 1, previous to carrying out the PEGylation step, does not have a positive influence on the specific activity of the conjugated or PEGylated

factor IX (cf. point 2.2 *supra*). Accordingly, the board considers that the results presented in Annex II do not allow to conclude that an improved *in vivo* function of factor IX (decreased immunogenicity and longer half-life compared to non-PEGylated factor IX; higher specific activity compared to PEGylated factor IX with no previous immobilization) cannot be achieved in a straightforward way by applying the process of claim 1.

3.3 It is also common general knowledge that the degree of purity of a protein might well influence its specific activity resulting from a PEGylation method (cf. *inter alia* paragraph [0010] of the patent-in-suit). Although both factor VIII and factor IX used in Annex II are recombinant products, different techniques have been used for their production (Advate manufacturing process for factor VIII and CHO cell-lines for factor IX) and there is no information in Annex II on their respective degree of purity.

4. It follows from these considerations that the respondent's argumentation as regards the objection of lack of sufficiency of disclosure is not supported by verifiable facts and thus, the claimed subject-matter is considered to fulfil the requirements of Article 83 EPC.

Entitlement to the claimed priority

5. The respondent argues that the claimed subject-matter is not entitled to the claimed priority (cf. Section X *supra*). No comments have been made by the opposition division in the decision under appeal on the merits of this objection.

6. Claims 1 to 16 of the priority document are directed to "*a process for chemical modification of a polypeptide by covalent binding a biocompatible polymer to the said polypeptide*", wherein said process is characterized by method steps identical to those of granted claim 1. Claim 3 of the priority document further specifies the polypeptide as being factor IX. However, claims 1 and 3 are not restricted to processes resulting in an improvement of the *in vivo* function of factor IX.

7. Nevertheless, it is clearly derivable from the section "*Summary of the invention*" present in the priority document that the purpose of immobilizing a polypeptide on a group-specific adsorbent prior to the conjugating reaction is to retain the specific activity of the chemically modified polypeptide. This is also the purpose mentioned in the patent-in-suit. Moreover, by reference to the known prior art, the priority document also acknowledges the advantageous effects of PEGylation, namely an increased *in vitro* stability, an improved *in vivo* half-life and a reduction of the immunogenicity of the modified or PEGylated polypeptide (cf. page 1, last two paragraphs under the section "*Background of the invention*" of the priority document). In fact, this is an implicit disclosure that the process disclosed in the priority document actually intends to improve the *in vivo* function of a polypeptide such as factor IX. Therefore, the board concludes that the subject-matter of the claims as granted is at least implicitly, but directly and unambiguously, disclosed in the priority document.

8. As for the absence in the priority document of any example of the disclosed process using factor IX, the same reasons as those given above regarding Article 83 EPC apply also to the disclosure of the priority document.

9. Therefore, the claimed subject-matter is considered to be entitled to the claimed priority date.

Article 100(a) EPC in connection with Article 54(2) EPC

10. The respondent holds that the subject-matter of the granted claims is anticipated by the disclosure of document D5 (cf. Section X *supra*). The board, however, agrees with the conclusions of the opposition division in the decision under appeal and considers that the disclosure of document D5, which does not mention factor IX at all, cannot anticipate the subject-matter of the granted claims which is directed to a process for improving the *in vivo* function of factor IX (cf. Section I *supra*). Decision T 26/85 (*supra*), referred to by the respondent and concerning the novelty of overlapping ranges, does not apply to the present case in which the relevant issue concerns the novelty of a specific disclosure (factor IX) over a generic disclosure (polypeptides) and wherein the specific disclosure has not been disclosed at all.

11. Moreover, document D5 refers only to a "*specific binder substance*" or to a second substance that "*specifically binds*" to the domain of a first bioactive substance which is responsible for the activity of this first substance and wherein this first substance - which is defined as any molecule having a desired activity,

typically a protein or a glycoprotein - is to be conjugated with a polymer. However, there is no reference to "*a group-specific adsorbent carrying anionic-exchange ligands*" and, even though the definition of "*a group-specific adsorbent carrying anionic-exchange ligands*" may be broadly interpreted (*infra*), it does certainly not embrace any of the (second) substances mentioned in document D5 (cf. *inter alia* pages 7 and 8 of document D5).

12. Thus, the claimed subject-matter is considered to fulfil the requirements of Article 54 EPC.

Article 100(a) EPC in connection with Article 56 EPC

13. Document D5 or, alternatively, document D8 have been cited by the respondent as closest prior art (cf. Section X *supra*). Document D8 was published on May/June 1996 - after the priority date of the patent (29 September 1995) and, since the claimed priority is considered to be valid (cf. points 5 to 9 *supra*), this document is not prior art citable under Article 54(2) EPC. The board, however, agrees with the appellant that document D6 is the most suitable starting point for the discussion of inventive step (cf. Section IX *supra*).

14. Both documents D5 and D6 disclose methods for improving the *in vivo* function of proteins by means of PEG conjugation. However, only in document D6 are such methods disclosed specifically in relation to factor IX, while factor IX is not even mentioned in document D5. Accordingly, document D6, disclosing methods for improvement of the *in vivo* function of factor IX, is

considered by the board to represent the closest prior art.

15. The underlying technical problem may be seen in the provision of an alternative method for improving the *in vivo* function of factor IX. The process of claim 1 provides a solution to this problem and differs from the method disclosed in document D6 in that, previous to the PEGylation, factor IX is immobilized in a column comprising a group-specific adsorbent carrying anion-exchange ligands. By immobilizing factor IX prior to its conjugation, the negative impact of PEGylation on the biological function of factor IX can be advantageously avoided or reduced. Although in the patent the effect is not demonstrated for factor IX, it is clearly shown for factor VIII. Example 3 shows that, adsorbing recombinant Factor VIII to Q Sepharose™ FF (a strong anion-exchanger on a Sepharose/Agarose matrix) before conjugation with PEG, results in a higher retention of its specific activity in comparison to the PEGylation of factor VIII carried out in Example 2 without prior immobilization of factor VIII. Other advantages of both economical and clinical nature are also referred to in the patent-in-suit (cf. paragraph [0013] of the patent-in-suit).

16. Although the deficiencies and problems associated with protein PEGylation were well-known to a skilled person, in particular the impairment of the *in vivo* function of the PEGylated protein, the board is convinced that, in view of the prior art on file, the solution disclosed in the patent was not obvious to a skilled person. Indeed, a skilled person faced with the problem underlying the patent-in-suit and looking for

appropriate solutions would most likely have turned its attention to the teachings of documents D4 and D5, both disclosing protein PEGylation methods with protection of the protein active site by shielding it with a specific ligand.

17. Document D4 discloses the PEGylation of serine proteases, wherein the active site of these proteases is protected by shielding it with benzamidine, a specific inhibitor of the serine proteases of the trypsin family, which is immobilized on a highly hydrated insoluble polysaccharide (Sepharose) (cf. page 3, lines 5 to 29 of document D4).

17.1 It could be argued that, since benzamidine binds to several proteases belonging to the group of serine proteases, benzamidine is a "*group-specific adsorbent*". Moreover, since benzamidine has an amidino group in its structure, it could also theoretically function as an "*anionic-exchange ligand*". Thus, benzamidine could be seen as being encompassed within the general definition of "*a group-specific adsorbent carrying anionic-exchange ligands*" used in claim 1(a) as granted and broadly characterized in paragraphs [0011] and [0028] of the patent-in-suit. If this was the case, the solution as claimed would be obvious in the light of document D4, since factor IX, which is not mentioned at all in document D4, was however known to be a serine protease of the trypsin family.

17.2 However, the appellant convincingly argued that benzamidine has a very basic pK around 11 and thus, would not be suitable for use as an anionic-exchange ligand in a process in which the function of a protein

is to be preserved (cf. Section IX *supra*). There is also no evidence on file to show or support that benzamidine has ever been used as an anionic-exchange ligand. Therefore, benzamidine is considered not to fall within the general definition used in the method step (a) of claim 1.

