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Datasheet for the decision of 6 December 2007

Case Number: T 0405/06 - 3.3.08

Application Number: 93919098.9

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IPC: C12N 15/13

Language of the proceedings: EN

Title of invention:
Immunoglobulins devoid of light chains

Patentee:
VRIJE UNIVERSITEIT BRUSSEL

Opponent:
DOMANTIS LIMITED

Headword:
Immunoglobulins/BRUSSEL

Relevant legal provisions (EPC 1973):
EPC Art. 54, 56, 83, 84, 123

Keyword:
"Main request: added matter (yes)"
"Auxiliary request 1: sufficiency of disclosure (no)"
"Auxiliary request 2: added matter (no)"
"Clarity (yes)"
"Sufficiency of disclosure (yes)"
"Novelty (yes)"
"Inventive step (yes)"

Decisions cited:
T 0190/99, T 0100/01

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0405/06 **-** 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 6 December 2007

Appellant I: (Patent Proprietor)
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 31 January 2006 concerning maintenance of European patent No. 0656946 in amended form.

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
C. Heath

Summary of Facts and Submissions

I. The patent proprietor (appellant I) and the opponent (appellant II) each lodged an appeal against the interlocutory decision of 31 January 2006, whereby European patent No. 0 656 946, which had been granted on European patent application No. 93 919 098.9 originating from an international application published as WO 94/04678 (referred to as the application as filed), was maintained on the basis of the first auxiliary request filed on 30 August 2005.

II. The main request then on file had been refused by the Opposition Division for lack of inventive step (Article 56 EPC).

III. The patent had been opposed on the grounds as set forth (i) in Article 100(a) EPC that the invention was not new (see Article 54 EPC) and did not involve an inventive step (see Article 56 EPC), (ii) in Article 100(b) EPC that the patent did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (see Article 83 EPC), and (iii) in Article 100(c) EPC that the subject-matter of the patent extended beyond the content of the application as filed (see Article 123(2) EPC).

IV. The statements setting out the grounds of appeal were filed. A main request and two auxiliary requests were also filed by appellant I in replacement of the requests on file.

V. Each of the appellants submitted a reply to the other's statement of grounds of appeal.

VI. On 27 February 2007 the Board issued a communication expressing provisional and non-binding opinions and summoned the parties to oral proceedings scheduled on 5 July 2007.

VII. With a letter dated 26 March 2007, appellant I requested postponement of the oral proceedings which was refused with a communication dated 12 April 2007.

VIII. With a letter dated 18 May 2007, appellant II filed further submissions which were accompanied by a first scientific report.

IX. With a letter dated 31 May 2007, appellant I requested postponement of the oral proceedings in order to be in the position to prepare a response to the experimental data submitted by appellant II.

X. With a communication dated 8 June 2007, the Board informed the parties that the oral proceedings were postponed until 6 December 2007.

XI. With a letter dated 5 June 2007, appellant I filed further submissions which were accompanied by three auxiliary requests to replace the auxiliary requests on file.

XII. With a letter dated 5 June 2007, appellant II filed further submissions.

XIII. Observations under Article 115 EPC were received on 15 June 2007 on behalf of the Department of Cell Biology, Erasmus MC.

XIV. With a letter dated 5 November 2007, appellant II filed further submissions which were accompanied by a second scientific report.

XV. With a letter dated 6 November 2007, appellant I made further submissions which were accompanied by a main request and seven auxiliary requests (1 to 7) to replace the main and the auxiliary requests then on file. Experimental data and comments on the second scientific report of appellant II were enclosed.

Claims 1 and 11 of the **main request** which were identical to claims 1 and 11 as granted read:

"1. Immunoglobulin characterized in that it comprises two heavy polypeptide chains **capable of recognizing and binding one or several antigens**, wherein the heavy polypeptide chains are devoid of a so-called first domain in their constant region (CH1), this immunoglobulin being devoid of light polypeptide chains."

(emphasis added by the Board)

"11. Fragment corresponding to a polypeptide of a heavy chain of an immunoglobulin, which contains an amino acid residue at position 45 of said heavy chain which is a charged amino acid or a cysteine residue, said fragment forming a determined antigen binding site."

