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**Datasheet for the decision
of 28 November 2006**

Case Number: T 1372/05 - 3.3.08

Application Number: 98104238.5

Publication Number: 0860504

IPC: C12N 15/48

Language of the proceedings: EN

Title of invention:

Polypeptides of feline T-cell lymphotropic lentivirus

Applicant:

IDEXX LABORATORIES, INC.

Opponent:

-

Headword:

FIV immunoassay/IDEXX

Relevant legal provisions:

EPC Art. 83

Keyword:

"Sufficiency of disclosure (no)"

Decisions cited:

T 0206/83, T 0226/85, T 0158/91, T 0234/93, T 0639/95,
T 0890/02, T 0891/02

Catchword:

-



Case Number: T 1372/05 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 28 November 2006

Appellant: IDEXX LABORATORIES, INC.
One Idexx Drive
Westbrook, ME 04092 (US)

Representative: Taormino, Joseph Paul
Hoffman Eitle,
Patent- und Rechtsanwälte
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 23 June 2006
refusing European application No. 98104238.5
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: C. Rennie-Smith
Members: M. R. Vega Laso
F. Davison-Brunel

Summary of Facts and Submissions

- I. European Patent Application No. 98 104 238.5, published as EP 0 860 504 A1 with the title "Polypeptides of feline T-cell lymphotropic lentivirus", is a divisional application of European patent application No. 90 907 657.2 filed on 30 April 1990.
- II. By a decision of the examining division posted on 23 June 2005, the application was refused under Article 97(1) EPC. The examining division considered that the subject-matter of the claims then on file, which were directed to, *inter alia*, an immunoassay for detecting infection with feline immunodeficiency virus (FIV) and FIV *env* gp130 polypeptide fragments for use in the assay, did not meet the requirements of Articles 83 and 84 EPC and did not involve an inventive step within the meaning of Article 56 EPC.
- III. In relation to Article 83 EPC, the examining division observed that neither the amino acid sequence of the FIV gp130 protein nor any peptides derived therefrom were disclosed in the application as filed. The examining division considered that, in view of the lack of disclosure in this respect, the skilled person was left with the task of determining which fragments of the gp130 protein were suitable as antigen for detecting the presence of FIV antibodies in a serum sample. For these reasons, the application was considered not to disclose the claimed invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. The examining division also remarked that in the framework of assessing whether the requirements of Article 83 EPC

are met, experimental data filed during examination proceedings could only be taken into account if said data confirmed statements present in the application as filed.

- IV. The appellant (applicant) filed a notice of appeal against the decision of the examining division and paid the appeal fee. In the statement setting out the grounds of appeal, the appellant pursued as its sole claim request the set of claims which led to the refusal of the application. As a subsidiary request, oral proceedings under Article 116 EPC were requested.

- V. The examining division did not rectify its decision and the appeal was remitted to the boards of appeal (Article 109 EPC).

- VI. The appellant was summoned to oral proceedings. In a communication under Rule 11(1) of the Rules of Procedure of the Boards of Appeal attached to the summons, the board expressed its provisional opinion on the issues discussed in the decision under appeal, and gave the appellant the opportunity to submit comments and/or file amended claim requests.

- VII. No comments or claim requests were received within the time limit set by the board. However, a new representative was appointed.

- VIII. Oral proceedings were held on 28 November 2006 in the presence of the new representative. During the proceedings, an amended claim request (claims 1 to 4) was filed in replacement of the set of claims previously on file.

IX. Claim 1 of the amended main request read:

"1. An enzyme-linked immunosorbent assay (ELISA) method for detecting an antibody to feline immunodeficiency virus (FIV) within a sample comprising contacting a purified polypeptide fragment of at least 5 amino acids of FIV *env* gp130 which has an epitope of FIV *env* gp130 with the sample under conditions suitable to allow an antibody/polypeptide complex to form between antibodies within said sample and the polypeptide fragment, and further detecting the formation of such a complex."

Dependent claim 2 was directed to a specific embodiment of the method of claim 1. Independent claim 3 related to a polypeptide fragment as defined in claim 1 which was capable of being bound by an antibody to FIV *env* gp130 in the claimed method. Independent claim 4 was directed to a nucleic acid encoding the polypeptide fragment of claim 3.

