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**Datasheet for the decision
of 30 May 2018**

Case Number: T 0301/12 - 3.3.08

Application Number: 05741681.0

Publication Number: 1751276

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Language of the proceedings: EN

Title of invention:
VACCINE COMPRISING AN ATTENUATED PESTIVIRUS

Patent Proprietor:
Boehringer Ingelheim Vetmedica GmbH

Opponent:
Intervet International B.V.

Headword:
Attenuated pestivirus/BOEHRINGER INGELHEIM

Relevant legal provisions:
EPC Art. 100(a), 104(1), 111(1), 113(1)
EPC R. 100(1), 88(1)
RPBA Art. 16(1)

Keyword:

Patent as granted - inventive step (yes)

Apportionment of costs - (yes)

Decisions cited:

T 0024/81, T 0930/92, T 0937/04, T 0123/05, T 0053/06,

T 0212/07, T 0854/09, T 2179/09, T 0258/13, T 1663/13

Catchword:



Beschwerdekammern
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Case Number: T 0301/12 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 30 May 2018

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 8 December 2011
rejecting the opposition filed against European
patent No. 1751276 pursuant to Article 101(2)
EPC.**

Composition of the Board:

Chairman B. Stolz
Members: M. R. Vega Laso
R. Winkelhofer

Summary of Facts and Submissions

I. European patent No. 1 751 276 with the title "Vaccine comprising an attenuated pestivirus" was granted on the European application No. 05741681.0.

II. The patent was granted with 38 claims. Claim 1 reads as follows:

"1. An attenuated pestivirus, having at least one mutation in the coding sequence for glycoprotein E^{ms}[sic] and at least another mutation in the coding sequence for N^{pro}, wherein said mutation in the coding sequence for glycoprotein E^{ms}[sic] leads to inactivation of RNase activity residing in E^{ms}[sic] and said mutation in the coding sequence for N^{pro} leads to inactivation of said N^{pro}, [sic]"

Dependent claims 2 to 25 are directed to various embodiments of the attenuated pestivirus of claim 1. Claims 26 to 29 and 38 relate to compositions comprising the attenuated pestivirus. Claims 30, 31 and 38 concern the use of a Bovine Viral Diarrhoea Virus (BVDV) according to the invention in the manufacture of a vaccine. Claims 32 to 34 are directed to a nucleic acid molecule comprising the nucleic acid encoding a live attenuated BVDV of the invention, and claims 35 to 37 to a method for attenuating a pestivirus.

III. The patent was opposed on the ground for opposition of Article 100(a) in conjunction with Article 56 EPC.

IV. In a decision under Article 101(2) EPC posted on 8 December 2011, the opposition division found that the subject-matter of the claims of the patent as granted

involved an inventive step within the meaning of Article 56 EPC and, thus, the ground for opposition of Article 100(a) EPC did not prejudice the maintenance of the patent as granted. Consequently, the opposition division rejected the opposition.

- V. The opponent (appellant) lodged an appeal against the decision of the opposition division and submitted a statement setting out the grounds of appeal.
- VI. The patent proprietor (respondent) replied to the grounds of appeal and submitted new documentary and experimental evidence.
- VII. As a subsidiary request, both parties requested oral proceedings.
- VIII. The parties were summoned to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) sent in preparation of the oral proceedings, the board provided some comments on the submissions of the parties and expressed its provisional opinion on procedural issues and substantive issues concerning Article 56 EPC.
- IX. In reply to the communication, the appellant informed the board that, while it maintained all its requests, including the request for oral proceedings, it would "*... probably not be represented at the oral proceedings on 30 April 2018*". The appellant did not make any submissions in substance, but only referred to its submissions in the notice of opposition and the statement of grounds of appeal.
- X. Two weeks before the scheduled oral proceedings, the registrar of the board contacted the representative of

the appellant by telephone, asking whether the appellant would be represented at the oral proceedings. The representative informed the registrar that "*most likely*" the appellant would not be represented.

XI. In the afternoon of the day before the oral proceedings the registrar tried to contact the representative. The representative was not available at that time, but his assistant remarked on the telephone that, since a flight to Munich had not been booked, it appeared that the representative did not intend to attend the oral proceedings.