17.3 Moreover, the method of document D4 is, conceptually, completely different from the claimed process. Whereas the former relies on a direct and specific binding of a substance (benzamidine) to the active site of a protein (serine proteases), the latter does not specifically target the active site of the (serine protease) factor IX but relies on the presence of accessible negative charged amino acids on its surface to interact - in a more general manner - with the "*group-specific adsorbent carrying anionic-exchange ligands*". As stated in paragraph [0028] of the patent, group-specific adsorbents "*often bind less strongly and elution can be performed under milder conditions than with mono-specific adsorbents, the latter binding to a single or a very small number of polypeptides*" - as is the case for benzamidine.

18. Document D5 discloses a process for the preparation of a conjugate between a polymer and a first substance having a biological activity, the process comprising binding the first substance with a second substance that specifically binds the domain mediating the biological activity of the first substance, conjugating a polymer to the first substance having the second substance bound thereto, and freeing the second substance from the first substance having the polymer

conjugated thereto (cf. page 5, line 20 to page 6 line 3 and claim 1 of document D5).

18.1 Document D5 explicitly states that "*[t]he invention relies upon the use of a second substance that specifically recognizes a domain that mediates the desired biological activity of a first substance which is to be derivatized. The second substance can be viewed as a specific binder substance*" (cf. page 6, lines 14 to 18) and further exemplifies the second substance as being "*an antigen or antidiotypic antibody, receptor or anticytokine antibody, antibody, enzyme substrate, receptor or ligand. In each case the second substance specifically binds to the first substance to shield the domain of the first substance which is responsible for the activity of the first substance*" (cf. page 7, lines 8 to 14). Accordingly, the method of document D5, as that of document D4, involves shielding the active site of the (first) biologically active substance to be conjugated, and requires, as an essential feature, that said shielding is made by binding a specific (second) binder substance to the active site of the first substance.

18.2 Factor IX is not mentioned at all in document D5 and, as for document D4, the board is convinced that there is no hint or indication in document D5 that could lead a skilled person to the claimed subject-matter in an obvious manner. The method of document D5 is conceptually and technically more closely related to that described in document D4 than to that of claim 1 (cf. point 17.3 *supra*).

19. Thus, the board considers the claimed subject-matter to fulfil the requirements of Article 56 EPC. Neither the disclosure in document D6 alone or in combination with any of documents D4 or D5 render the solution proposed by the claimed subject-matter obvious.

Reimbursement of the appeal fee (Rule 103(1)(a) EPC)

20. The appellant alleges that the opposition division committed a substantive procedural violation (Article 113(1) EPC) because it reached a decision which was based on a wrong application of established legal principles. Moreover, the opposition division, having issued twice a favourable opinion on sufficiency of disclosure, came to a negative conclusion only at the oral proceedings based on the same facts and evidence that were on file before. Finally, the patentee was deprived of the possibility of providing experimental data to overcome the alleged deficiency of the patent and it was left with the only possible remedy of appeal (cf. Section IX *supra*).

21. Although the opposition division expressed an opinion on the issue of sufficiency of disclosure in favour of the patentee in two communications (cf. point 5 of the communication dated 3 November 2006 and point 8 of the communication dated 26 October 2007 annexed to the summons to the oral proceedings), this opinion was clearly labelled as being preliminary and non-binding. It is also worth noting that, following the aforementioned communications of the opposition division, the opponent filed submissions on 28 February 2007 and on 8 February 2008, respectively, in which it clearly stated that its objections raised under

Article 83 EPC were maintained and some further developments on that issue were added. To this extent, the appellant could have legitimately expected that the opponent would try to reverse the preliminary and non-binding opinion of the opposition division during the oral proceedings.

22. A preliminary, provisional (positive) opinion does not prevent a party to make its complete case. It is the responsibility of a party to ensure that the facts and evidence filed are not only unequivocally clear but also as complete as possible. If a party decides to retain or not to file further evidence to support its case, it runs the risk that an adverse decision may be issued based only on the available (incomplete) evidence on file.

23. The alleged wrong indications of the opposition division which the appellant considered to be contrary to the Guidelines and the established case law may well amount to an error of judgment by the opposition division but they do not constitute a procedural non-compliance or violation, let alone a substantial one.

24. Thus, the request for the reimbursement of the appeal fee is rejected.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is maintained as granted.

3. The request for reimbursement of the appeal fee is rejected.

The Registrar: The Chairman:

A. Wolinski M. Wieser