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Datasheet for the decision of 8 October 2015

Case Number: T 2238/11 - 3.3.04

Application Number: 05798217.5

Publication Number: 1751187

IPC: C07K14/705

Language of the proceedings: EN

Title of invention:
Canine CD20 compositions

Applicant:
Idexx Laboratories, Inc.

Headword:
Antibody against the extracellular domain of canine CD20/IDEXX

Relevant legal provisions:
EPC Art. 56, 113
EPC R. 103(1)(a)
RPBA Art. 11

Keyword:
Inventive step of all requests - (no)
Substantial procedural violation - (no)

Decisions cited:
T 0951/92, T 0725/05, T 0726/10

Catchword:

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Case Number: T 2238/11 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 October 2015

Appellant: (Applicant)	Idexx Laboratories, Inc. One Idexx Drive Westbrook, Maine 04092 (US)
Representative:	Müller-Boré & Partner Patentanwälte PartG mbB Friedenheimer Brücke 21 80639 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 28 March 2011 refusing European patent application No. 05798217.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	M. Montrone
	M. Blasi

Summary of Facts and Submissions

I. The appeal was lodged by the applicant (hereinafter "the appellant") against the decision of the examining division to refuse European patent application No. 05798217.5. The application was filed as international application and published as WO 2006/007202 (hereinafter "the application as filed") with the title "*Canine CD20 compositions*".

II. The impugned decision dealt with a single claim request. The examining division considered that the subject-matter of claims 1 to 10 lacked inventive step. In a paragraph with the heading "*Further Remarks*" the examining division held that "*Post-proceedings analysis of documents revealed evidence filed after the date of priority that, contrary to the Affidavit submitted during oral proceedings, anti-human CD20 to the extracellular domain (Rituximab) can bind to canine CD20 in in vitro immunohistochemistry, but not in flow-cytometric assays (D16,* [...]*; D17,* [...]*).*" Therefore, the examining division was of the opinion that the subject-matter of claim 1 lacked novelty in view of the disclosure in document D4 (all documents are identified in section VII below).

III. With the statement of grounds of appeal, the appellant submitted a main and an auxiliary request. The main request corresponded to the request dealt with in the decision under appeal, the only difference being that claim 5 was deleted.

Claim 1 of the main request reads:

"1. An isolated antibody or antigen binding portion thereof that specifically binds SEQ ID NO: 10."

Claim 1 of auxiliary request 1 reads:

"1. An isolated antibody or antigen binding portion thereof that specifically binds SEQ ID NO: 10, wherein the isolated antibody or antigen binding portion thereof specifically binds canine CD20 positive B-lymphocytes."

IV. In a subsequent submission the appellant raised the objection that the examining division had committed a substantial procedural violation: it had contravened the requirements of Article 113(1) EPC by not giving the appellant an opportunity to comment on its finding of lack of novelty set out in the "*Further Remarks*" section of the decision under appeal which would justify an immediate remittal of the case.

V. The board informed the appellant of its preliminary view in a communication pursuant to Article 15(1) RPBA. The board indicated *inter alia* that the subject-matter of claim 1 of the main and the auxiliary request lacked inventive step and that it did not consider that the examining division had committed a substantial procedural violation.

VI. In reply to the board's communication the appellant submitted two further auxiliary requests and *inter alia* documents D21 and D22 (identified in section VII below).

Claim 1 of auxiliary request 2 reads:

"1. An isolated antibody or antigen binding portion thereof that specifically binds only to a predominant extracellular domain of canine CD20 as set forth in SEQ ID NO: 10, wherein the isolated antibody or antigen binding portion thereof specifically binds canine CD20 positive B-lymphocytes."

Claim 1 of auxiliary request 3 reads:

"1. An isolated antibody or antigen binding portion thereof that specifically binds SEQ ID NO: 10 for use in treating canine CD20+ B-cell lymphoma."