XVI. Oral proceedings took place on 6 December 2007 at which appellant I filed new auxiliary requests 1 and 2 and withdrew previous auxiliary requests 1 to 7.

Claim 1 of auxiliary request 1 read:

"1. Immunoglobulin characterized in that it comprises two heavy polypeptide chains **sufficient for the formation of a complete antigen binding site, or several antigen binding sites** wherein the heavy polypeptide chains are devoid of a so-called first domain in their constant region (CH1), this immunoglobulin being devoid of light polypeptide chains."

(emphasis added by the Board)

Auxiliary request 2 consisted of 36 claims.

Claims 1 and 10 read:

"1. Immunoglobulin characterized in that **it is obtainable from Camelids** and in that it comprises two heavy polypeptide chains sufficient for the formation of a complete antigen binding site, or several antigen binding sites wherein the heavy polypeptide chains are devoid of a so-called first domain in their constant region (CH1), this immunoglobulin being devoid of light polypeptide chains."

(emphasis added by the Board)

"10. Fragment which is a heavy polypeptide chain of an immunoglobulin according to claim 1 or a fragment which

is the variable region of a heavy chain of an immunoglobulin according to claim 1, both of which fragments contain an amino acid residue at position 45 of said heavy chain which is a charged amino acid or a cystéine [sic] residue, said fragment forming a determined antigen binding site."

Claims 2 to 9, 12 to 20 and 28 to 33 were dependent on claim 1 and directed to particular embodiments thereof.

Claim 11 was directed to a further fragment of an immunoglobulin according to anyone of claims 1 to 9.

Each of claims 21 and 22 was directed to a nucleotide sequence encoding all or part of an immunoglobulin according to anyone of claims 1 to 20.

Claims 23 and 24 were respectively directed to a process for the preparation of a monoclonal antibody or antibodies according to anyone of claims 1 to 20.

Claims 25 to 27 concerned particular embodiments of claim 24.

Claim 34 was directed to a recombinant vector comprising a nucleotide sequence according to claim 21 or claim 22.

Claim 35 was directed to a recombinant cell or non-human organism modified by a vector according to claim 34.

Claim 36 was directed to a cDNA library composed of nucleotide sequences coding for a heavy-chain immunoglobulin according to anyone of claims 1 to 20.

XVII. The following documents are referred to in the present decision:

(D1) H. Ungar-Waron et al., Isr. J. Vet. Med., Vol. 43, No. 3, March 1987, Pages 198 to 203

(D2) E. Sally Ward et al., Nature, Vol. 341, 12 October 1989, Pages 544 to 546

(D3) F. Prelli and B. Frangione, J. Immunol., Vol. 148, No. 3, 1 February 1992, Pages 949 to 952

(D6) C. Hamers-Casterman et al., Nature, Vol. 363, 3 June 1993, Pages 446 to 448

(D12) R. Sitia et al., Cell, Vol. 60, 9 March 1990, Pages 781 to 790

(D24) "Immunology", I. M. Roitt et al., Churchill Livingstone, Gower Medical Publishing, London, New-York, 1991, Second Edition, Pages 5.1 to 5.11

(D43) S. M. Azwai et al., J. Comp. Path., Vol. 109, 1993, Pages 187 to 195

XVIII. The submissions made by appellant I, insofar as they are relevant to the present decision, may be summarised as follows:

Main request (claim 1)
(added matter; Article 123(2) EPC)

The term "complete" used on page 4 of the application as filed did not convey any other information but the fact that an unexpected difference was observed between the claimed immunoglobulins and the conventional immunoglobulin with a four-chain structure, the antigen binding sites of the claimed immunoglobulins being formed exclusively by the heavy chains.

Thus, the expressions "*capable of recognizing and binding one or several antigens*", as used in present claim 1, and "*sufficient for the formation of a complete binding site*", as used in claim 1 as originally filed, were equivalent.