XII. Oral proceedings were held on 30 May 2018 in the absence of the appellant.

XIII. The following documents are referred to in this decision:

- (1): EP 1 104 676 A1, published on 6 June 2001;
- (2): WO 03/023041 A2, published on 20 March 2003;
- (3): EP 1 013 757 A2, published on 28 June 2000;
- (4): Canadian Patent No. 2 363 493, published on 22 May 2002;
- (6): D. Mayer et al., *Vaccine*, 2004, Vol. 22, 317 to 328; and
- (14): Technical declaration by Prof Dr Gregor Meyers, dated 28 November 2012.

XIV. The submissions made by the appellant in its statement of grounds of appeal concerning issues relevant to this decision, were essentially as follows:

Articles 100 (a) and 56 EPC - inventive step

Document (1) was aimed at providing a BVDV vaccine strain that was safe for the foetus upon vaccination of the pregnant cow, and protected the foetus from infection from wild-type field viruses. It described a live attenuated BVDV E^{rns} mutant that was not transmitted from the placenta to the foetus.

The differences between the teaching of document (1) and the alleged invention were (a) the pathogenic nature of the BVDV strains to be attenuated, and (b) the additional inactivation of the N^{pro} gene. The technical problem to be solved was the provision of attenuated pestiviruses that were safe, such that they did not cross the placenta of pregnant cows, and efficacious, such that they were capable of inducing a (sterile) immune response in the cow that protected the foetus from infection by field viruses. The patent provided only one example of such viruses, the XIKE-B-NdN strain in which the E^{rns} and N^{pro} genes were inactivated. The contribution of the invention to the art was thus restricted to the provision of that specific BVDV type 2 (BVDV-2) strain of a high-virulence level, that when attenuated by inactivating the E^{rns} and N^{pro} genes fulfilled a "delicate balance of safety and efficacy". This balance was by no means a general feature of any BVDVs having those two genes inactivated.

The problem underlying the invention was not solved by all embodiments covered by the claims. The opposition

division found that the technical effect underlying the claimed invention was (i) the retention of efficacy (vis-à-vis a comparable single mutant vaccine virus) whilst (ii) improving the safety of the vaccine by providing a further safety net against reversion or (iii) possible low-level trans-placental transmission. With regard to (i), it was *highly* questionable whether efficacy was retained when an in itself already low-virulence BVDV-1 strain was further attenuated through the addition of an N^{Pro} deletion. In fact, the patent proprietor had admitted that the low-virulence BVDV-1 strain CP7 described in document (1) could not provide sufficient protection against highly pathogenic BVDV-1 strains, leave alone against BVDV-2 strains, and that the higher a virus was attenuated, the less efficient would it be as a vaccine. Hence, more than serious doubts existed as to whether the anticipated effect of the claimed viruses of eliciting an immune response that was sufficient to protect the foetus against field infection, could be readily obtained for the whole range claimed.

Moreover, the claimed subject-matter was obvious. A person skilled in the art would have applied the teaching of document (1) to high-virulence BVDVs of type 2, as described in document (2) for the NY 93/C strain. He/she would have then observed that for such viruses the attenuation principle described in document (1) would not result in a safe vaccine because the virus was not sufficiently attenuated to prevent trans-placental transmission. This would have motivated the skilled person to further attenuate high-virulence BVDVs. In view of documents (3) and (4) which described the N^{Pro} gene - the only other known virulence factor in BVDVs - and two N^{Pro} BVDV mutants with a different level of attenuation, it was obvious to the skilled

person to inactivate also the N^{pro} gene in order to bring the virulence down and increase the safety of the vaccine.

The skilled person would not have considered an E^{rns} and N^{pro} double mutant to be too attenuated. There was no reason to assume that the N^{pro} mutant dN6 described in document (4) would behave too attenuated when the E^{rns} gene was additionally deleted. The fact that the BVDVdN1 virus described in Example 4 of document (3) induced a neutralizing serum indicated that a vaccine comprising this virus could protect animals against BVDV of both type 1 and 2. Contrary to the opposition division's view, the viral dose used in Example 4 was a normal dose for use in a vaccine. The N^{pro} mutant dN6 described in document (4) would be considered by a skilled person to be an ideal starting point for a virus having both an N^{pro} and an E^{rns} deletion.