VII. The following documents are cited in this decision:

D2: Stamenkovic et al., J. Exp. Med., 167, p. 1975-1980, (1988)

D4: Rastetter et al., Ann. Reviews of Medicine, 55, p. 477-503, (2003)

D5: Jubala et al., Vet. Pathology, 42, p. 468-476, (July 2005)

D9: Venta et al., Biochem. Genetics, 34, p. 321-341, (1996)

D10: WO 02/062946

D16: Crow et al., Cancer Therapy, 6, p. 181-186, (2008)

D17: Impellizeri et. al., Vet. J., 171(3), p. 556-558, (2006)

D19: US 2002/0041847

D21: WO 2004/035607

D22: Teeling et al., J. Immunol., 177, p. 362-371, (July 2006)

VIII. Oral proceedings before the board were held on 8 October 2015. At the end of the oral proceedings the chairwoman announced the board's decision.

IX. The appellant's arguments may be summarised as follows:

Immediate remittal of the case (Article 11 RPBA)

The objection of the examining division that the antibodies disclosed in document D4 - when assessed in the light of the data of the two post-published documents D16 and D17 - anticipated the claimed antibodies had been raised for the first time in the "*Further Remarks*" section of the decision under appeal. This had deprived the appellant of an opportunity to comment on this issue, contrary to the requirements of Article 113(1) EPC, and therefore was a substantial procedural violation justifying immediate remittal of the case to the examining division (in a different composition).

The terms "decision" and "grounds" in Article 113(1) EPC were not to be interpreted in a narrow sense and an applicant had to be informed about all objections during the grant proceedings, *i.e.* before a final decision was taken, see decision T 951/92.

Also, the considerations on novelty in the "*Further Remarks*" section might have influenced the examining division's decision on inventive step.

Inventive step

Main request

The disclosure in document D19 of anti-CD20 antibodies conjugated to, for example, toxins or radioactive compounds, *i.e.* the so-called anti-CD20 immunoconjugates, represented the closest prior art, not the disclosure in the same document of unconjugated anti-CD20 antibodies.

This was so because, firstly, the disclosure concerning the conjugated antibodies was the central teaching of document D19 (see examples 3 and 4).

Secondly, the skilled person would have doubts that the experimental and clinical data disclosed in document D19 in relation to the unconjugated antibodies were correct. It was known at the priority date of the application that antibodies raised against human or mouse CD20 did not normally cross-react with CD20 on canine B-cells, see the reference in the application as filed, page 1, second paragraph to the antibody Rituximab and the disclosure in documents D5, D16, D17 and D22. In contrast, document D19 reported that two unconjugated anti-CD20 antibodies which had both been raised against human CD20 bound in an *in vitro* assay better to canine than human lymphocytes (see Table in example 1). Moreover, the successful treatment of a dog suffering from B-cell lymphoma with one of the two unconjugated antibodies (see example 2) did not allow any conclusion to be drawn regarding the therapeutic efficacy of this antibody, since only a single dog had been treated and therefore placebo effects could not be ruled out.

The claimed antibodies differed from the conjugated anti-CD20 antibodies disclosed in document D19 in that they were unconjugated, bound specifically to the extracellular domain of canine CD20 as defined by SEQ ID NO: 10 and depleted canine CD20-positive B-cells.

The objective technical problem was thus the provision of alternative means for the treatment of CD20-positive B-cell lymphomas in dogs.

Solving this problem by the claimed antibodies was not obvious. The skilled person would not have expected that unconjugated anti-CD20 antibodies could deplete canine CD20-positive B-cells. Therefore, the skilled person would rather have attempted to provide alternatives to the immunoconjugates disclosed in document D19, for example by modifying the conjugated part.

Even if the skilled person had been motivated to provide unconjugated antibodies binding specifically to the canine CD20 extracellular domain, he would not have arrived at them, as only a fragment of the gene encoding canine CD20 had been cloned at the priority date of the application. In other words, the extracellular domain *per se* which was necessary for generation of the claimed antibodies was not available to the skilled person.

Assuming nevertheless that the skilled person would have cloned and sequenced the complete canine CD20 gene by standard technology, for example by using the primers disclosed in document D9, he would not have been able to identify the extracellular domain defined by SEQ ID NO: 10 in the canine CD20 gene by aligning it with the known human and mouse CD20 genes (see documents D2 and D10). This was so because the CD20 extracellular domain differed significantly between the three animal species

with regard to sequence and length. Moreover, the canine CD20 had two extracellular domains and only one of them, the predominant, *i.e.* longer one, had the sequence of SEQ ID NO: 10.