Auxiliary request 1
Sufficiency of disclosure (Article 83 EPC)

The description of the patent disclosed the isolation of the immunoglobulins of the invention starting from serum of camelids or their production by expression of nucleotide sequences encoding them. The disclosed process for the isolation of the immunoglobulins was not specific for camelids, but rather designed to enable the specific separation of immunoglobulins, especially through the use of fraction adsorption on Protein A or Protein B Sepharose. Once, (i) the existence of the new type of immunoglobulins essentially different from the conventional four-chain immunoglobulins was known, (ii) the associated basic structure of this new type of immunoglobulins was characterised, and (iii) means to assay their antigen

binding capacity and a process to isolate those immunoglobulins or to prepare them by expression of their sequences were disclosed, nothing could prevent the skilled person from repeating the same isolation and assay steps with the serum of species other than camelid species for detecting similarly defined immunoglobulins.

Auxiliary request 2

Added matter (Article 123(2) EPC)

The wording "obtainable from" used in claim 1 found a support on page 19, second sentence, of the application as filed.

Clarity (Article 84 EPC)

The wording "obtainable from" as used in claim 1 was clear. The claimed immunoglobulins were defined by both clearly understandable structural and functional features.

Claims 13, 14, 20, 23 and 36 corresponded to granted claims 17, 18, 24, 27 and 40. They had the same wording. Therefore, they were not objectionable for lack of clarity.

Sufficiency of disclosure (Article 83 EPC)

The application as filed, in particular in the experimental part of the description, provided a detailed and sufficiently clear and complete disclosure

of the structure and preparation of the camelid immunoglobulins to which claim 1 was directed.

Novelty (Article 54 EPC)

Document D1 taken alone was not relevant for the assessment of the novelty of claim 1. It did not contain any information as to the identity of the protein corresponding to the protein band of 40 kDa seen on the electophoregram of Fig. 2.

Inventive step (Article 56 EPC)

Not document D2 as decided by the opposition division but document D24 represented the closest state of the art. Document D24 was a hallmark publication describing the commonly accepted conventional four-chain structure and functions of immunoglobulins. It did not contain any statement that it could be beneficial to envisage or look for a different fundamental structure for functional immunoglobulins. Starting from document D24, it was impossible to conceive any other structure than the four-chain one.

If document D1 were to represent the closest prior art, the technical problem would be the determination of the structure of the camel immunoglobulins. The skilled person would not have contemplated any structure other than the conventional four-chain one as it was the only structure described in the document.

XIX. The submissions made by appellant II, insofar as they are relevant to the present decision, may be summarised as follows:

Main request (claim 1)
(added matter; Article 123(2) EPC)

Claim 1 at issue failed to qualify the binding as "complete". Thus, it went beyond the original disclosure, according to which such a qualification was mandatory.

Auxiliary request 1 (claim 1)
Sufficiency of disclosure (Article 83 EPC)

In the application as filed the structure and the preparation of non-camelid immunoglobulins were not disclosed in a manner sufficiently clear and complete. The experimental part of the description as a whole was dedicated to the characterisation and the preparation of specific camelid immunoglobulins only. As explained in the scientific reports provided with the appellant II's letters of 18 May and 5 November 2007, the inventors had merely determined the structure of the camelid V_{HH} immunoglobulins. In an attempt to generalise this teaching, the inventors analysed the sequence differences between camelid V_{HH} antibodies and mammalian V_H domains, and erroneously concluded that the presence of a charged amino acid position 45 was essential for a V_H domain to function properly in absence of a light chain. The differences were in fact far more complex than a single amino acid change and in non-camelid single-chain V_H immunoglobulin domains it appeared that position 45 was frequently occupied by an uncharged amino acid.

Auxiliary request 2

Added matter (Article 123(2) EPC) and clarity (Article 84 EPC)

The wording "obtainable from" taken in the broad context of claim 1 had no support in the application as filed. It encompassed *inter alia* situations where camelids would have been made transgenic for the expression of genes encoding human immunoglobulins, i.e. immunoglobulins not normally produced by them. This showed also that the said wording rendered unclear the subject-matter for which protection was sought as non-camelid immunoglobulins could also be encompassed by the claim.

Claims 13, 14, 20, 23 and 36 lacked clarity due to the use of the optional terms "especially, "for instance" and "for example".

Sufficiency of disclosure (Article 83 EPC)

Insofar as, in view of the expression "obtainable from Camelids" used therein, claim 1 encompassed non-camelid immunoglobulins, the objections were the same as for auxiliary request 1.

Novelty (Article 54 EPC)

Claim 1 lacked novelty in view of document D1, interpreted in the light of documents D6 and D43. The skilled person would have found that the protein corresponding to the band of 40 kDa observed upon

SDS-PAGE in document D1 was an immunoglobulin as recited in claim 1.

Inventive step (Article 56 EPC)

Claim 1 lacked inventive step. Document D2 represented the closest state of the art. The technical problem to be solved over document D2 was the provision of improved immunoglobulins lacking light chains and solving the problem of stickiness or the provision of alternative immunoglobulin structures to the accepted four-chain IgG structure and also solving the problem of stickiness. There was no general solution applicable to the technical problem across the whole scope of the claim.

If document D1 were to represent the closest prior art, the technical problem would be the determination of the structure of the camel immunoglobulins. It was obvious from Figure 2 of document D1 that, in view of its apparent molecular weight, the protein corresponding to the band of 40 kDa lacked light chains.

XX. Appellant I (patentee) requested that the decision under appeal be set aside and the patent be maintained on the basis of either the main request as filed with the letter of 6 November 2007, or one of auxiliary requests 1 or 2 as filed during the oral proceedings.

XXI. Appellant II (opponent) requested that the decision under appeal be set aside and the patent be revoked.

Reasons for the Decision

Main request (claim 1)

Added matter (Article 123(2) EPC)

1. Whereas in the application as filed the immunoglobulins for which protection is claimed are characterised as comprising two heavy polypeptide chains "*sufficient for the formation of a complete antigen binding site*" (see the passage bridging pages 3 and 4, as well as claim 1 of the application as filed) in claim 1 at issue the two heavy chains are simply required to be "*capable of recognizing and binding one or several antigens*".

2. As stated on page 4, third full paragraph, of the application as filed, by "*a complete antigen binding site*" it is meant "*a site which will alone allow the recognition and complete binding of an antigen*", this being "*verified by any known method regarding the testing of the binding affinity*".

3. The qualification of the binding of an antigen as "complete" in the application as filed is understood by the skilled person as emphasising that the binding is "as great in degree or amount as it possibly can be". This underlines the fact that the immunoglobulins which are disclosed in the patent in suit should comprise two heavy chains "sufficient for the formation of a complete antigen binding site", i.e. the site should contain all the structural parts which ensure such a binding. Claim 1 at issue merely requires an "unqualified binding" and, thus, covers also situations in which binding is not "as great as it possibly can

be". This, in the Board's judgement, amounts to an extension of the subject-matter of the application beyond the content of the application as filed.

4. Appellant I argues that the term "complete" does not convey any other information but the fact that there is an unexpected difference between the claimed immunoglobulins and the conventional four-chain ones. The argument is not tenable for the reason that it is not in line with the afore-mentioned definition of a complete antigen binding site given in the application as filed (see point 2, supra) which indicates that the immunoglobulins of the invention are required to offer an optimised binding site allowing a "complete" binding of the antigen.

5. Thus, the main request does not meet the requirements of Article 123(2) EPC and should be refused.

Auxiliary request 1 (claim 1)

Formal requirements (Articles 84 and 123 EPC)

6. Although appellant II has formulated no objections in this respect, the Board makes an assessment as follows. Claim 1 at issue differs from claim 1 of the main request (i.e. claim 1 as granted) in that the phrase "*capable of recognizing and binding one or several antigens*" has been replaced by the phrase "*sufficient for the formation of a complete antigen binding site, or several antigen binding sites*". A support for that amendment is found in the paragraph bridging pages 3 and 4 of the application as filed in which the same phrase is used. Thus, the requirements of Article 123(2)

EPC are met. As explained on page 4 of the application as filed, by "a complete antigen binding site" it is meant a site which will alone allow the recognition and complete binding of an antigen. Therefore, claim 1 at issue features a narrower embodiment of the more general concept addressed by claim 1 as granted. Thus, the requirements of Article 123(3) EPC are met. Furthermore, claim 1 is not only supported by the description but also clear and concise. Thus, the requirements of Article 84 EPC are also met.

Sufficiency of disclosure (Article 83 EPC)

7. Claim 1 is directed to an immunoglobulin which, while being devoid of light chains, comprises two heavy polypeptide chains, the latter chains lacking a CH_1 domain and being sufficient for the formation of a complete binding site.

8. The question to be answered is whether a skilled person would have found at the filing date in the application as filed a sufficiently clear and complete disclosure of the precise structure of such an immunoglobulin in order to be in a position to prepare it over the broad range of the claim. In other terms, one should assess whether all the features compensating for the absence of the CH_1 domain and the light chains are disclosed.

9. The experimental part of the description as a whole and the corresponding figures (see pages 34 to 55 and Figures 1 to 8 in the application as filed) deal exclusively with camel immunoglobulins. However, claim 1 is not limited to immunoglobulins obtained from camelids.

10. Also the general part of the description contains no complete disclosure of any non-camelid immunoglobulin. Indeed, the replacement by camelid specific residues such as those at position 45 and the frequent presence of a cysteine in the CDR_3 region associated with a cysteine in the CDR_1 position 31 or 33 or FW_2 region at position 45 (see page 13, last paragraph) are the only pieces of information made available especially for non-camelid immunoglobulins. These data *per se* do not amount to a disclosure which is sufficiently clear and complete to enable the skilled person to identify the minimal structural features that a non-camelid immunoglobulin comprised only of two heavy polypeptide chains should have in order to form a complete antigen binding site, in the sense that said site allows alone the recognition and complete binding of an antigen.

11. Appellant I argues that the experimental part of the description contains ample information which while relating to the preparation of camelid immunoglobulin could have been easily extended to the preparation of non-camelid immunoglobulins. The argument is not tenable for the reason that - as indicated in point 10, supra - it leaves the skilled person with the task and burden to find how the teaching related to camelid immunoglobulins can be extended to products of different origins (e.g. human immunoglobulins) which also fall under the broad area of claim 1.

12. Thus, auxiliary request 1 does not meet the requirements of Article 83 EPC and should be refused.

Auxiliary request 2

Requirements of Article 123(2) EPC

13. Claim 1 of auxiliary request 2 differs from claim 1 of auxiliary request 1 in that the wording "*it is obtainable from camelids*" has been added (see Section XVI, supra). The claim is objected to under Article 123(2) EPC by appellant II because in its view, due to this wording, it would also cover immunoglobulins which are not related to the immunoglobulins of camelids. It is in particular submitted that claim 1 would encompass for example immunoglobulins secreted by the cells of a camelid rendered transgenic for the expression of genes encoding immunoglobulins of human origin.

14. In the Board's judgement, the expression "obtainable from camelids" means that the claimed immunoglobulin is an immunoglobulin displaying the stated features **and** being "as it would be obtained from a camelid". Such immunoglobulins are disclosed in detail in the experimental part of the application as filed. The rather complicated hypothetical construction depicted by appellant II in support of its "added matter" and "clarity" objections (see point 13 supra and point 21 infra) amounts to a mere allegation: firstly, no such products are specifically claimed or described here; secondly, it is a construction which would not occur to a mind willing to understand when reading the claim (see decision T 190/99 of 6 March 2001). Thus, in the Board's judgement, there is no issue of Article 123(2) EPC here.

15. Claim 10 is directed to two fragments, namely a heavy chain of a camelid immunoglobulin according to claim 1

and the variable region of such a chain, i.e. to a so-called V_{HH} region. The description of the application as filed provides ample and sufficient support also for such fragments (see Example II on pages 41 to 55). Therefore, claim 1O does not contain subject-matter which extends beyond the content of the application as filed.

16. Thus, auxiliary request II complies with the requirements of Article 123(2) EPC.

Requirements of Article 123(3) EPC

17. Auxiliary request 2 differs from the main request (claims as granted) essentially in that claims 1 and 11 (now claim 10) have been substantially amended (see Sections XV and XVI, supra).

18. The wording "*it is obtainable from camelids*" found in claim 1 at issue has a limiting effect, compared to claim 1 of auxiliary request 1 as granted. Therefore, there is no violation of the provisions of Article 123(3) EPC.

19. Similarly, the re-wording of claim 11 as granted has resulted in claim 10 at issue having a more limited scope, with only fragments of an immunoglobulin obtainable from camelids being claimed. The amendments contained in present claim 10 have not extended the protection conferred by the patent as granted.

20. Thus, auxiliary request II complies with the requirements of Article 123(3) EPC.

Clarity (Article 84 EPC)

21. The wording of claim 1 provides an unambiguous definition of the immunoglobulins for which protection is sought. These are immunoglobulins having the features of IgG2 and IgG3 of camelids as schematically represented in Figure 6 of the patent. For the reasons explained in point 14 (see supra), the expression "obtainable from camelids" is considered to have a clear meaning. The objection made by appellant II in this respect is not tenable. Thus, claim 1 meets the clarity requirement of Article 84 EPC.

22. Claims 13, 14, 20, 23 and 36 are objected to by appellant II in view of the presence therein of terms ("especially" in claims 13, 20, 27 and 36, "for instance" in claim 14 and "for example" in claim 23) which render unclear the subject-matter for which protection is sought. Nevertheless, the defect was present in the corresponding granted claims 17, 18, 24, 27 and 40. Lack of clarity not being a ground for opposition (see Article 100 EPC) the objections are not admissible. Other claims contain erroneous back-references. But, for the same reason as for claims 13, 14, 20, 23 and 36, they cannot be objected to and any attempt to remedy the deficiency would have contravened Rule 57a EPC.

Sufficiency of disclosure (Article 83 EPC)

23. As indicated in point 14 (see supra), in the Board's judgement, claim 1 is directed to immunoglobulins with the stated features and as they would be obtained from a camelid. For such immunoglobulins a sufficiently

clear and complete disclosure is provided in the experimental part of the application as filed (see points 9 and 15, supra).

24. The appellant II's argument that non-camelid immunoglobulins are not sufficiently disclosed needs not be considered as, indeed, claim 1 does not cover such immunoglobulins (see point 14, supra).

25. Therefore, auxiliary request 2 meets the requirements of Article 83 EPC.

Novelty (Article 54 EPC)

26. Appellant II objects to claim 1 for lack of novelty over document D1, interpreted in the light of documents D6 and D43.

27. Document D1 describes the sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) under reducing conditions of a camel-IgG preparation recovered after chromatography on a DEAE-Sephacel column of camel serum precipitated with 50% ammonium sulfate. On the picture of the SDS-PAGE represented on Figure 2 (see page 200), three components are identified corresponding to (as enumerated in the sentence bridging pages 199 and 200) "*a γ-like heavy chain of AMW [apparent molecular weight] 55 kd, an L-chain of 22 kd and* ***an additional protein band of 40 kd***" (emphasis added by the Board). This latter band is not further characterised in the rest of the document.

28. Appellant II argues that this latter band corresponds to a protein which is an immunoglobulin as recited in claim 1, the presence of a similar band in a SDS-PAGE electrophoregram having been later on confirmed in document D43 and structurally identified in document D6:

28.1 Document D6, which is dated 3 June 1993 and, therefore, does not belong to the state of the art, reports that its contributors, including the designated inventors of the patent, have "*investigate[d] the presence of considerable amounts of IgG-like material of M_r 100K in the serum of the camel (Camelus dromedarius)*[6]" (see the abstract on page 446 with citation "6" being document D1). These molecules were found to yield upon reduction only heavy chains of respectively, 46 kDa (IgG_2 fraction) and 43 kDa (IgG3 fraction), devoid of light chains and lacking CH_1 domains (see the abstract on page 446 and the left-hand column on page 448).

28.2 Document D43, which was published after document D6 (see the footnote on page 195, the citation "*Hamers-Casterman et al., 1993*" as referred to therein being D6) and, therefore, is not part of the state of the art, describes the isolation and provides a preliminary characterisation of camel immunoglobulins. It contains a reference to document D1 (see the citation "Ungar-Waron *et al.*, 1987" in the "Introduction" on page 187). It reports that SDS-polyacrylamide gel electrophoresis of either the IgG fraction collected from ACA-34 gel filtration separation of an ammonium sulfate precipitate of camel serum or the three major peaks produced by an ion exchange chromatography of the same on an FLPC Mono-Q

(DEAE) column showed a protein band of 42kDa (see pages 190 to 191).

29. The appellant II's argument is not tenable for the following reasons:

29.1 As pointed out in decision T 100/01 of 5 February 2004, when considering how far the teaching in a written description of an allegedly novelty-destroying document also makes available certain features which are not explicitly stated, i.e. implicit or intrinsic features, all that matters is the whole contents of the said document **alone** as read and interpreted by the skilled person on the background of common general knowledge, i.e. the knowledge generally available at the relevant filing date, not later.

29.2 In the present case, a skilled person would have only derived from document D1 that an undetermined protein of an apparent molecular weight of 40 kDa as determined by SDS-PAGE under reducing conditions was present in the camel serum examined. Moreover, as it is unlikely that the experiments of documents D6 and D43, both published after the relevant filing date (here the priority date) in 1993, i.e. six years after the publication of document D1, were performed starting from the serum obtained from the same adult female camels as referred on page 198 of that document, the skilled person would not have been in a position to inevitably derive from document D1 that the undetermined protein was a camel IgG2 or IgG3. One can even not exclude that he/she could have thought it was not an immunoglobulin but a contaminant protein.

30. Therefore, the subject-matter of claim 1 is new. As the other claims are either dependent on claim 1 or contain a back-reference thereto, auxiliary request 2 meets the requirements of Article 54 EPC.

Inventive step (Article 56 EPC)

31. Appellant II objects to claim 1 for lack of inventive step on the basis of document D2 taken as the closest state of the art.

32. Neither document D2 nor document D24, which is proposed by appellant I, but document D1 represents the closest state of the art. Indeed, D2 reports the results of an investigation in which the interactions with antigen of individual domains of anti-lysozyme antibodies were analysed, a matter which is far from the key subject-matter of the patent, and D24 is a textbook which generally describes the immunoglobulins as molecules consisting of two heavy polypeptide chains associated with two light chains. Neither of these two documents alone or in combination can have a bearing on the inventive step discussion. In contrast, document D1, as explained above (see point 27), is directly concerned with the isolation and characterisation of camel immunoglobulins. It describes the presence in the camel serum examined of an undetermined protein of an apparent molecular weight of 40 kDa as measured by SDS-PAGE under reducing conditions, without any indication of whether it is an immunoglobulin, let alone an immunoglobulin lacking light chains, or a contaminant protein (see point 29.2, supra).

33. In view of document D1, the technical problem to be solved may be seen as being the identification and characterisation of immunoglobulins of the camel family, in particular of the IgG component described in document D1 as having an apparent molecular weight of 40 kDa as determined by SDS-PAGE. The solution proposed in the claims is the finding in camelids of functional immunoglobulins comprising two heavy chains lacking the CH_1 domain and devoid of light chains.

34. The question to be answered is whether this particular structure would have been suggested to the skilled person by document D1 in combination with further prior art or whether its finding would have been the inevitable result of further obvious experimental steps starting from the 40 kDa component of document D1.

35. At the relevant filing date, the only prior art documents describing naturally produced (in contrast to bioengineered) immunoglobulins not having the conventional accepted four-chain structure with two complete heavy chains and two complete light chains were immunoglobulins produced by cells in the context of a disease. Exemplary of such immunoglobulins are those described in documents D3 and D12. In document D3, immunoglobulin lacking a CH_1 domain produced by mouse myeloma cells are described while document D12 reports that immunoglobulin heavy chain fragments not associated with immunoglobulin light chains and lacking the entire CH_1 domain (but not proved to be involved in antigen-antibody interactions) were found in the urine of a patient having developed a common clinico-pathologic presentation of H Chain Disease

(HCD). Therefore, it is unlikely that the skilled person might have found any guidance in such documents.

36. The remark made on page 192 of post-published document D43, that the finding of a protein band of 42 kDa (see point 28.2, supra) "*requires further investigation to determine whether this protein is an integral part of the camel immunoglobulin molecule or an associated molecule, such as a complement molecule*", reinforces the Board's view that it was unlikely that a person skilled in the art trying at the relevant filing date with further experiments to identify the structure of camel immunoglobulins would have directly and inevitably arrived at the structure indicated in claim 1.

37. Therefore, it is concluded that the subject-matter of claim 1 involves an inventive step. Thus, as the other claims are either dependent on claim 1 or contain a back-reference thereto, auxiliary request 2 meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is remitted back to the first instance with the order to maintain the patent based on the set of claims of auxiliary request 2 as filed during the oral proceedings and a description to be adapted thereto.

The Registrar | The Chairman

A. Wolinski | L. Galligani