X. The following documents are mentioned in the present decision:

D2: T.P. O'Connor et al., Journal of Clinical Microbiology, March 1989, Vol. 27, No. 3, pages 474 to 479;

D3: R.A. Olmsted et al., Proc. Nat. Acad. Sci. USA, April 1989, Vol. 86, No. 7, pages 2448 to 2452;

Annex B1: Printout of the NCBI record no. NP_040976 dated 12 January 2004;

B2: R.A. Olmsted et al., Proc. Nat. Acad. Sci.
USA, October 1989, Vol. 86, No. 20,
pages 8088 to 8092.

XI. The arguments put forward by the appellant, as far as they are relevant for this decision, may be summarized as follows:

A person skilled in the art was able to work the claimed subject-matter on the basis of the instructions provided in the application and his or her common general knowledge. If reasonable technical guidance how to work the invention was provided in the application, it was not required under the EPC to disclose the best mode to carry out the invention. Since the application was addressed to the person skilled in the art, it was neither necessary nor desirable that details of known ancillary features should be given. In the present application, the skilled person was instructed to choose an amino acid sequence comprising at least five amino acids from the gp130 protein sequence known at the time, and to use available techniques to confirm its usefulness for diagnostics.

At the filing date, a person skilled in the art could retrieve the amino acid sequence of the *env* gp130 polypeptide or the encoding nucleic acid sequence from appropriate databases, eg NCBI (cf. Annex B1) or from document D2. He or she, applying the common general knowledge at the time, was able to determine sequences of high or low antigenicity either on the basis of the amino acid sequence or by experimentally testing them. A reasonable amount of trial and error was permissible

in doing so, and an incidental failure of a method did not affect its feasibility.

The experimental data filed as Annex B showed polypeptide fragments of *env gp130* which were able to detect FIV antibodies and, thus, were suitable for the method of detection of feline immunodeficiency virus according to the invention. These data represented the proof that the claimed invention was indeed enabled.

- XII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 4 of the sole main request filed during the oral proceedings.

Reasons for the Decision

Admission of the amended main request into the proceedings

1. The amended main request (sole request on file) was filed during the oral proceedings. In spite of the fact that this set of claims was clearly late-filed, for the following reasons the board decided to admit the amended main request into the proceedings.
2. Claims 1 to 4 of the amended main request correspond essentially to claims 1, 2, 7 and 6 of the claim request underlying the decision under appeal, except for claim 1 being restricted to an enzyme-linked immunosorbent assay (ELISA) method, and for the language of claims 1 and 3 being partially reformulated. The amended claims do not contain any subject-matter which has not been claimed before, nor do they raise

any issues which the board could not reasonably be expected to deal with without adjournment of the oral proceedings (cf. Article 10b(3) RPBA). Furthermore, the introduced amendments are manifestly allowable from a formal point of view, in particular in respect of the issues of added matter (Article 123(2) EPC) and clarity (Article 84 EPC). In fact, the amended claims represent a serious attempt at remedying severe clarity deficiencies present in the previous claim request as well as at establishing an inventive step over the teaching of document D2.

3. The amended main request was thus admitted into the proceedings.

Sufficiency of disclosure (Article 83 EPC)

4. The immunoassay method of claim 1, which is based on the detection of the humoral immune response induced by FIV in infected cats, comprises as a first step contacting a sample from the animal with a purified fragment of at least 5 amino acids of the FIV env gp130 polypeptide, which fragment contains an epitope of the gp130 polypeptide. In a second step of the method, formation of an antibody/polypeptide complex between the polypeptide fragment and antibodies in the sample is allowed under suitable conditions, detection of such complex formation indicating the presence of antibodies in serum in response to FIV infection.
5. Although during oral proceedings the issue of inventive step in respect of the immunoassay of claim 1 was discussed to some extent, the decisive question in the present case is whether or not the claimed subject-

matter fulfils the requirements of Article 83 EPC, ie whether a person skilled in the art, taking into account the guidance provided by the application as filed and the common general knowledge at the time the disclosure was made, would have arrived at the invention as claimed, without an undue burden of experimentation and without exercising any inventive skill.

6. In defining whether or not the required experimentation amounts to an undue burden, the boards of appeal have acknowledged that, when it comes to the sufficiency of disclosure in an unexplored or difficult field, a reasonable amount of trial and error is permissible. However, there must be adequate instructions available in the specification or on the basis of common general knowledge which would lead the skilled person necessarily and directly towards success through the evaluation of initial failures or through an acceptable statistical expectation rate in case of random experiments (cf. T 639/95 of 21 January 1998, point 1 of the Reasons; and T 226/85, OJ EPO 1988, 336, point 8 of the Reasons).

7. The assessment whether a European application fulfils the requirements of Article 83 EPC has to be conducted in each case on its own merits (cf. decisions T 158/91 of 30 July 1991, point 2.3 of the Reasons; T 639/95 of 21 January 1998, point 3 of the Reasons; and T 891/02 of 29 October 2003, point 3 of the Reasons). In the present case, for carrying out the immunoassay of claim 1 the skilled person should have had the required means readily available, in particular a fragment of at

- least 5 amino acids of the FIV env gp130 polypeptide that contains an epitope of this polypeptide.
8. However, as observed by the examining division in the decision under appeal, the application discloses neither the amino acid sequence of the FIV env gp130 polypeptide, nor any fragments derived therefrom that contain an epitope of the gp130 polypeptide.
 9. This has not been disputed by the appellant. In its statement setting out the grounds of appeal, the appellant nevertheless argued that, at the filing date of the application, a person skilled in the art was in the position to obtain the amino acid sequence of the FIV env gp130 polypeptide or the nucleotide sequence encoding it, either from document D2 or via a search in the appropriate databases, eg the NCBI database (cf. printout of the record no. NP_040976 filed as Annex B1 to the statement of grounds of appeal). Once the amino acid sequence had been obtained, it was allegedly a matter of routine experimentation to obtain suitable fragments of the FIV env gp130 polypeptide containing an epitope of this polypeptide.
 10. The board notes that document D2, a scientific publication authored by, among others, the present inventors, is not mentioned in the present application, and that, not being a textbook or general technical literature, the content of this document cannot be considered to be part of the common general knowledge of the person skilled in the art which he/she may use to supplement the information given in the application (cf. in particular decisions T 206/83, OJ EPO 1987, 5, point 5 and T 234/93 of 15 May 1997, point 4). Moreover,

document D2, whilst identifying the gp130 polypeptide as the sole FIV polypeptide which reacts with all serum samples obtained from 14 cats experimentally infected with FIV, does not provide **any** sequence information for the polypeptide in question.

11. As regards the NCBI database record (cf. Annex B1), which discloses the amino acid sequence of an envelope polypeptide of the feline immunodeficiency virus, nowhere in the application is there a reference to this record. Thus, not being part of the disclosure content of the application itself, the sequence information contained in the record could only be used to supplement the disclosure if it was part of the common general knowledge of the skilled person at the filing date.

12. In its communication sent in preparation for the oral proceedings, the board expressed its doubts concerning the probative value of the Annex B1 in respect of the alleged public availability of the amino acid sequence of the gp130 polypeptide at the filing date of the application, and drew the attention of the appellant to the fact that the sole date indicated in the record was 12 January 2004, ie roughly fourteen years after the filing date. The board also pointed to the reference made in the record to a scientific publication by Olmsted et al. (cf. document B2 *supra*) published in October 1989, ie prior to the filing date of the application. However, the appellant did not submit any arguments in response to these observations, either in writing or at the oral proceedings.

13. On the basis of the evidence on file, the board is not in the position to acknowledge that the sequence information contained in the record no. NP_040976 of the NCBI database (cf. Annex B1) belongs to the common general knowledge of the skilled person for the purpose of assessing sufficiency of disclosure in respect of the present application.

14. First, there is no conclusive evidence on file in respect of the actual date on which the database record in question was made available to the public. Consequently, the appellant's allegation that, at the filing date of the application, the amino acid sequence contained in the record of the NCBI database was available to a person skilled in the art cannot be accepted.

15. And secondly, even if it is assumed that the database record and the sequence information contained in it were made available to the public shortly before or after the scientific publication to which the record refers (document B2 published in October 1989, ie 7 months before the filing date of the application), the board is not convinced that the required information, ie the amino acid sequence of the gp130 polypeptide, is provided in the record in a straightforward and unambiguous manner so that supplementary searches were not needed (cf. decision T 890/02, OJ EPO 2005, 497, point 9 of the Reasons). The NCBI database record does not identify the amino acid sequence contained in it as corresponding to the *env* **gp130** polypeptide of the feline immunodeficiency virus; rather, one of the CDS features in the record reads `"/locus_tag="FIVgp5"`, which appears to indicate

that the disclosed sequence may correspond to a different FIV envelope polypeptide. This ambiguity cannot be clarified by document B2, to which reference is made in the database record, because in document B2 only three FIV envelope polypeptides are mentioned: a 140 kDa polypeptide, designated gp140 (precursor), a 100 kD polypeptide, designated gp100 (outer membrane) and a gp36 polypeptide (transmembrane). *Prima facie*, none of these polypeptides appears to correspond to the gp130 polypeptide mentioned in claim 1.