Auxiliary requests 1 and 2

Document D19 did not teach the skilled person how to arrive at antibodies which bound either (i) specifically to a canine protein defined by SEQ ID NO: 10 on CD20-positive B-cells (auxiliary request 1), or (ii) to only the predominant extracellular domain of canine CD20 as defined by SEQ ID NO: 10 on CD20-positive B-cells (auxiliary request 2). The generation of the claimed antibodies in auxiliary requests 1 and 2 required the use of the protein defined by SEQ ID NO: 10 as antigen which was neither available from the prior art nor identifiable in the full-length CD20 sequence, for the reasons set out for the main request.

Auxiliary request 3

Document D19 disclosed that there was a need to develop an immunotherapy for, *inter alia*, B- and T-cell malignancies in domestic animals and suggested that markers equivalent to those on human B- and T-cells might serve as useful targets. However, it was not suggested that the extracellular domain of canine CD20 as defined by SEQ ID NO:10 was a suitable target which should moreover be used to generate antibodies binding specifically thereto. Furthermore, it was surprising that only these antibodies triggered the depletion of canine CD20-positive lymphoma B-cells. Therefore, the subject-matter of auxiliary request 3 involved an inventive step.

X. The appellant requested as its main request that the decision under appeal be set aside due to a substantial procedural violation by the examining division, and that the case be immediately remitted to the examining division in a different composition for further prosecution.

As auxiliary request the appellant requested that the decision under appeal be set aside and that the case be remitted to the examining division with the order to grant a patent on the basis of the main request, or alternatively on the basis of auxiliary request 1, both filed with the statement of grounds of appeal, or as a further alternative, on the basis of one of auxiliary requests 2 or 3, both filed with the letter of 23 September 2015. The appellant also requested§ that the appeal fee be reimbursed.

Reasons for the Decision

Immediate remittal of the case (Article 11 RPBA)

1. Pursuant to Article 11 RPBA, a board shall remit a case to the department of first instance if fundamental deficiencies are apparent in the first instance proceedings, unless special reasons present themselves for doing otherwise.

2. The appellant argued that a fundamental deficiency had occurred in the first instance proceedings in view of the "*Further Remarks*" section in the decision under appeal. In this section, the examining division had surprisingly concluded that the claimed subject-matter lacked novelty. As shown by the examining division's reference to "*Post-proceedings analysis...*", the

appellant had not been heard on this aspect during the proceedings and thus its right to be heard pursuant to Article 113(1) EPC had been violated. Since the terms "decision" and "grounds" in Article 113(1) EPC were not to be interpreted in a narrow sense, an applicant had to be informed about all objections during the grant proceedings, *i.e.* before a final decision was taken, as emphasised in decision T 951/92. This had not happened in the present case.

3. Article 113(1) EPC stipulates that decisions of the EPO may only be based on "grounds or evidence" on which the parties concerned have had an opportunity to present their comments. "Grounds or evidence" are to be understood as meaning the essential legal and factual reasoning on which the EPO has based its decision (see Case Law of the Boards of Appeal ("CLBA"), 7th edition 2013, III.B.1.2)

4. In the present case, the examining division refused the application because it was of the view that the subject-matter of claims 1 to 10 lacked inventive step. This objection was raised during the examination proceedings (see communication of the examining division of 23 July 2009 and annex to the summons dated 2 August 2010) and the appellant has not argued that it did not have the opportunity to comment on this objection.

5. The board considers that the "*Further Remarks*" section of the decision under appeal (see point 4 in the decision) is to be regarded as an *obiter dictum, i.e.* as voluntary information by the examining division which however does not form part of the grounds for refusing the application. Observations in such an *obiter dictum* might assist the applicant (or the board in case of an

appeal) by, for example, obviating the need for a remittal to the first instance in case of an allowable appeal.

5.1 Indications that the "*Further Remarks*" section in the decision under appeal does not form part of the actual decision are, in the board's view, (i) that the decision to refuse the application was taken during the oral proceedings and was based on lack of inventive step (see minutes, point 10), (ii) that this section follows the examining division's statement in the written decision that the application is to be refused (see point 3 of the decision), and (iii) that the section starts with the words "*Post-proceedings analysis...*".

5.2 As a party's right to be heard pursuant to Article 113(1) EPC is satisfied if it has had an opportunity to present its comments on all grounds or evidence on which a decision is based, this right is not violated if a party did not have the opportunity to comment on observations in an *obiter dictum* (cf. e.g. decisions T 726/10, point 9 of the reasons and T 725/05, point 6 of the reasons).

5.3 The board agrees with this approach, and concludes in view of point 5.1 above that no violation of the appellant's right to be heard has occurred in relation to the "*Further Remarks*" section. The board notes however that the present case shows that an *obiter dictum* referring for the first time to issues which had not been raised before may give a party the impression that its rights under Article 113(1) EPC have been ignored.

6. Nor can the board agree with the appellant that the negative opinion on novelty in the "*Further Remarks*"

section of the decision under appeal might have influenced the examining division in reaching its decision on inventive step. There are no facts derivable from either the decision itself or the minutes to support this view. On the contrary, as set out in point 5.1 above, the decision to refuse the application for lack of inventive step had clearly been taken at the oral proceedings and thus before the examining division made the "*post-proceedings*" analysis of the documents which it then summarised in the "*Further Remarks*" section.

7. That the (potential) novelty objection referred to in the "*Further Remarks*" section had not been raised during the grant proceedings cannot be regarded as a fundamental deficiency in the first instance proceedings either. Pursuant to Rule 71(2) EPC, a communication under Article 94(3) EPC shall contain a reasoned statement covering, *where appropriate*, all the grounds against the grant of the patent. Therefore, leaving out one of several possible grounds is not as such in breach of Rule 71(2) EPC or Article 94(3) EPC. If however the decision to refuse the application was subsequently based on this "omitted" ground, the requirements of Article 113(1) EPC would be contravened (cf. decision T 951/92, OJ EPO 1996, 53, Headnote II). As set out above, lack of inventive step, not lack of novelty, was the ground on which the decision under appeal was based, so the requirements of Article 113(1) EPC were not contravened in the present case.

8. The board therefore concludes that no fundamental procedural deficiency occurred. Thus, the requirements for a remittal of the case pursuant to Article 11 RPBA are not met.

Introduction of the invention

9. The application under consideration concerns antibodies binding specifically to the predominant, *i.e.* the larger of the two extracellular domains of the canine cluster of differentiation 20 (CD20) membrane protein which is primarily expressed on the surface of B-cells and is therefore considered as an important target for antibody-based therapies in the treatment of B-cell lymphomas in dogs (see page 1, second and third paragraphs of the application as filed). Large parts of the canine CD20 protein sequence, including both extracellular domains, were not known at the priority date of the application.

Inventive step (Article 56 EPC)

Main request

Closest prior art

10. In assessing whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal apply the "problem and solution" approach, which requires as a first step the identification of the closest prior art.

The closest prior art is generally a document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most technical features in common, *i.e.* requiring the minimum of structural modifications (see CLBA, *supra*, I.D.3.1).

11. The appellant has not disputed that document D19 could be considered as the closest prior art document since it discloses subject-matter conceived for the same purpose as the claimed subject-matter, *i.e.* the treatment of B-cell lymphomas in dogs. The appellant submitted however that the closest prior art was the disclosure in document D19 of anti-CD20 antibodies conjugated to other compounds, not the disclosure in the same document of unconjugated anti-CD20 antibodies.

12. Document D19 discloses antibodies binding to CD20 of domestic animals, including dogs. The antibodies do not bind exclusively to canine CD20; they are cross-reactive, *i.e.* also bind to human CD20, the protein against which they were generated (see paragraph [0066] and table in example 1 on page 14).

The antibodies are either unconjugated, *i.e.* "*naked*", which means that they are not linked to other compounds (see paragraph [0033]), or they are linked to other compounds, for example toxins or radioactive molecules, in which case they are referred to as "*immunoconjugates*" (see paragraph [0035]).

Also, it is explicitly mentioned throughout the document that for therapeutic applications conjugated and unconjugated antibodies are equally suitable (see e.g. paragraphs [0002], [0016], [0033], [0035], [0066], [0084] and [0114]) and that the therapeutic use "*entails the administration of antibodies directed against antigen determinants found on cells*" (see paragraph [0013]), this statement meaning that therapeutically useful antibodies should bind to extracellular epitopes of target proteins, e.g. *inter alia* to CD20 on B-cells (see paragraph [0016]).

The experimental part of document D19 reports that two unconjugated anti-CD20 antibodies, referred to as 1F5 and Biogenex, both raised against human CD20, bind *in vitro* in solution to purified lymphocytes derived from canine blood. In the board's view, this result would imply to the skilled person that both antibodies bind to extracellular epitopes of canine CD20 (see example 1, table and paragraphs [0146] and [0147]).

Furthermore, the 1F5 anti-CD20 antibody was used in a clinical study with a single dog for the treatment of B-cell lymphomas. After four weeks of treatment, lymphomas were no longer detectable (see example 2, paragraphs [0148] and [0149]), which, in the board's view, would imply to the skilled person that it was the antibody which depleted the malignant B-cells since this was the only therapeutic agent administered.

The document also reports that a single cat suffering from B-cell lymphomas benefited from the treatment with an immunoconjugate comprising a different anti-CD20 antibody and a radioactive compound (see example 4, paragraph [0152]).

13. The appellant submitted that the skilled person would have doubts concerning the correctness of the experimental and clinical data of document D19 in relation to the unconjugated, cross-reactive anti-CD20 antibodies because they were found to bind to canine CD20.

13.1 The board is not persuaded by this argument. At the priority date of the present application, there was no general teaching derivable from the prior art documents cited in the present proceedings that anti-CD20 antibodies generated against human CD20 did not bind to

canine CD20. The documents relied on in this context, namely documents D5, D16, D17 and D22, were all published after the priority date of the application and therefore could not have been taken into account when evaluating the data in question. Regarding the passage in the application on page 1 reporting a failure of the anti-human CD20 antibody Rituximab to bind to canine B-cells, the skilled person, knowing about species-specific differences in the sequence of the CD20 protein would, in the board's view, not expect either that each antibody which was generated against the human CD20 would necessarily bind to canine CD20 or that none of them would. That this is antibody-dependent is shown for example by document D19 itself, which reports that only two out of three cross-reactive anti-human CD20 antibodies tested bind to canine CD20-positive lymphocytes (see table in example 1, page 14).

13.2 Therefore, in the board's view, the skilled person had no reason to doubt the correctness of the experimental and clinical data concerning the unconjugated - and also the conjugated - anti-CD20 antibodies reported in examples 1, 2 and 4 of document D19 (see point 12 above). In addition, these data are consistent with the analogous concept known from humans at the relevant date of the present application, *i.e.* that antibodies binding to CD20-positive human B-cells can be successfully used to treat of human B-cell lymphomas (see e.g. document D4, abstract; document D19, paragraph [0010])).

14. Lastly, the appellant referred *inter alia* to a further clinical study, reported in example 3 of document D19, to support its view that the teaching in this document relating to conjugated antibodies was the closest prior art. It is disclosed that a single dog suffering from B-cell lymphomas was treated with an immunoconjugate

comprising the so-called L243 antibody and a radioactive compound. The animal benefited from the administration of the immunoconjugate (see example 3, paragraphs [0150] and [0151]).

15. However, this study does not relate to the present subject-matter, since the immunoconjugate used comprises an antibody which is directed against the so-called MHC class II protein (major histocompatibility complex class II protein), *i.e.* a B-cell surface protein unrelated to CD20 (see the table in example 1).

16. Hence, in summary, the board cannot concur with the appellant that the conjugated anti-CD20 antibodies are the central teaching of document D19 and that thus only they represent the closest prior art.

Rather, document D19 teaches that both conjugated and unconjugated cross-reactive anti-CD20 antibodies are equally suitable for the purpose of the present invention, *i.e.* the treatment of B-cell lymphomas in domestic animals, including dogs.

Therefore, both forms of these antibodies represent the closest prior art. This conclusion is justified also because the present claims are not limited to one form, *i.e.* they encompass both conjugated and unconjugated forms.

Technical problem and solution

17. The difference between the claimed antibodies and those disclosed in document D19 is that the claimed antibodies are not cross-reactive, *i.e.* they bind exclusively to the extracellular domain of canine CD20 defined by SEQ ID NO: 10. Since human CD20 is not present on B-cells of

dogs, the lack of any cross-reactivity of the claimed antibodies towards this human protein is under the circumstances of the present case not associated with any particular advantageous technical effect. Hence, the board agrees with the appellant that the objective technical problem to be solved is to be formulated as the provision of alternative antibodies as a means for the treatment of CD20-positive B-cell lymphomas in dogs.

18. The board is satisfied that this problem is solved by the antibodies of claim 1 in view of the examples in the application, which confirm that monoclonal antibodies generated by immunising mice with the protein defined by the sequence of SEQ ID NO: 10 bind specifically to canine CD20 (see example 3 and figures 11 to 13).

Obviousness

19. It is established case law of the boards of appeal that a course of action is considered obvious within the meaning of Article 56 EPC if the skilled person would have carried it out in expectation of some advantage or improvement. In other words, obviousness is present not only when the results are clearly predictable but also when there is a "reasonable expectation of success", which implies the ability of the skilled person to predict rationally, on the basis of the knowledge existing before a research project is started, the successful conclusion thereof within an acceptable amount of time (see CLBA,*supra*, point I.D.7.1).

20. Document D19 discloses therapeutically effective but cross-reactive anti-CD20 antibodies as a means for treating canine B-cell lymphomas and explicitly suggests that "*Animal equivalents of these* [human] *antigens, which may vary by species, are readily identifiable and*

their use is preferred" (see paragraph [0013]; emphasis added). In the board's view, the skilled person would derive from this passage that for immunotherapy in dogs it is preferable to use antibodies that were generated against species-specific antigens.

21. Therefore, and contrary to the appellant's view, the board considers that the skilled person has in the light of the teaching of document D19 ample motivation to provide as alternative antibodies those which are specifically directed against extracellular epitopes of canine CD20.

22. Since at the priority date of the application the complete gene encoding canine CD20 had not yet been cloned, the skilled person would in a first step have to isolate the complete canine CD20 protein in order to obtain its extracellular domain as an antigen for immunisation.

23. The skilled person was aware at the priority date that a fragment of the gene encoding canine CD20 and a pair of corresponding PCR primers existed (see document D9, page 338, table AII). It is within the normal skills of the skilled person to amplify with the help of this primer pair a part of the canine CD20 gene which then allows the subsequent cloning of the complete gene including the determination of its nucleic acid and corresponding protein sequence by standard technology. This was not contested by the appellant.

24. As the next step the skilled person would have to identify the extracellular domain within the complete canine CD20 gene. In this context, the appellant has not contested that the skilled person was aware of the human and mouse CD20 genes.

25. These genes share - as conserved structural motifs - four transmembrane domains that anchor the CD20 protein in the cytoplasmic membrane and a single extracellular domain located between the third and fourth transmembrane domain (see document D2, figure 2; document D10, page 9, lines 27 and 28, "mouse a1", SEQ ID NO: 48, figure 7). Document D2 predicts the position of the human CD20 extracellular domain between residues 142 and 182 (see figure 2, page 1976, last paragraph to page 1979, first paragraph), which was experimentally confirmed by epitope mapping studies of anti-CD20 antibodies detecting a critical extracellular epitope at positions 170 to 172 in the human and mouse CD20 protein (see document D21, page 94, line 28 to page 95, line 1).

26. In the board's view, considering that both human and mouse CD20 have conserved motifs, the skilled person would have reasonably predicted that the CD20 protein of another mammal, *i.e.* dogs, would by analogy, have the same motifs, including a large extracellular domain that is located at a similar if not identical position.

27. The appellant submitted that the skilled person would not have been able to identify the canine-specific extracellular domain in the complete CD20 gene by sequence alignment with the human and mouse gene because, as a matter of fact, (i) the sequence and length of the canine domain differed significantly from that of human and mouse and (ii) the canine CD20 contained two domains.

27.1 The board considers however that the fact that the individual domains differ from each other with respect to sequence and length is not a technical obstacle to aligning them. This is commonly done in the art, as shown for example in figure 7 of document D10 which

aligns different members of the CD20 protein family, including that of human, denoted "A1" and that of mouse, denoted "a1" (see page 9, lines 27 and 28). While the human and mouse CD20 extracellular domain in the complete CD20 sequence have the same length, they are aligned with the sequences comprising shorter extracellular domains of the other members of the CD20 protein family (see figure 7). This is possible because the standard sequence alignment algorithms introduce gaps to achieve the best overall alignment between the compared sequences. Therefore, in the board's view, the skilled person using a standard sequence alignment procedure to compare the complete canine CD20 sequence obtained with those of the corresponding human and mouse sequences would have readily identified the extracellular domain represented by SEQ ID NO: 10 in claim 1.

27.2 That canine CD20, unlike human and mouse CD20, has a second extracellular domain is irrelevant since, as observed above, the skilled person would have identified the one corresponding to the single human and mouse extracellular domain, and that is also the one which is claimed (see e.g. document D2, figure 2 and document D10, figure 7).

28. Lastly, in a final step, the skilled person would then have successfully raised antibodies against the isolated, extracellular domain of the canine CD20 protein by applying standard immunisation protocols. This too was not contested.

29. Thus, the board concludes from the observations in points 19 to 28 above that the skilled person would have provided the antibodies of claim 1 of the main request in an obvious manner in the light of the teaching of

document D19, combined with common general knowledge. The main request therefore lacks inventive step and does not fulfil the requirements of Article 56 EPC.

Auxiliary requests 1 and 2

30. The subject-matter of claims 1 of auxiliary requests 1 and 2 differs from that of the main request in that the feature "wherein the isolated antibody [...] specifically binds canine CD20 positive B-lymphocytes" has been added in both auxiliary requests and the further feature "binds only to a predominant extracellular domain of canine CD20 as set forth in" has been added in auxiliary request 2.

31. In the board's view, the addition of these features does not change the claims' subject-matter compared to that of the main request. By virtue of its structure it is inherent to any antibody that binds to the extracellular domain of canine CD20 defined by SEQ ID NO: 10, that it also binds to canine CD20-positive B-lymphocytes, to a predominant extracellular domain of canine CD20, and that it binds to that domain only.

32. In view of the above considerations, the board concludes that the reasoning set out in points 10 to 28 above for the antibodies of claim 1 of the main request, applies *mutatis mutandis* to the antibodies of claims 1 of the auxiliary requests 1 and 2.

33. Hence, for auxiliary requests 1 and 2 the board arrives at the same conclusion as for the main request, *i.e.* that they do not fulfil the requirements of Article 56 EPC.

Auxiliary request 3

34. The subject-matter of claim 1 of auxiliary request 3 differs from that of the main request in that it relates to a second medical use, the claim being in the format according to Article 54(5) EPC. The antibodies are applied in the treatment of canine CD20-positive B-cell lymphoma.

35. As set out in points 12 and 20 above, the closest prior art document D19 discloses that cross-reactive anti-CD20 antibodies directed against the extracellular domain of CD20 are administered to dogs for the treatment of CD20-positive B-cell lymphomas, and also suggests the use of the canine-specific CD20 as antigen and immune-therapeutic target.

Hence, for the same reasoning as set out in points 10 to 28 above the subject-matter of claim 1 of auxiliary request 3 is considered obvious.

36. The auxiliary request 3 does therefore not fulfil the requirements of Article 56 EPC.

Reimbursement of the appeal fee

37. The appellant requested that its appeal fee be reimbursed.

38. Pursuant to Rule 103(1)(a) EPC, the board orders reimbursement of the appeal fee in full if it finds the appeal to be allowable and, such reimbursement is equitable by reason of a substantial procedural violation.

39. In the present case, the appeal is not allowable and the prerequisite for ordering a reimbursement is thus not met. Moreover, the board has found that the examining division did not commit a substantial procedural violation (see point 8 above). Therefore, the board does not accede to the appellant's request for reimbursement of the appeal fee.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated