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**Datasheet for the decision
of 19 August 2010**

Case Number: T 0716/08 - 3.3.04

Application Number: 02785223.5

Publication Number: 1440086

IPC: C07K 14/11

Language of the proceedings: EN

Title of invention:

Infectious salmon anaemia virus vaccine

Applicant:

Intervet International BV

Headword:

Infectious salmon anaemia virus vaccine/INTERVET

Relevant legal provisions:

EPC Art. 54, 56, 83, 84, 123(2)

Keyword:

"Added subject-matter (no)"

"Clarity, support, sufficiency of disclosure, novelty (yes)"

"Inventive step - problem solved (yes)"

Decisions cited:

T 0939/92, T 0187/93, T 0792/00, T 0219/01, T 0210/02,
T 0609/02, T 0293/04, T 1306/04, T 1329/04, T 0665/05,
T 0903/05, T 0394/06, T 0391/07, T 0087/08

Catchword:

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Case Number: T 0716/08 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 19 August 2010

Appellant: Intervet International BV
Wim de Körverstraat 35
NL-5831 AN Boxmeer (NL)

Representative: Keus, Jacobus Albertus Ronald
Intervet International BV
Patent Department
P.O. Box 31
NL-5830 AA Boxmeer (NL)

Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 28 November 2007
refusing European patent application
No. 02785223.5 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: C. Rennie-Smith
Members: G. Alt
M. Wieser

Summary of Facts and Submissions

I. This is an appeal against the decision of the examining division dated 28 November 2007 whereby the European patent application No. 02 785 223.5, published as International application No. WO 03/035680, was refused pursuant to Article 97(1) EPC. The application has the title "Infectious Salmon anaemia virus vaccine".

II. The following documents are cited in the present decision:

D3 Journal of Virology, vol. 71, no. 12, 1997, pages 9016-9023, Falk, K. et al.

D4 Journal of General Virology, vol. 81, 2000, pages 143-150, Kibenge, F.S.B. et al.

D5 Journal of Virology, vol. 71, no. 10, 1997, pages 7681-7686, Mjaaland, S. et al.

D6 EP-A-1 094 069

D7 Experiments submitted with letter dated 18 April 2007.

III. The following decisions are cited in the present decision:

T 939/92 of 12 September 1995

T 187/93 of 5 March 1997

T 792/00 of 2 July 2002

T 219/01 of 15 December 2004

T 210/02 of 1 October 2004

T 609/02 of 27 October 2004

T 293/04 of 5 April 2006

T 1306/04 of 8 December 2005

T 1329/04 of 28 June 2005

T 665/05 of 10 October 2006

T 903/05 of 30 August 2007

T 394/06 of 28 July 2009

T 391/07 of 13 January 2009

T 87/08 of 11 February 2010

IV. The decision under appeal dealt with a single request with claims relating to a nucleic acid encoding a 48 kDa protein from infectious Salmon anaemia virus (hereinafter abbreviated as "ISAV") and related nucleic acid fragments, recombinant DNA molecules, live recombinant carriers and host cells (claims 1 to 6); to the 48 kDa protein and fragments thereof, their use as a vaccine and for manufacturing a vaccine and a vaccine comprising said proteins (claims 7 to 15); methods for the preparation of a vaccine (claim 16) and diagnostic kits (claim 17).

- V. The examining division decided that the subject-matter of claims 7 and 8 was not novel in view of either of documents D3 or D4 because both disclosed the "existence of the 48 kDa protein". The subject-matter of claims 1 to 6 was found to lack an inventive step in view of either of documents D3 or D4 in combination with either document D5, disclosing the isolation and analysis of genomic clones of ISAV and their use for the detection of ISAV or, alternatively, document D6, disclosing isolation and analysis of genomic clones of ISAV encoding the structural protein P1, its recombinant expression in a baculoviral system and its use for vaccinal and diagnostic purposes. Claim 9 was considered to be obvious in view of a combination of either of documents D3 or D4 with document D6.
- VI. Also claims 10 to 16, i.e. the vaccine-related claims, were refused for lack of inventive step. The examining division considered that the problem of inducing a protective immunity in vivo in fish susceptible of infection by ISAV had not been shown to be solved by the present invention. The examining division relied on decision T 1329/04 which stated that "the definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve". Consequently, the examining division reasoned that "in view of documents D3 and D4, the problem to be solved is to provide a vaccine against ISAV and the solution proposed is to use the 48 kDa protein (or nucleic acids thereof). However, the description does

not provide any evidence that the technical problem has been solved, i.e. that vaccination leads to immunity against ISAV in fishes. The Examples 4 and 5, for which the claimed priority is not valid, only report the reactivity of the produced protein with rabbit antiserum raised against two peptides, not a vaccinal challenge."

VII. Moreover, in view of decisions T 1329/04, T 792/00 and T 1306/04 the examining division did not accept data submitted by the appellant in the course of the examination proceedings (document D7), aimed at demonstrating that the problem was solved. It was stated in particular with reference to decisions T 1329/04 and T 1306/04, that "inventive step has to be ascertained at [the] effective date. If the post-published document is the first disclosure going beyond speculation, this document may not be taken into account to assess inventive step."

VIII. The examining division added however that even if the evidence in document D7 was taken into consideration, it did not make the therapeutic effect plausible because "[t]he mortality/protection reported in Table 3 with a cumulative mortality in tank 4 [of] respectively 60% with treatment and 75% without treatment (saline solution) does not give very significant results, and certainly not a very significant level of protection".

IX. Furthermore, the argument that document D4 disclosed that the 48 kDa protein was not detected by a rabbit serum against ISAV and therefore did not provide an incentive to use the protein in a vaccine preparation was dismissed. In this context it was stated that "in

any case, immunogenicity in rabbits does certainly not provide a basis to a claim to vaccines for fishes."

- X. Finally, claim 17 relating to a diagnostic kit was refused because its subject-matter was obvious in view of a combination of document D5, disclosing the use of a cloned fragment of ISAV cDNA for viral detection, or document D6, disclosing a diagnostic kit relying on the SP-1 protein from ISAV, with either of documents D3 or D4.
- XI. With the statement of the grounds of appeal the appellant filed a new main request containing only claims 10 to 16 of the request dealt with in the decision under appeal.
- XII. In a communication the board informed the appellant of its preliminary opinion (i) that it considered document D6 as the closest prior art document, (ii) that it considered it to be common general knowledge that structural viral proteins were good candidates for the preparation of a vaccine and (iii) that, with regard to the interpretation of the disclosure in document D4, this would not have taught the skilled person that the lack of reactivity of the 48 kDa protein in the Western blot as reported in document D4 was due to the absence of antibodies against that protein in the serum.
- Moreover, the board asked for re-written claims.
- XIII. With a letter sent by telefax on 4 August 2010 the appellant sent a re-written set of claims comprising fourteen claims.

XIV. Oral proceedings were held on 19 August 2010.

The appellant filed a new main request addressing objections of lack of clarity raised by the board at the oral proceedings.

Independent claims 1, 3, 5, 6, 13 and 14 of this request read:

"1. Use of an 48 kD infectious Salmon anaemia virus (ISAV) protein or an immunogenic fragment of said protein, said protein or immunogenic fragment thereof having an amino acid sequence that is at least 70% homologous to the amino acid sequence as depicted in SEQ ID NO: 2, for the manufacturing of a vaccine for combating ISAV infections.

3. Use according to claim 1 or 2, characterised in that said protein or immunogenic fragment thereof is encoded by a nucleic acid sequence or part thereof having at least 70% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1.

5. Vaccine for combating ISAV infection, characterized in that it comprises a nucleic acid sequence as described in claim 3 or 4, a stretch of nucleotides carrying such nucleic acid sequence, a recombinant DNA molecule comprising such nucleic acid sequence or such a stretch of nucleotides, a live recombinant carrier comprising such nucleic acid sequence or such a stretch of nucleotides or such recombinant DNA molecule, a host cell comprising such nucleic acid sequence or such a stretch of nucleotides or such recombinant DNA molecule

or such live recombinant carrier, and a pharmaceutically acceptable carrier.

6. Vaccine for combating ISAV infection, characterised in that it comprises an 48 kD ISAV protein or an immunogenic fragment of said protein, said protein or immunogenic fragment thereof having an amino acid sequence that is at least 70% homologous to the amino acid sequence as depicted in SEQ ID NO: 2, and a pharmaceutically acceptable carrier.

13. Method for the preparation of a vaccine according to claim 5, said method comprising the admixing of a nucleic acid sequence as described in claim 3 or 4, a stretch of nucleotides carrying such nucleic acid sequence, a recombinant DNA molecule comprising such nucleic acid sequence or such a stretch of nucleotides, a live recombinant carrier comprising such nucleic acid sequence or such a stretch of nucleotides or such recombinant DNA molecule, a host cell comprising such nucleic acid sequence or such a stretch of nucleotides or such recombinant DNA molecule or such live recombinant carrier and a pharmaceutically acceptable carrier.

14. Method for the preparation of a vaccine according to any of claims 6-9, said method comprising the admixing of a protein or immunogenic fragment thereof as described in claims 6-9 or antibodies against the protein described in claims 6-9 and a pharmaceutically acceptable carrier."

XV. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis

of claims 1 to 14 of the main request filed at the oral proceedings.

XVI. The appellant's arguments submitted in writing and at the oral proceedings, as far as they are relevant for the present decision, may be summarized as follows:

Inventive step

The 53 kDa structural protein of ISAV disclosed in document D4 was equivalent to the 48 kDa protein of the application.

It was agreed with the board's view that document D6 was the closest prior art document disclosing a vaccine comprising the 74 kDa structural protein of ISAV.

The problem to be solved was the provision of an alternative ISAV vaccine.

The skilled person would consider structural viral proteins as candidates to be included in vaccines. This was however not the only possibility of solving the problem underlying the application.

Even if it was assumed that the skilled person had considered to use a structural protein, the skilled person had no motivation to use the 48 kDa protein of ISAV.

This was so, because document D4 disclosed that it did **not** react in a Western blot probed with an antiserum obtained from rabbits injected with ISAV.

The skilled person would have regarded the two reasons stated in document D4 for the failure of the 48 kDa protein to react in the Western blot - a too low quantity of the protein on the Western Blot membrane or the loss of a conformational epitope in the denatured protein - as highly unlikely.

Therefore, the skilled person would have inferred from the absence of reactivity of the 48 kDa protein in the Western blot disclosed in document D4 that in fact, antibodies against this protein had not been generated upon immunisation with ISAV in rabbits, i.e. that the 48 kDa protein was not immunogenic and hence was not a candidate for a vaccine.

The post-published experiments of document D7 demonstrated a cumulative mortality of 57% in the vaccinated groups whereas it was 75% in the control group, thus proving a protective effect of the 48 kDa protein.

Reasons for the Decision

Article 84 EPC

1. The claims of the sole request are clear. In particular, the skilled person would understand that the expression in claims 1 and 6 "[u]se of an 48 kD infectious Salmon anaemia virus (ISAV) protein or an immunogenic fragment of said protein, said protein or immunogenic fragment thereof having an amino acid sequence that is at least 70% homologous to the amino acid sequence as depicted in SEQ ID NO: 2", or the

expression in claims 3 and 8 "characterised in that said protein or immunogenic fragment thereof is encoded by a nucleic acid sequence or part thereof having at least 70% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1" means that the parameter of a 70% sequence homology is to be determined in relation to the entire sequence depicted in SEQ ID Nos. 1 and 2, in the case of both the whole protein and the fragment. This interpretation is in conformity with the statements on page 7, lines 1 to 3 and 12 to 13 of the description that "[o]ne form of this embodiment relates i.a. to 48 kD ISAV proteins and to immunogenic fragments thereof, that have an amino acid sequence that is at least 70% homologous to the amino acid sequence as depicted in SEQ ID NO: 2" and that "[a]nother form of this embodiment relates to such 48 kD ISAV proteins and immunogenic fragments of said protein encoded by a nucleic acid sequence according to the invention."

2. Moreover, the claims are supported both formally (for example page 9, line 16 to page 10, line 20) and substantially (see the examples, in particular Example 2, see points 17 to 26 below) by the description.
3. The requirements of Article 84 EPC are fulfilled.

Article 123(2) EPC

4. All of the present claims are based on combinations of claims as filed.

In particular:

Claims 1 to 4 are based on claim 11 combined with claims 7, 8, 9 and 1, or 9 and 2, respectively.

Claims 5 to 12 are based on claim 12 in combination with claims 1 to 6, 7, 8, 9, 1 and 9 (both claims 8 and 9), 14, 15 or 16, respectively.

Claims 13 and 14 are based on claim 17 or on a combination of claims 17 and 13.

5. The requirements of Article 123(2) EPC are fulfilled.

Article 54 EPC

6. In the decision under appeal the subject-matter of the claims corresponding to present claims 1 to 14 (then claims 10 to 16) was not objected to for lack of novelty (see section VI above).

The board considers that the present claims fulfil the requirements of Article 54 EPC with regard to the documents currently on file.

Article 56 EPC

7. Claims 1 to 14, corresponding to claims 10 to 16 of the claims dealt with in the decision under appeal, relate to the use of a protein for manufacturing a vaccine, to a vaccine and to a method for the preparation of a vaccine.

8. In the decision under appeal documents D3 or D4 were considered as closest prior art documents for these "vaccine-claims".
 - 8.1 Documents D3 and D4 disclose the characterization of ISAV.
9. In contrast, document D6, a European patent application, discloses the isolation of SP-1, a structural protein of ISAV, and suggests its usefulness for vaccination against ISAV infection.
10. In the board's view, therefore, when taking into account well-established case law saying that the primary criterion for determining the closest prior art document for assessing inventive step is that it discloses subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention, document D6 has to be considered as the closest prior art document.
11. Starting from document D6 and in the absence of evidence of an improvement over the subject-matter disclosed in that document, the problem to be solved is considered to be the provision of an alternative vaccine against ISAV.
12. The solution to this problem as stated in the claims is the use of a 48 kDa protein having the sequence described in SEQ ID No. 2, variants thereof or related compounds, such as recombinant DNA molecules.
13. A first issue in the present case is whether or not the disclosure in the application provides evidence that

the problem formulated in point 14 above has been solved. In the decision under appeal the examining division held that it was not plausible, on the basis of the disclosure in the application and in particular Examples 4 and 5, that the solution, as then claimed in claims 10 to 16, solved the problem underlying the application.

14. The boards have regularly considered in the context of the evaluation of inventive step whether or not "the problem is solved" (see for example decision T 187/93, point 19 of the reasons or decision T 939/92, points 2.4.1 or 2.5.1 of the reasons) and have in cases where they were not satisfied that this was so, i.e. that what was claimed was de facto a solution to the problem, denied an inventive step (see for example decision T 210/02, point 5, paragraph 10 et seq. of the reasons or decision T 1329/04, points 6 to 11 of the reasons) or required a reformulation of the problem (see for example decision T 939/92, points 2.5 and 2.6, last paragraph of the reasons or decision T 87/08, point 6.3 of the reasons).

15. The verification of whether or not the claimed solution actually solves the problem, i.e. that the claimed subject-matter actually provides the desired effect, is according to decision T 1329/04 to be made on the basis of data in the application (point 12 of the reasons). Common general knowledge at the priority date may be used to interpret the teaching in an application or a patent (see for example decision T 293/04, point 21 of the reasons or decision T 665/05, point 16 of the reasons). Post-published evidence can only be used to back-up the teaching derivable from the application

(for example decision T 1329/04, point 12 of the reasons).

16. As to the quality of the evidence, "absolute proof" of the achievement of an effect is not required for the effect to be "plausible". Thus, in the case of a vaccine, it is not required that protective immunity is actually demonstrated in the target organism. It suffices that the data indicate that a compound could be a useful candidate for a vaccine (for example decision T 903/05, point 19, last paragraph of the reasons; decision T 0391/07, point 20 of the reasons; decision T 394/06, point 13 of the reasons in combination with page 6, last paragraph to page 8, first paragraph of "Facts and Submissions".)
17. The present application discloses in Example 2 that the 48 kDa protein of ISAV was found by screening of a bacteriophage lambda cDNA library with an anti-ISAV polyclonal rabbit serum.
18. In a lambda bacteriophage cDNA library each bacteriophage particle expresses on its surface a protein corresponding to the cDNA contained in that particle. By probing such a library with a monoclonal antibody preparation or a polyclonal serum, proteins reacting with the antibodies, and thus also the corresponding cDNAs, are identified.
19. In the present case the antibodies used for probing the library are in the form of a polyclonal serum obtained from rabbits immunized with whole ISAV particles.

20. At the priority date it was known from document D4 that ISAV had four structural proteins having molecular masses as determined on an SDS-gel of 74, 53, 43 (or 46 depending on the virus isolate) and 26.5 kDa (see for example Table 2 or Figure 5).

21. The appellant submits that the 53 kDa protein disclosed in document D4 is equivalent to the 48 kDa protein of the application. The board has no reason to doubt this submission. Thus, it is concluded that the 48 kDa protein of the application is one of the four viral structural proteins of ISAV as disclosed in document D4.

22. It is, as the appellant agreed at oral proceedings, common general knowledge that structural proteins of a virus, i.e. the proteins involved in formation of the viral capsid, or in the case of enveloped viruses, additionally those situated in the viral envelope, are potential candidates for the inclusion in subunit vaccines. This is so because structural proteins are present at the outside of the virion and are thus exposed to the immune system. Therefore, it is expected that upon infection with ISAV, antibodies are preferably elicited against these structural proteins and that these antibodies may achieve neutralization of the virus. Therefore, vaccine preparations containing, instead of for example the whole inactivated virus, only one (or more) of the structural proteins, i.e. so-called subunit vaccines, would also be expected to have the same effect, i.e. to elicit neutralizing antibodies.

23. That common general knowledge of the skilled person is reflected by the disclosure in document D6. It reports that one of the structural proteins of ISAV, SP-1 which, as submitted by the appellant at the oral proceedings, corresponds to the 74 kDa protein disclosed in document D4, was identified by screening with a polyclonal anti-ISAV rabbit serum (paragraph [0042] and that this protein is expected to induce a protective immune response in fish against infection with ISAV (paragraphs [0019] and [0053]).

24. In view of the case law referred to in points 15 and 16 above and in the light of the observations in points 17 to 23, in particular point 22 above, the board considers that the mere presence of antibodies against the 48 kDa protein in the rabbit serum used for screening the lambda bacteriophage cDNA library according to Example 2 of the application is evidence that the 48 kDa protein is antigenic and, consequently, could also be a useful constituent of a subunit vaccine.

25. The polyclonal serum according to the application was obtained after immunisation of rabbits with ISAV particles. The target organism for vaccination with the 48 kDa protein is however salmon. In the decision under appeal the examining division states that immunogenicity in rabbits does not provide a basis to a claim to vaccines for fish (see section IX above). The board notes however, that there is no evidence before it demonstrating that the properties of the immune system of salmon and rabbits are of a totally different nature.

26. Thus, in conclusion the board is satisfied in view of Example 2 that the subject-matter of the claims is a solution to the problem formulated above, i.e. the provision of an alternative vaccine against ISAV.
27. As a consequence the post-published evidence, i.e. document D7, is not needed to back up the disclosure in the application. However, for completeness, the board notes the following with regard to the examining division's view on document D7 (see section VIII above).
28. Document D7 discloses that salmon were vaccinated with the 48 kDa protein expressed in E. coli (two groups) or with saline (two groups), respectively. All groups were challenged eight weeks after vaccination by infection with ISAV. The cumulative mortality of the saline group was 75%, that of the vaccinated group 57% (calculated from Table 3). Thus, in the board's view, these data demonstrate that the E. coli-expressed 48 kDa ISAV protein has a protective effect against IASV infection. Whether or not this effect is "very significant" is irrelevant, since absolute proof of the usefulness of the compound as a vaccine is not necessary (see point 16 above).

Obviousness

29. According to established case law an invention is considered as obvious if the skilled person trying to solve a technical problem would - and not simply could - have arrived at the invention following promptings in the prior art or from common general knowledge.

30. Thus, in the present case the question is whether or not the skilled person faced with the problem of providing an alternative anti-ISAV vaccine would be motivated to use the 48 kDa structural ISAV protein.

31. At the oral proceedings the appellant submitted that the use of a structural protein of ISAV as a vaccine different from the one according to the closest prior art document D6, i.e. the 74 kDa protein, and in particular the use of the 48 kDa protein was only one of the many possible solutions for the underlying problem. Other options were for example the improvement of the vaccine known from document D6 by, for example, the preparation of a combination vaccine, by using a different expression system or by shortening the protein. Thus, the skilled person was in a situation where he/she could, but would not have been motivated to provide a different structural protein of ISAV as an alternative ISAV vaccine (see point 29 above).

32. When examining whether or not the skilled person nevertheless would have chosen a structural ISAV protein different from the 74 kDa protein according to document D6 and, in particular the 48 kDa protein, to solve the technical problem underlying the present application, document D4 is the most relevant document among those available in these proceedings.

33. It discloses the analysis of structural proteins of ISAV in a Coomassie blue-stained SDS polyacrylamide gel and a Western blot. Lane 1 of the SDS-polyacrylamide gel contains purified "Back Bay 98" virus isolate. Lanes 2 and 3 contain moderately purified and ultra-pure RPC/NB-877 virus isolate, respectively. For the

Western blot the proteins were transferred from the gel to a nitrocellulose membrane. The membrane was probed with rabbit antiserum raised against ISAV isolate Back Bay 98 (see "Materials and Methods": "Gel electrophoresis of viral proteins and Western blotting").

34. It is stated on page 148, second column of document D4: "As shown in Fig. 5(b), the blot of the homologous virus [lane 1] showed protein bands of 74, 46, 43, and 26.5 kDa, whereas the blot of the heterologous virus isolate RPC/NB-877 [lanes 2 and 3] had protein bands of 74 and 46 kDa only. **The 53 kDa protein** [i.e. the 48 kDa protein of the application] **was not detected by Western blot analysis in any purified ISAV preparations.**" (emphasis and notes in [...] added).
35. Document D4 discloses on page 149, second column, second paragraph: "Failure to detect the major protein bands of 53 kDa in both Back Bay 98 and RPC/NB-877 viruses and 26.5 kDa in RPC/NB-877 virus in Western blots may be due to the conformational nature of epitopes in these proteins. Alternatively, the lack of reaction of the 53 and 26.5 kDa bands could be due to small amounts of antigen in the Western blots."
36. The skilled person knows on the basis of his/her common general knowledge that due to the experimental set up of a Western blot assay the non-reactivity of a protein with a given antiserum does not immediately indicate the underlying reason for this result. The skilled person would prima facie see several reasons which may be grouped into two main categories. First, antibodies to a particular protein are present in the polyclonal

serum - implying that the protein is immunogenic - but, for example, they do not react with the blotted protein or reactivity cannot be detected with the method applied; and second, antibodies to the particular protein are absent from the polyclonal serum because none have been generated upon immunisation - implying that the protein is not immunogenic, i.e. that it is not a candidate protein for a vaccine (see point 22 above).

37. Thus, it follows from the passage cited above in point 35 that the authors of document D4 see the reason for the non-reactivity of the 53 kDa protein (i.e. the 48 kDa protein of the application) in the Western blot in the first of the two categories mentioned in point 36 above. In other words, they do not ascribe it to the absence of antibodies to the protein in the polyclonal serum. Hence, *prima facie*, document D4 teaches that the 48 kDa protein is immunogenic.
38. However, as submitted by the appellant at the oral proceedings, the skilled person who is presumed to read and interpret prior art documents on the basis of his/her background knowledge would have considered the explanations in document D4 for the failure of the 48 kDa protein to react with the antiserum in the Western blot assay as highly unlikely and would instead have inferred that the absence of reactivity comes from the absence of antibodies to the 48 kDa a protein in the serum.
39. Concerning the conformational nature of the epitopes in the 48 kDa protein, the appellant explains that large proteins such as the 48 kDa protein usually have many

antigenic determinants, some of them of a linear and some of a conformational nature. Usually a polyclonal serum, in contrast to a monoclonal antibody preparation, does not contain antibodies against only one but against many of the antigenic determinants. Thus, if it is assumed, as the authors of document D4 do, that there are antibodies against the 48 kDa protein in the rabbit serum, the explanation given in document D4 would mean that the structure of the 48 kDa protein on the Western blot membrane is modified to such an extent that all of the antigenic determinants to which antibodies are directed are destroyed, so that none of the different antibodies existing in the polyclonal anti-ISAV serum would react. The skilled person would consider this highly unlikely.

40. Concerning the too small amount of the 48 kDa protein on the Western blot membrane, the appellant submits that it can be seen in Figure 5 that the 26.5 kDa protein of ISAV is present on the SDS gel in a higher concentration than the 48 kDa protein. Moreover, it has a lower molecular weight. Both these conditions speak for a more efficient transfer from the gel onto the nitrocellulose membrane of the 23.6 kDa protein compared to the 53 kDa protein. The reactivity with the Black Bay 98 serum (lane 1) demonstrates that the transfer from the gel to the membrane has in fact worked (see point 34 above). For that reason and also because the 26.5 kDa protein would be more efficiently transferred to the membrane, the skilled person would view the suggestion in document D4 that the absence of reactivity of the 26.5 kDa protein with the anti RPC/NB-877 virus serum was due to a too small amount of the protein as highly unlikely. Therefore, the skilled

person would also have called into doubt the credibility of the same explanation with regard to the 48 kDa protein.

41. Hence, in the appellant's view, the skilled person after reading document D4 would not be under the impression that the failure of the 48 kDa protein to react in the Western blot assay was due to the concentration or structure of the protein, but would consider that it was due to the absence of antibodies against the 48 kDa protein in the serum.

42. The board finds this argumentation persuasive.

It thus considers that the skilled person would have interpreted the teaching in document D4 such that the failure of the 48 kDa protein to react in the Western blot is due to the absence of antibodies to the 48 kDa protein in the rabbit serum and that therefore the 48 kDa protein is not immunogenic and hence is not a candidate for a vaccine.

43. Therefore, the skilled person trying to solve the technical problem underlying the patent and being in the situation described in point 31 above where he/she had many suitable alternatives for solving the problem, would not be motivated by the disclosure in the prior art documents available to the board in these proceedings to replace the 74 kDa ISAV protein-containing vaccine disclosed in the closest prior art document D6 by one containing the 48 kDa ISAV protein. He/she would therefore not arrive at the claimed subject-matter in an obvious way.

44. Consequently, the subject-matter of claim 1 is considered to involve an inventive step. This conclusion extends to claims 2 to 14 which are either dependent on claim 1 or relate to the 48 kDa protein and its vaccinal use.

45. The requirements of Article 56 EPC are fulfilled.

Article 83 EPC

46. Article 83 EPC requires that the European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. In particular, as regards claims to a so-called first or second medical use, it is not only necessary for acknowledging that the requirements of Article 83 EPC are fulfilled, that the skilled person is enabled on the basis of the disclosure in the application to make the compounds to be used, but also that there is evidence in the application and or on the basis of common general knowledge that the therapeutic effect is achieved (for a first medical use see decision T 219/01 point 4 of the reasons, for second medical use, T 609/02, point 9 of the reasons.)

47. The application discloses the nucleic acid and amino acid sequence of the 48 KDa protein of ISAV. The therapeutic effect is credible for the reasons given in point 24 above. Hence, the board concludes that the requirements of Article 83 EPC are fulfilled.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent on the basis of claims 1 - 14 of the main request filed at the oral proceedings, figures 1 - 3 as filed and a description yet to be adapted thereto.

The Registrar:

The Chairman:

G. Nachtigall

C. Rennie-Smith