16. At oral proceedings, the appellant argued further that the skilled person could obtain the information required to clone and sequence the genome of FIV, and in particular the nucleotide sequence encoding the gp130 polypeptide, from document D3. However, as in the case of document D2 discussed above (cf. point 10), no reference is made in the application to document D3. Since this document is a scientific publication, not a textbook or an encyclopaedia, and since no reasons have been put forward why this document should exceptionally be considered to form part of the common general knowledge at the filing date, the appellant's argument cannot be accepted.

17. Furthermore, the board judges that, even if the skilled person could, in principle, have tried to clone and sequence the genome of the feline immunodeficiency virus, with or without the guidance provided in document D3, the whole amount of experimentation required not only for cloning and sequencing the gene encoding the *env* gp130 polypeptide, but also for finding fragments of this polypeptide containing an

- epitope, which fragments could be as short as five amino acids, would have amounted to an undue burden.
18. A further line of argument of the appellant relied on the passage on page 5, lines 12ff. of the application, in which the isolation of antigenic glycopeptides of FIV using a Lentil Lectin Sepharose 4B column is described. In the appellant's view, following the instructions given in this passage the skilled person could isolate the gp130 polypeptide and, by partial digestion, obtain polypeptide fragments from which the sequence could be determined using techniques well known in the art. Isolating and testing the polypeptide fragments for antigenicity required only routine experimentation.
19. The board disagrees with this view. It is apparent from the application that, among the FIV polypeptides reacting with sera of all 14 cats experimentally infected with FIV, three are glycoproteins, namely gp40, gp47 and gp130 (cf. page 5, lines 4 and 5). The method disclosed in the application for the isolation of glycopeptides is not specific for any of these three glycoproteins. Consequently, further purification steps would be necessary to isolate the gp130 polypeptide. However, only rather general references to HPLC and affinity chromatography using polyclonal or monoclonal antibodies, but no detailed instructions are provided in the application in this respect. Moreover, there is no specific guidance in the application either with respect to the proteolytic digestion of the isolated gp130 polypeptide or the purification of the polypeptide fragments obtained after digestion. The skilled person is also left to his or her own resources

when it comes to the selection of polypeptide fragments of gp130 having an epitope of this polypeptide, as neither specific epitopes of the gp130 polypeptide nor monoclonal antibodies that bind to them have been described.

20. In sum, in order to obtain polypeptide fragments derived from the FIV *env* gp130 polypeptide that have an epitope of this polypeptide, a person skilled in the art would have to embark on a research program, for which the application provides very little guidance. Even if each individual step *per se* can be considered to be feasible with a certain amount of trial and error, the total amount of experimental effort necessary to obtain the means for carrying out the invention is regarded as undue for the skilled person (cf. T 639/95 of 21 January 1998, point 15 of the Reasons). Consequently, the disclosure of the application is considered to be insufficient as regards the means for carrying out the invention as claimed.

21. The experimental evidence presented by the appellant (cf. Annex B to the statement of grounds of appeal) cannot change the board's finding. By this evidence, the appellant intended to show that two specific fragments derived from the FIV *env* gp130 polypeptide and corresponding to amino acids 398-410 and 599-615, could be used in the immunoassay of claim 1 for the detection of FIV seropositive samples, and that using these fragments the claimed assay was at least as reliable as the PetCheck Anti-FIV test kit.

22. The board notes that the two specific gp130 fragments used in the experiments of Annex B are not disclosed in the application as filed, and that the fact that sixteen years after the filing date of the application two fragments of the FIV *env* gp130 polypeptide suitable for carrying out the claimed invention are described, cannot remedy the insufficient guidance provided in the application for isolating such fragments.
23. The board thus concludes that the sufficiency requirements of Article 83 EPC are not satisfied in respect of the means necessary for carrying out the invention as claimed, in particular in respect of the provision of suitable fragments of the FIV *env* gp130 polypeptide having an epitope of this polypeptide. Since the findings in the decision under appeal with regard to Article 83 EPC were justified, the appellant's request to set aside this decision cannot be granted.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Wolinski

C. Rennie-Smith