Since the mutant BVDV strains described in document (2) were not sufficiently attenuated to prevent trans-placental transmission in high virulence BVDV strains, the only option left for the skilled person was to start looking for further attenuation options. Documents (3) and (4) provided attenuated BVDV viruses having a deletion in the N^{pro} gene and vaccines comprising those viruses which were capable of protecting animals against BVDV infection as they induced serum that neutralized both type 1 and type 2 viruses. The viruses described in document (4) had a level of growth comparable to that of the wild-type virus. Thus, starting from document (2) and looking for a further attenuated BVDV the skilled person would be highly motivated to apply the teachings of document (4). He/she had no reason to fear that the double mutant would be over-attenuated. By combining

the teachings of documents (2) and (4), the skilled person would arrive at pestiviruses falling within the scope of the claims, without exercising any inventive effort. Hence, the claimed subject-matter did not involve an inventive step.

- XV. The submissions by the respondent, insofar as they are relevant to the present decision, may be summarised as follows:

Articles 100 (a) and 56 EPC - inventive step

Claim 1 of the patent encompassed both BVDV-1 and BVDV-2 mutants. As concerned BVDV-1 mutants, document (1) was the closest state of the art. The single E^{rns} mutant B-349-d described therein was considered to be safe because trans-placental transmission was not observed at the time of vaccination. However, in the absence of a challenge with the wild-type virus, no information on efficacy could be derived from document (1).

The opposition division correctly found that the invention solved the technical problem of providing an attenuated pestivirus strain with a similar efficacy to an E^{rns} inactivated mutant, but having improved safety characteristics, over the whole breadth of the claim, in particular as regards both low- and high-virulence BVDV. The problem underlying the invention was solved by all embodiments covered by the claims. The experimental evidence in document (14) demonstrated that the E^{rns} N^{pro} double mutant KE9-B-NdN derived from the low-virulence BVDV-1 strain KE9 was safe because, upon inoculation of pregnant heifers, no virus could be detected in foetal tissues. It was also efficacious as it provided full protection for the foetuses against a BVDV-1 challenge.

Starting from the mutant virus of document (1), the skilled person had no motivation at all to introduce an additional mutation in the N^{pro} gene. Document (3) described a BVDV-1 virus mutated in the N^{pro} gene but did not provide any evidence regarding its efficacy as a vaccine *in vivo*. In view of the lower replication rate of the N^{pro} mutant in cell culture, the skilled person would not expect a sufficient immune protection. The seroconversion data provided in document (3) were not conclusive with regard to efficacy. Thus, the person skilled in the art would not have considered combining the teachings of documents (1) and (3). Nor would he/she have combined document (1) with document (4).

Document (2), which was the closest state of the art as concerned BVDV-2 mutants, described an E^{rns} mutant (XIKE-B), but provided no experimental data that would allow assessing trans-placental safety of a vaccine based on this mutant. Although documents (3) and (4) identified the safety aspect as a potential problem, they did not provide any hint, let alone a solution to the problem. Thus, the claimed subject-matter was not obvious to the skilled person in view of a combination of document (2) with either document (3) or (4).

Apportionment of costs

In its communication, the board had expressed a provisional opinion favourable to the position of the respondent. However, the appellant had not filed any substantive reply. While it had informed the board that it would "probably" not be represented at the oral proceedings, the appellant had not withdrawn its request for such proceedings. Such a behaviour amounted

to an abuse of procedure because, left in doubt about the attendance of the appellant, the respondent had no other choice than to instruct its representative to prepare the case and attend the oral proceedings. Under these circumstances, the costs incurred by the respondent to be represented at the oral proceedings should be reimbursed by the appellant.

XVI. The appellant (opponent) requests that the decision under appeal be set aside and the patent be revoked.

XVII. The respondent (patent proprietor) requests dismissal of the appeal and apportionment of the costs it incurred for the oral proceedings before the board.

Reasons for the Decision

Additional evidence filed in appeal proceedings

1. Document (14) is a technical report by Prof Meyers including experimental evidence concerning the safety and efficacy of the E^{rns} N^{pro} mutant KE9-B-NdN derived from the low-virulence wild-type BVDV type 1 strain KE9. This document, which was submitted by the respondent together with its reply to the statement of grounds of appeal, is considered to be a direct response to the objection that the invention does not solve the technical problem over the whole scope of the claims, in particular as far as the claimed subject-matter concerns BVDV type 1.
2. It is apparent from the file - and has not been disputed by the appellant - that the objection in question had been raised for the first time during the oral proceedings before the opposition division. Since the patent proprietor (the present respondent) could

not be reasonably expected to present the experimental evidence in the proceedings before the opposition division, the board holds that document (14) has been filed in due time. Hence, this evidence must be considered by the board when arriving at its decision on the appeal.

The claimed invention

3. The invention relates to attenuated pestiviruses, in particular bovine viral diarrhoea viruses (BVDVs) and their use for the manufacture of a vaccine. BVDV is an economically important pathogen that causes gastrointestinal, respiratory, and reproductive disease in cattle. BVDV strains are differentiated into two types, type 1 and type 2, which differ both antigenically and at the level of genomic sequences.

4. While BVDV vaccines based on attenuated live viruses can be generally considered to be more efficacious in eliciting a protective immune response than other types of viral vaccines, they may involve safety problems. If pregnant cows at early stages of gestation are vaccinated, the vaccine viruses may cross the placenta and lead to clinical manifestations in the foetus, abortion and/or induction of persistently infected calves. For this reason, at the priority date such vaccines could not be applied to herds that included pregnant cows. Further safety problems associated with the use of attenuated live viruses as vaccine may arise if the viruses revert to the virulent wild-type, which is often the case when attenuation is achieved by conventional multiple passaging (see paragraph [0007] of the patent).

5. The invention provides an attenuated pestivirus, preferably BVDV having at least one mutation in the E^{rns} gene and at least another mutation in the N^{pro} gene. Such improved attenuated pestivirus does not cross the placenta itself and induces an immunity that prevents viral transmission across the placenta and thereby prevents pregnancy problems like abortion of the foetus or birth of persistently infected hosts, such as calves in the case of BVDV infection (see paragraph [0009] of the patent).

6. The patent provides experimental evidence supporting the claimed invention. While inoculation of pregnant heifers with a N^{pro} BVDV-2 mutant (XIKE-A) or a E^{rns} BVDV-2 mutant (XIKE-B) lead to either abortion or infection of the foetus (see Example 1 of the patent), when pregnant heifers were inoculated with a E^{rns} N^{pro} BVDV-2 mutant (XIKE-B-NdN) according to the invention the virus was not detected in the foetus (see Example 3, in particular paragraph [0168]). In a second experiment, the heifers were inseminated four weeks after vaccination with XIKE-B NdN. 60 to 90 days after insemination they were challenged with a heterologous BVDV-2 strain (KE-13). Whereas all non-vaccinated controls were BVDV viremic and the foetuses BVDV positive, the vaccinated animals were fully protected against the heterologous strain, both in terms of viremia and transmission to the foetus (see paragraphs [0181] and [0182] of the patent).

Articles 100(a) and 56 EPC - inventive step

Document (2) as the closest state of the art

7. In the decision under appeal, the opposition division considered that each of documents (1) to (4) and (6)

related to the problem of providing improved pestivirus strains for use in vaccination, but that document (2) was to be regarded as the closest state of the art because it related to the attenuated forms of more virulent strains of BVDV (BVDV type 2) that, when used as a vaccine, may provide improved cross-protection against different antigenic groups of BVDV (see page 4, second paragraph of the decision).

8. Document (2), a patent application filed by the present respondent, addresses the technical problem of providing an infectious attenuated BVDV type 2 of defined genetic identity (see page 2, lines 18 to 22 and paragraph bridging pages 8 and 9). It describes two BVDV mutant clones derived from the wild-type BVDV-2 strain New York '93/C by either deletion of the codon for histidine at position 349 of the amino acid sequence of the E^{rns} gene (H349Δ; XIKE-B), or substitution of the codon for histidine at position 300 by a codon for leucine (H300L; XIKE-C). For animal experiments, the XIKE-B mutant was given precedence over the XIKE-C mutant to minimize the danger of a genomic reversion to wild-type (see page 30, lines 18 and 19).
9. It is described in document (2) that, when 7 to 10 weeks old calves were inoculated with XIKE-B, the virus was found in buffy coat preparations and neutralizing antibodies were detected in the serum from day 14 after infection. The calves developed only mild respiratory symptoms (see Example 1, section under the heading "Animal experiment with XIKE-B and XIKE-A"). In Example 3, the efficacy of BVDV isolates to prevent foetal infection after a heterologous BVDV type 1 challenge is assessed. Heifers immunized with XIKE-B were inseminated and challenged with BVDV-1 strain KE#9

between day 60 to 90 of pregnancy. The XIKE-B mutant was effective in eliciting an immune response that prevented foetal infection after challenge with a heterologous virus belonging to the BVDV type 1 antigenic group (see page 38, lines 8 to 10).

The technical problem

10. It is undisputed that the sole difference between the XIKE-B mutant described in document (2) and the attenuated pestivirus according to claim 1 is the presence of at least a mutation in the coding sequence for N^{Pro} which leads to inactivation of N^{Pro}. In the decision under appeal, the opposition division found that the technical effect associated with this difference was the "*... retention of efficacy (vis-à-vis a comparable single mutant vaccine virus) whilst improving the safety of the vaccine by providing a further safety-net against reversion or possible low level trans-placental transmission*" (see section 2.2.3, last paragraph of the decision).
11. The appellant contested this finding arguing that the improvement of the safety of the vaccine by providing a further safety net against reversion could not be considered as a technical effect underlying the invention because it was not mentioned in the patent as a problem.
12. The board cannot share this argument. It is common general knowledge in the field of vaccines that reversion is a crucial safety issue affecting live attenuated vaccines, including those based on a well-defined mutation. In fact, the danger of genomic reversion to wild-type was considered by the authors of document (2) to be a relevant issue (see page 30,

lines 18 and 19 of this document). Although not expressly mentioned in the specification, the effect of improving safety as regards reversion is apparent to a person skilled in the art reading the patent in the light of the common general knowledge. The skilled person immediately realizes that a double mutant, in particular a mutant as disclosed in the patent which has a mutation or deletion in one gene and an extensive deletion in a different gene, is much safer from the point of view of reversion than a mutant with a single mutation or deletion as those described in document (2).

13. On this account, the board shares the opposition division's view that the problem to be solved starting from document (2) can be regarded to be "*... the provision of an attenuated pestivirus strain with similar efficacy to an E^{rns} inactivated mutant, but having improved safety characteristics*" (see page 8, first paragraph of the decision under appeal).

The problem is solved by all embodiments covered by the claims

14. In the decision under appeal, the opposition division held that, in view of the data in the patent in suit it was credible that the technical problem is solved across the whole breadth of the claim, "*... in particular insofar as it covers both low and high virulence BVDV isolates*" (see page 8, second paragraph of the decision). In appeal proceedings, the appellant contested this finding arguing that, if a low-virulence BVDV strain having an E^{rns} mutation is further attenuated by a deletion in the N^{pro} gene, efficacy may not be retained.

15. The appellant has not provided any experimental evidence that supports its objection. In contrast, the experimental evidence submitted by the respondent as document (14) shows that an E^{rns} N^{pro} mutant of a BVDV type 1 strain KE9 (KE9-B-NdN) is not only safe, but also efficacious. When pregnant heifers were vaccinated with KE9-B-NdN, foetal infection was not detected (see Group 1 in Table 2 on page 5 of document (14)). In the efficacy study, non-pregnant heifers were vaccinated with KE9-B-NdN and inseminated seven months later. Between day 60 to 90 of pregnancy, 12 pregnant heifers were challenged with a heterologous BVDV-1 strain (Pec515NCP). Two months after the challenge the animals were slaughtered and foetal tissues were examined. All the foetuses from vaccinated heifers were found to be virus-negative (see Group 1 in Table 6 on page 10 of document (14)), whereas foetuses from non-vaccinated animals (Group 2 in Table 6) contained virus, in most cases in all analysed tissues. These results clearly show that vaccination with an E^{rns} N^{pro} double mutant of a BVDV type 1 is efficacious in preventing infection of the foetus.
16. The board considers this experimental evidence, which was not challenged by the appellant, to be conclusive. Thus, the appellant's objection that the technical problem is not solved over the whole scope of the claims is without merit.

The claimed subject-matter is not obvious

17. In the decision under appeal, the opposition division observed that both parties appeared to consider that the skilled person would "*inadvertently*" come across the problem, as it had not been suggested that the recognition of the problem could *per se* involve an

inventive step. The board remarks that, apart from the general statement in the chapter "Background of the invention" (see page 2, lines 3 to 5) that live BVDV vaccines, although attenuated, are most often associated with safety problems because the viruses cross the placenta of pregnant cows and lead to clinical manifestations in the foetus and/or induction of persistently infected calves, document (2) does not mention, let alone provide experimental evidence concerning the possible trans-placental transmission of the XIKE-B and XIKE-C mutants to the foetus upon vaccination of a pregnant heifer.

18. Contrary to the appellant's view, this information is not implicit in the experimental data provided in Example 3 of document (2). At the time of vaccination with XIKE-B, the heifers were not pregnant; in fact, they were inseminated 4 weeks after vaccination. The experimental data provided in document (2) only show that immunization with XIKE-B virus was effective in eliciting sterile immunity and preventing foetal infection when the heifers were challenged with a heterologous BVDV type 1 (see Example 3 starting on page 33, in particular page 38, lines 8 to 10). It cannot be concluded from the data whether the vaccine virus would cross the placenta of immunized pregnant heifers and infect the foetus.

19. The board has doubts whether - as the appellant contends - a person skilled in the art reading document (2) would be prompted to vaccinate pregnant heifers with the mutant XIKE-B virus described therein, and to test for the presence of the mutant virus in the foetus. Even if, for the sake of argument, it is assumed that the statements in the section "Background of the invention" would motivate the skilled person to

do so, the question arises whether the skilled person, when confronted with the finding that - as shown in the patent in suit - the XIKE-B virus is able to cross the placenta and infect the foetus, finds in document (2) any hint how to modify the XIKE-B virus to prevent trans-placental transmission. Document (2) does not suggest a further attenuation of the XIKE-B virus, let alone how to achieve it, whether by introducing additional mutations in the E^{INS} gene or mutating another viral gene.

20. The appellant argued that, starting from document (2) the skilled person would have tried to further attenuate the XIKE-B virus described therein by mutating the N^{PRO} gene as described in documents (3) and (4). This argument is not persuasive. As stated above, the skilled person does not find in document (2) any hint towards further attenuation to solve the problem of trans-placental transmission. Moreover, as stated in the decision under appeal neither document (3) nor document (4) include any test for trans-placental infection of the foetus in vaccinated pregnant cows. Hence, the skilled person could not derive from either document whether the introduction of a mutation in the N^{PRO} gene would prevent infection of the foetus upon vaccination of the pregnant cow with the mutant virus.

21. Even if the board were to share appellant's argument that a person skilled in the art could try to further attenuate the mutants described in document (2) by an additional mutation/deletion in the N^{PRO} gene as described in documents (3) and (4), the board is not convinced that he/she would have a reasonable expectation of maintaining efficacy, let alone of preventing trans-placental transmission to the foetus.

The skilled person in the field of attenuated live vaccines would be well aware of the risk of over-attenuation which could result in the loss of efficacy in protecting the animals against BVDV infection.

22. In sum, the appellant's line of argument is based on an *ex post facto* analysis of documents (2), (3) and (4), an approach which, according to the jurisprudence of the Boards of Appeal, is not admissible (see, e.g., decision T 24/81, OJ EPO 1983, 133). The appellant failed to persuade the board that the skilled person would combine the teaching of document (2) with the teaching of either document (3) or (4). Such a combination would only be made with the benefit of hindsight knowledge of the invention.

23. Hence, the claimed subject-matter was not obvious to a person skilled in the art in view of documents (2), (3) and (4).

Document (1) as the closest state of the art

24. In the decision under appeal, the opposition division observed that document (1) could be considered to be a possible starting point for the assessment of inventive step as regards attenuated viruses derived from BVDV type 1 (see page 4, second paragraph of the decision). In its statement of grounds of appeal, the appellant seemed to combine the teachings of document (1) with those of document (2) to create a new closest state of the art, which was then combined with the teachings of document (3) and/or (4).

25. Document (1) describes attenuated live BVDVs for the preparation of a vaccine for use in the prevention and/or treatment of BVDV infections in breeding stocks of

cattle, pregnant cows and for foetal protection in pregnant cows (see page 2, lines 5 to 7). The attenuation principle, which is said to be applicable to both type 1 and type 2 BVDVs, is the inactivation of the RNase activity of the protein encoded by the E^{rns} gene. It is shown in the examples that BVDV type 1 strain B-349-d, which is attenuated in this manner, does not cross the placental barrier and does not lead to clinical manifestations of BVDV infection in the foetus (see page 3, lines 48 and 49).

26. Document (1) is not concerned with the issue of efficacy of an attenuated live BVDV vaccine and, accordingly, experimental data in this respect are not provided. Thus, the problem to be solved starting from document (1) can be formulated as providing an attenuated pestivirus with the safety characteristics of an E^{rns} mutant which is efficacious as a vaccine, i.e. protects the vaccinated animal against a wild-type infection.

27. As the appellant itself argued, it is questionable whether further attenuation of an in itself already low virulence BVDV-1 strain by introducing an additional mutation in the N^{pro} gene would lead to a strain with the same efficacy as a strain having only the E^{rns} mutation. A person skilled in the art, who is aware of the fact that further attenuation is likely to have an adverse effect on efficacy, would be discouraged from trying to further attenuate the mutant virus described in document (1), in particular by introducing a mutation in the N^{pro} gene as described in documents (3) and (4). In fact, it is quite surprising that, when heifers inseminated seven months after vaccination with a E^{rns} N^{pro} BVDV-1 mutant according to the invention are challenged with a wild-type BVDV-1 virus, the foetus is

protected from infection, as the experimental data in document (14) show.

28. For these reasons, the claimed subject-matter cannot be considered to be obvious in view of document (1).

Further documents cited as the closest state of the art in opposition proceedings

29. In its statement of grounds of appeal, the appellant referred to the facts and evidence put forward in the notice of opposition, which it considered to be still valid and thus part of the appeal.
30. The appellant's understanding as to the requirements for submissions in appeal proceedings is not correct. Pursuant to Article 12(1) of the Rules of Procedure of the Boards of Appeal (RPBA), appeal proceedings shall be based on (a) the notice of appeal and statement of grounds of appeal, (b) any written reply of the other party or parties to be filed within four months of the notification of the grounds of appeal, and (c) any communication sent by the board and any answer thereto filed pursuant to directions of the board. The statement of grounds of appeal shall contain the appellant's **complete** case (see Article 12(2) RPBA).
31. In the board's view, this requirement is not fulfilled by a passing reference to the facts and evidence put forward in opposition proceedings. It is not for the board to identify issues which arose in opposition proceedings and may (or may not) still be a matter of dispute in appeal proceedings, but for the appellant to put forward in the statement of grounds of appeal its line(s) of argument and each of the facts and evidence on which it relies in appeal proceedings.

32. Nevertheless, since in the decision under appeal the opposition division found that an approach starting from a N^{pro} mutant as described in document (3) would lead to the same conclusion as the approach starting from a E^{ns} mutant as described in document (2) (see section 2.2.6 of the decision under appeal), the board has considered summarily the different lines of argument put forward in the opposition brief based on any of documents (3), (4) and (6) as the closest state of the art, all these documents describing N^{pro} pestivirus mutants for use as an attenuated live vaccine. The board shares the opposition division's view that a further attenuation of these mutant viruses by introducing a mutation in the E^{ns} gene was not obvious to a person skilled in the art. Documents (3), (4) and (6) are concerned with the efficacy of various N^{pro} pestivirus mutants as a vaccine and do not provide any hint as to the safety of the vaccine for the foetus. None of these documents suggests further attenuation in order to prevent the vaccine virus from crossing the placenta and infecting the foetus, nor how to achieve it. Although it was known from document (1) that vaccination of pregnant cows with an E^{ns} BVDV-1 mutant is safe for the foetus, a conservative and cautious person skilled in the art being aware of the risk of over-attenuation which may result in a loss of efficacy, would refrain from introducing additionally an E^{ns} mutation. Hence, also starting from document (3), (4) or (6) as closest state of the art, the claimed subject-matter cannot be considered to be obvious.

Conclusion

33. The claimed subject-matter involves an inventive step. Thus, the finding in the decision under appeal that the ground for opposition of Article 100(a) in conjunction with Article 56 EPC does not prejudice the maintenance of the patent as granted, is correct.

Article 113(1) EPC - right to be heard

34. In its communication pursuant to Article 15(1) RPBA, the board provided a reasoned provisional opinion on some of the issues to be discussed at the oral proceedings. The grounds and evidence on which the present decision is based, are essentially those on which the decision under appeal and/or the board's provisional opinion were based. Hence, they are known to the appellant. Even though it was given the opportunity to make written and/or oral submissions thereon, the appellant neither replied in substance to the board's communication nor attended the oral proceedings.

Apportionment of costs

35. In opposition appeals proceedings the board may, for reasons of equity, deviate from the principle of each party bearing its own costs, and order their different apportionment (Article 104(1) in conjunction with Article 111(1), second sentence, Rule 100(1) EPC, and Article 16(1) RPBA. Such reasons of equity exist, when a party's costs arise from culpable actions of an irresponsible or even malicious nature by another party (Case Law of the Boards of Appeal, 8th ed. 2016, IV.C. 6.2; cf. also Bostedt in Singer/Stauder, EPÜ, 7th ed., Art. 104 Rn 7).

36. Each party is subject to an equitable procedural obligation to give notice, in good time and as early as possible, if not attending oral proceedings to which it has been duly summoned. If a party only knows shortly before the specified time for the oral proceedings that it is not going to attend, such equitable obligation extends also to informing any other parties to the appeal proceedings of such non-attendance. Failing which, an apportionment of costs in favour of another party, who has attended as summoned, may be justified for reasons of equity (see for example decisions T 930/92, OJ EPO 1996, 191, and T 937/04 of 21 February 2006).
37. In the present case, both parties to the appeal proceedings had requested oral proceedings under the condition that the board was not inclined to concur with their respective positions. In the board's communication accompanying the summons to oral proceedings, the board in some detail dealt with the appellant's arguments submitted upon appeal, concluding that the appeal was likely to be dismissed. From the board's communication, it was not only clear to the appellant that oral proceedings would take place, but also that its conditions for the holding of oral proceedings had been fulfilled (cf. decision T 53/06 of 21 February 2018). Under these circumstances, the appellant could, in order to properly pursue its case, either have raised further arguments in writing to defend its position, or present them at the latest at the scheduled oral proceedings.
38. In reply to the board's communication, the appellant announced in writing that it "*... will probably not be represented at the oral proceedings ...*", while at the

same time explicitly upholding the request for oral proceedings, and without providing further arguments on the substance. This submission was forwarded to the respondent. It remained the only, written or other, submission informing the respondent of the appellant's intention. However, this submission is worded in terms which are, deliberately or not, unclear and leave the respondent in the dark as to the appellant's true intentions.

39. In view of appellant's unclear statement, the respondent had no alternative than to properly prepare for the case of the appellant attending the oral proceedings.
40. Had the appellant ever clearly and unmistakably aired its decision not to attend the oral proceedings, or had it even explicitly withdrawn the request for oral proceedings, the board would have been in a position to cancel them and issue a decision in writing (cf. decisions T 930/92, *supra*, and T 212/07 of 18 November 2009); alternatively, it could have still held such oral proceedings, if possibly in the absence of both parties. In any case, the respondent would not have been left in the dark about the appellant's intentions, and - if the oral proceedings would still have been held - could have made an informed decision whether or not to attend them at its own costs (cf. decision T 123/05 of 24 May 2007).
41. Against this backdrop, the appellant's failure to clearly state its intentions as regards its attendance at the oral proceedings, is to be regarded as a culpable failure in its duties. Apart from arguably rendering the oral proceedings unnecessary, in particular as the respondent - in the absence of any

submissions from the appellant additional to the grounds of appeal - had nothing to add, the respondent's time and expenditures for preparation and attendance have been wasted.

42. Under the specific circumstances of this case, for reasons of equity, an apportionment of costs in favour of the respondent is appropriate (cf. decisions T 53/06, *supra*; T 212/07, *supra*; T 2179/09 of 19 March 2013; T 258/13 of 11 January 2017; and T 1663/13 of 14 July 2016).

43. Under Rule 88(1) EPC, the decision on the apportionment of costs shall only consider a party's expenses necessary to ensure the proper protection of its rights involved. In particular, this may include the costs reasonably charged to the party by a single professional representative for the preparation of and attendance at oral proceedings, including travel and accommodation, if needed (cf. Article 16(2) RPBA and decisions T 854/09 of 11 March 2011; T 258/13, *supra*; and T 1663/13, *supra*). However, in the absence of exceptional circumstances, the further attendance of accompanying persons at the oral proceedings is regularly a matter of deliberate choice, but not a necessity in the sense of Rule 88(1) EPC (decision T 258/13, *supra*; cf. also decision T 930/92, *supra*, where the presence of one member of the respondent's company was considered justified under the circumstances of the case).

44. In the present case, no such exceptional matters had arisen that would have justified the apportionment also comprising the costs of the two persons (experts) accompanying the respondent's due representative. In particular, based on the submissions on file, no expert

discussion was to be expected. Nor did the respondent announce the presence of the two technical experts at the oral proceedings beforehand.

45. The board's competence comprises not only the apportionment of costs, on principle, but also the fixing of their specific amount (Rule 88(2) in conjunction with Article 111(1), second sentence, and Rule 100(1) EPC, and Article 16(2) RPBA). The specific amount of costs to be paid will be fixed at a later stage as no detailed bill of costs and no supporting evidence have been provided by the respondent as of yet, let alone the appellant having had an opportunity to comment thereupon.

Order

For these reasons it is decided that:

1. The appeal is dismissed.
2. The appellant shall bear the costs incurred by the respondent for the preparation and attendance of the oral proceedings by the representative.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated