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Datasheet for the decision of 4 March 2016

Case Number: T 0222/11 - 3.3.04

Application Number: 03732280.7

Publication Number: 1420822

IPC: A61K39/285, A61K39/245

Language of the proceedings: EN

Title of invention:
Modified Vaccinia Virus Ankara for the vaccination of neonates

Patent Proprietor:
Bavarian Nordic A/S

Opponents:
Emergent Product Development Germany GmbH
Sanofi Pasteur

Headword:
Maturation of the immune system in neonates/BAVARIAN NORDIC

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 123(2), 123(3)
EPC R. 80, 115(2)
RPBA Art. 12(1), 12(4), 15(3)

Keyword:
Sole request - requirements of the EPC met (yes)

Decisions cited:
G 0007/93, T 0167/93, T 0934/91, T 0283/11

Catchword:

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Case Number: T 0222/11 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 4 March 2016

Appellant I: (Patent Proprietor)	Bavarian Nordic A/S Bøgeskovvej 9 3490 Kvistgaard (DK)
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Appellant II: (Opponent 01)	Emergent Product Development Germany GmbH Am Klopferspitz 19 82152 Martinsried (DE)
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Respondent: (Opponent 02)	Sanofi Pasteur 2, avenue Pont Pasteur 69007 Lyon (FR)
Representative:	Bösl, Raphael Konrad Isenbruck Bösl Hörschler LLP Patentanwälte Prinzregentenstraße 68 81675 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2010 concerning maintenance of the European Patent No. 1420822 in amended form.**

Composition of the Board:

Chairman	B. Claes
Members:	M. Montrone
	M. Blasi

Summary of Facts and Submissions

I. Appeals were lodged by the patent proprietor (hereinafter "appellant I") and opponent 01 (hereinafter "appellant II") against the interlocutory decision of the opposition division concerning maintenance of the European patent No. 1 420 822. The patent has the title "*Modified Vaccine virus Ankara for the vaccination of neonates*".

II. In the opposition proceedings, the grounds for opposition according to Article 100(a) EPC (lack of novelty and lack of inventive step), and Articles 100(b) and 100(c) EPC were evoked.

III. The opposition division decided not to admit the main request into the proceedings since it did not meet the requirements of Rule 80 EPC, and that the auxiliary request met the requirements of the EPC.

IV. With its statement of grounds of appeal appellant I submitted a main request (identical to the main request dealt with in the impugned decision) and auxiliary requests I to V. The auxiliary requests were later replaced by auxiliary requests I to XV in reply to appellant II's statement of grounds of appeal.

V. With its statement of grounds of appeal appellant II submitted ten documents. Subsequently, appellant II filed further documents, including D79 and D122, the latter in reply to appellant I's statement of grounds of appeal (the documents are identified in section X below).

VI. The parties were summoned to oral proceedings. Opponent 02 subsequently announced that it would not be attending. No other comments or requests were received by opponent 02.

VII. The board expressed its preliminary view on the case in a communication pursuant to Article 15(1) RPBA.

VIII. In preparation of the oral proceedings, appellant I submitted a main request and auxiliary requests 1 to 31 which replaced all claim requests filed earlier. The main request and auxiliary request 16 were subsequently replaced by corrected versions with a further letter.

IX. Oral proceedings before the board took place on 3 and 4 March 2016, in the absence of opponent 02. At the end of the oral proceedings, appellant I made auxiliary request 15 its sole request, withdrew all other claim requests, and submitted amended pages 3, 3a and 4 to 15 of the description to bring it in line with the claims of the sole request. For further details as to the course of the oral proceedings reference is made to the minutes. At the end of the oral proceedings the chairman announced the board's decision.

Claim 1 of the sole main request reads:

"1. Use of Modified vaccinia virus Ankara (MVA), wherein the MVA is strain MVA-BN deposited at the European Collection of Cell Cultures (ECACC), Salisbury (UK) under number V00083008 or derivatives thereof wherein said Ankara strain MVA-BN and its derivatives are characterized (i) in being capable of reproductive replication in chicken embryo fibroblasts (CEF) and the Baby hamster kidney cell line BHK but not capable of reproductive replication in the human cell lines HaCat,

HeLa and 143B and (ii) by a failure to replicate in a mouse strain that is incapable of producing mature B and T cells and as such is severely immune compromised and highly susceptible to a replicating virus, for the preparation of a medicament for the treatment of a neonatal animal including a human, wherein the MVA is a virus that abortively infects the neonatal animal including a human and wherein the treatment induces or enhances the maturation of the immune system, wherein said maturation is correlated with an increase in the number of dendritic cells and their precursor cells."

Claims 2 to 9 are dependent on claim 1.

X. The following documents are cited in this decision:

D1: WO 02/42480

D4: Study Report by the University of Zurich, dated March 2006

D5: Study Report by R. Drillien, dated 22 February 2006

D6: Study Report by BN-M, dated 10 July 2007

D8: Vilsmeier *et al.*, Berl. Münch. Tierärztl. Wschr., 112, 1999, 329-33

D19: WO 98/13500

D21: VIVACS report, dated 29 June 2005

D61: Drexler *et al.*, J. Gen. Virol., 79, 1998, 347-352

D62: Sutter *et al.*, Vaccine, 12, 1994, 1032-1040

D64: Declaration by Dr. Jacobs, dated 16 July 2010

D79: Study Report Baxter, (MVA0014E01), dated 13 April 2011

D122: Study Report Baxter, (MVA0016T01), dated 14 July 2011

XI. Appellant I's arguments may be summarised as follows:

Admission of the sole claim request and documents D79 and D122 into the proceedings

Appellant I had filed the sole request earlier, as auxiliary request 15 in reply to appellant II's statement of grounds of appeal (see section IV above). The request was thus not late-filed and should be admitted into the proceedings.

Documents D79 and D122 were late-filed and also not *prima facie* relevant. They should therefore not be admitted into the proceedings.

Res iudicata

The principle of *res iudicata* as established e.g. by decision T 167/93 applied to the present case, in which appellant II had submitted the same facts and arguments as those it had already presented in a previous case underlying decision T 283/11.

Sufficiency of disclosure

The decision of the opposition not to admit into the proceedings the argument relating to the deposit of the virus pursuant to Article 114(2) EPC was correct; that

argument had been filed too late. Accordingly, it should also not be admitted by the board into the present proceedings.

Derivatives of the deposited MVA-BN strain were reliably obtainable by the replication assays disclosed in the patent in suit.

Novelty

The subject-matter of claim 1 was novel over the disclosure in document D8. The MVA575 isolate used to induce paramunity in baby mice, as disclosed in document D8, replicated in HaCat cells (see e.g. documents D1, D4 and D5), contrary to the functional properties defined in feature (i) of claim 1. Also, the induction or enhancement of the maturation of the immune system as referred to in claim 1 was different from the induction of paramunity in new-born animals reported in document D8.

Inventive step

Document D8, disclosing native MVA575 for the induction of paramunity in baby mice, represented the closest prior art. However, the paramunity disclosed therein provided only short-term protection against viral infections, unlike the subject-matter of claim 1 which induced long-term protection mediated by the maturation of the immune system. Also, document D8 rather proposed the use of inactivated MVA575 - *i.e.* of strains that no longer abortively infected new-born mice - for the immunisation since the inactivation of MVA575 increased the immunogenicity of the virus.

The technical problem was the provision of means for inducing long-term immunity in neonates. The subject-matter of claim 1 solved this problem since the use of native MVA-BN or its derivatives for immunising neonates increased the number of dendritic cells (DCs) which induced or accelerated the maturation of the immune system, providing long-term protection against viral or bacterial pathogens. Neither the effect of MVA-BN on DCs nor the effect of DCs on the maturation of the immune system had been known from the prior art. These effects were surprising; accordingly, the subject-matter of claim 1 involved an inventive step.

XII. Appellant II's arguments may be summarised as follows:

Admission of the sole claim request and documents D79 and D122 into the proceedings

The sole request was late-filed and should therefore not be admitted into the proceedings.

The evidence contained in documents D79 and D122 showed that the deposited MVA-BN virus according to claim 1 did not exhibit the replication properties defined in feature (ii) of claim 1. Accordingly, both documents should be admitted into the proceedings in view of their *prima facie* relevance.

Sufficiency of disclosure

The MVA-BN strain according to claim 1 had not been deposited by the applicant, and the requirements of the EPC which applied when the depositor and the applicant were not identical were not met.

Moreover, the claimed treatment of the patient group "neonatal animals" by "MVA derivatives" according to claim 1 was not sufficiently disclosed in the patent in suit over the whole ambit of claim 1, since both terms were unclear. Firstly, the patent in suit did not exactly define what neonates were. Therefore, the skilled person could not determine who was suitable for the claimed therapy. Secondly, the patent in suit did not provide information allowing the skilled person to obtain MVA-BN derivatives, in particular with the replication properties defined in feature (i) of claim 1. Although the patent in suit mentioned in reference to document D1 an MVA replication test in HaCat cells, the test, did not however make it possible to reliably distinguish MVA strains known from the prior art from MVA-BN or its derivatives and was thus not suitable to identify derivatives of MVA-BN virus (documents D4 and D6).

Novelty

Document D8 disclosed *inter alia* native MVA575 virus, *i.e.* a virus that abortively infected animals, for the induction of paramunity in baby mice which protected the mice from infection by vesicular stomatitis virus. The maturation of the immune system was an implicit feature of paramunity and the native MVA575 virus was not distinguishable from derivatives of the deposited MVA-BN virus according to claim 1, since it had the same functional properties as those defined by features (i) and (ii) (see e.g. document D6). Accordingly, the subject-matter of claim 1 was not novel over the disclosure of document D8.

Inventive step

The disclosure in document D8 represented the closest prior art. There was no evidence on file disclosing an advantage of the virus MVA-BN or its derivatives according to claim 1 over the MVA575 virus in inducing the maturation of the immune system in neonates.

The technical problem was thus the provision of an alternative vaccinia virus for the claimed therapeutic application. MVA-F6 virus was an MVA isolate known in the prior art and could be used as an alternative to the MVA575 virus. Moreover, MVA-F6 was closely related to MVA-BN as disclosed in document D19 and was even indistinguishable from MVA-BN in relation to the functional features (i) and (ii) of claim 1, as demonstrated in documents D61, D62 and D64, the latter in reference to document D21. Accordingly, by using MVA-F6 the skilled person would had have arrived at the subject-matter of claim 1 in an obvious manner.

XIII. Appellant I requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the sole request pending before the board at the end of the oral proceedings, a description with pages 3, 3a and 4 to 15 as filed during oral proceedings, and the figures as granted.

Appellant II requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. As announced, opponent 02 was not present at the oral proceedings. The board decided to continue the

proceedings in its absence, in accordance with Rule 115(2) EPC and Article 15(3) RPBA.

Admission of the sole claim request and documents D79 and D122 into the proceedings

2. The sole claim request had already been filed by appellant I in reply to appellant II's statement of grounds of appeal, as auxiliary request XV (see section IV above). According to Article 12(1) and (4) RPBA, the request would therefore normally be, as a rule, part of the appeal proceedings. With reference to Article 12(4) RPBA, however, the board notes that this rule does not apply under all circumstances, since the provision refers to the power of the boards of appeal to hold inadmissible, *i.e.* exclude, *inter alia* requests filed for the first time in reply to the statement of grounds of appeal of the other party and which could have been filed during the first instance proceedings.

3. The board notes that the request under consideration addresses objections under Article 123(2) EPC raised by appellant II in its statement of grounds of appeal (see in particular point 3.2 in combination with point 3.15 and 3.10 of appellant I's letter dated 25 August 2011 (section IV above) and points 6.1.1 to 6.3.2 of appellant II's statement of grounds of appeal (section V above)). Appellant I could thus not reasonably have filed the present request earlier than with its reply. Therefore, the board decided not to exclude the sole request from the proceedings pursuant to Article 12(4) RPBA.

4. Although documents D79 and D122 were not filed by appellant II with its statement of grounds of appeal,

they were filed prior to or in reply to appellant I's statement of grounds of appeal (see section V above).

5. Whilst appellant I requested that documents D79 and D122 not be admitted into the proceedings, appellant II requested their admission because of their *prima facie* relevance; they provided evidence that the deposited Modified vaccinia virus Ankara-BN (MVA-BN) strain disclosed in the patent in suit replicated in a severely immune-compromised mouse, contrary to the replication properties defined in feature (ii) of claim 1.

6. The board notes that, considering the history of the file, that there is no indication that documents D79 and D122 could not have been filed at an earlier stage of the proceedings, notably during the opposition proceedings. Both documents contain experimental data concerning MVA-BN and its replication properties in relation to feature (ii) of claim 1. This feature was already referred to in claim 2 of the patent as granted and appellant II has not raised objections with regard to this issue during the opposition proceedings. Appellant II filed both documents only at the beginning of the appeal proceedings and argued that the documents were not available to it at an earlier moment. The board is aware of the fact that both documents are dated either April or July 2011, respectively. However, what appears relevant in this context is that the issue in respect of which the documents were filed was already on the table from the beginning of the opposition proceedings and that their submission does not arise directly from the arguments and/or reasons given in the decision under appeal. That the studies disclosed in documents D79 and D122 were made only

after the opposition proceedings cannot therefore be to the benefit of appellant II.

7. With respect to the relevance of documents D79 and D122, the board notes that they report on a neurovirulence study of MVA-BN virus which is administered intra-cerebrally to baby SCID mice, *i.e.* mice which are incapable of producing mature B and T-cells (see abstract of both documents). However, the patent in suit determines the failure of MVA-BN to replicate in an immune compromised mouse strain according to feature (ii) of claim 1 by administering the virus intra-peritoneally to these mice (see paragraph [0030]). Consequently, the experimental conditions applied in documents D79 and D122 for assessing the MVA-BN replication properties differ fundamentally from those disclosed in the patent in suit. Hence, both documents are technically unrelated to the patent in suit and thus also lack relevance.

8. Therefore the board decided not to take documents D79 and D122 into consideration during the appeal proceedings pursuant to Article 12(4) RPBA and Article 114(2) EPC.

Res iudicata

9. Appellant I submitted that the principle of *res iudicata* applied to the present case, because appellant II had already submitted the same facts and arguments in a previous case leading to decision T 283/11 of 5 November 2014. The board hearing that case had already investigated these facts and arguments and decided that the subject-matter of the claims under consideration met the requirements of the EPC. Re-opening an

investigation of this matter in the present case was contrary to the criteria established in decision T 167/93 (OJ EPO 1997, 229, point 2.5 of the Reasons), in particular since the claimed subject-matter in the present case was very similar to that under consideration in decision T 283/11 *supra*.

10. *Res iudicata* is a generally recognised principle in the contracting states and applied by the boards of appeal (see e.g. decisions T 167/93 *supra* and T 934/91, OJ EPO 1994, 184, point 3 of the Reasons). According to decision T 167/93 *supra*, *res iudicata* is only at stake if several criteria are fulfilled, one being that "*the issues of fact are the same*" (see point 2.5 of the Reasons, criterion (d)). Similarly, in decision T 934/91 *supra* it was held that "*...a final judgement by a court of competent jurisdiction* [...] *constitutes an absolute bar to a subsequent legal action involving the same claim, demand or cause of action, and the same parties or privies*" (see point 3 of the Reasons, emphasis added).

11. Decision T 283/11 *supra* concerns European patent No. 1 335 987, originating from European patent application No. 01991753.3, which is different from and unrelated to the patent in suit (see bibliographic data and section I of decision T 283/11). Moreover, the subject-matter of claim 1 of the sole request before the board differs significantly from that of claim 1 underlying decision T 283/11 *supra*, in that it refers to a second medical use of deposited MVA-BN and derivatives thereof for treating neonatal animals, wherein the virus abortively infects the claimed patient group, thereby inducing or enhancing the maturation of the immune system, which maturation correlates with an increase in the number of dendritic

cells and their precursors. Claim 1 underlying decision T 283/11 *supra* related solely to a product concerning the deposited MVA-BN and derivatives thereof (see section XVII of the Facts and Submissions). The subject-matter of claim 1 considered by the board in decision T 283/11 *supra* is therefore not the same as that of claim 1 now being considered by this board.

12. Accordingly, the principle of *res iudicata* does not apply and decision T 283/11 *supra* is therefore not a final judgement preventing this board from considering facts and arguments even if they were the same as those already submitted in decision T 283/11 *supra*. Appellant I's argument must therefore fail.

Sole claim request

Rule 80, Articles 84, 123(2), and (3) EPC

13. Appellant II did not raise any objections under Rule 80 and Articles 84, 123(2) and 123(3) EPC against the subject-matter of claims 1 to 9 of the sole claim request. The board has no objections either.

14. Thus, the sole claim request meets the requirements of Rule 80 and Articles 84, 123(2) and 123(3) EPC.

Sufficiency of disclosure

15. Appellant II argued that the deposition of the virus MVA-BN at the European Collection of Cell Cultures (ECACC), Salisbury (UK) under number V00083008 according to claim 1 did not meet the requirements of Article 83 EPC, since the biological material had been

deposited by a person other than the applicant and the requirements of the EPC which applied in these circumstances were not met. The objection was highly relevant since it put into question the compliance of patent in suit with the EPC and it should therefore be admitted into the proceedings. Accordingly, in not admitting this objection into the opposition proceedings the opposition division had exercised its discretion wrongly.

16. The board notes that the opposition division considered this objection to be a new and late-filed fact, since opponent 02 submitted it only one day prior to the oral proceedings (see page 2, paragraphs 5 and 6 of the minutes). Accordingly, in exercising its discretion pursuant to Article 114(2) EPC, the opposition division declined to admit the objection into the proceedings (see page 2, point 21, and page 18, point 77(d) of the decision under appeal).

17. The board concurs with appellant II that relevance is indeed one of the principal factors governing the admission of late-filed facts, evidence and arguments. However, it is not the sole decisive factor, since otherwise Article 114(2) EPC, giving opposition divisions discretion over whether to admit late-filed submissions, would be superfluous. Moreover, the discretion conferred by Article 114 EPC necessarily implies that the department of first-instance must have a certain degree of freedom when exercising its discretion, without undue interference from the boards of appeal. Accordingly, it is established case law that a board of appeal should overrule the way in which a department of first-instance has exercised its discretion only if it comes to the conclusion either that the first-instance department in its decision has

not exercised its discretion in accordance with the right principles, or that it has exercised its discretion in an unreasonable way, and has thus exceeded the proper limits of its discretion (see decision G 7/93, OJ EPO 1994, 775, point 2.6 of the Reasons).

18. In the present case, the new objection was raised by opponent 02 only one day prior to the oral proceedings before the opposition division (see point 15 above), although the subject-matter of claim 1, *i.e.* the use of the deposited virus strain and derivatives thereof for the claimed therapeutic application, had not changed since the onset of the opposition proceedings. Appellant II did not give reasons why this argument could not have been raised earlier.

19. In these circumstances, the board concludes that the objection could have been raised earlier in the opposition proceedings. Accordingly, considering the principles established in the case law and mentioned in point 16 above, the board has no reason to overrule the opposition division's decision not to admit it. The objection of appellant II under Article 83 EPC in relation to the deposit is therefore not taken into account in the appeal proceedings (Article 12(4) RPBA).

20. In a second line of argument in relation to insufficiency of disclosure, appellant II submitted that the patent in suit provided no definition for the term "neonatal". Therefore, the skilled person could not determine who was eligible for the claimed therapy. Furthermore, the replication assays referred to in the patent in suit were not suitable to distinguish MVA-BN or its derivatives according to claim 1 from MVA viruses known from the prior art. Accordingly, the

information provided in the patent in suit was insufficient for the skilled person to identify MVA-BN derivatives characterised by the replication properties defined in feature (i) of claim 1 (documents D4 and D6).

21. At the priority date of the patent in suit it was common general knowledge that the immune system of neonatal animals was immature and that this made them susceptible to infectious diseases (see e.g. paragraphs [0009] and [0010] of the patent in suit). Moreover, the patent in suit provides information regarding the age at which the immune system of different mammals can be considered as mature and at which the MVA-BN should preferably be administered for the maturation of the immune system in accordance with the invention (see paragraph [0070]). Accordingly, and contrary to the view of appellant II, the board considers that the patent in suit contains ample information about how to select the appropriate neonate patient group for the claimed therapeutic application.

22. As regards whether or not the skilled person could reliably identify and obtain derivatives of the deposited MVA-BN strain as referred to in claim 1, the board notes first that the patent in suit refers in paragraph [0029], in the context of defining "*not capable of reproductive replication in the cell line HaCAT*", to prior art disclosing an MVA replication assay based on the human cell line HaCat. Appellant II has not disputed that such an assay was available to the skilled person.

23. Secondly, the patent in suit defines "reproductive replication" as the ratio of virus produced by infected human HaCat cells, *i.e.* the "output", in relation to

the amount of virus used to infect the cells, *i.e.* the "input", with an output to input ratio of less than 1 indicating a lack of reproductive replication as defined in feature (i) of claim 1 (see paragraph [0029]). The patent itself discloses no experimental data in relation to MVA-BN replication in HaCat cells. However, documents D1, D4 to D6 and D21 report experimental data showing consistently that MVA-BN, unlike other MVA viruses known from the prior art and tested, replicates in HaCat cells with an output to input ratio of below 1. This therefore means, in view of the definition referred to above, that MVA-BN does not reproductively replicate in HaCat cells (see documents D1, Table 1 on page 57; D4, page 11, Table 4; D5, Table 7 on page 11; D6, the table on page 11; D21, Tables 1 and 2 on page 11). In this context, the board observes that the HaCat cell replication assay disclosed in documents D1, D4 to D6 and D21 was performed by a number of different persons skilled in the art, who all reproducibly arrived at the same result.

24. In view of the considerations above, the board concludes that the definition of reproductive replication in a HaCat replication assay as disclosed in the patent in suit allows the skilled person to reliably differentiate between MVA-BN virus and its derivatives according to claim 1 and MVA viruses known from the prior art, and is thus suitable to identify and obtain derivatives of MVA-BN with the functional properties defined in feature (i) of claim 1. The argument of appellant II must therefore fail.

25. It was uncontested that the deposited MVA-BN virus and its derivatives as defined in claim 1 are suitable for the claimed therapeutic application. Also, the board is

satisfied that the viruses according to claim 1 are suitable for the induction or acceleration of the maturation of the immune system in neonates in view of the experimental data provided in examples 1 and 2 of the patent in suit.

26. The patent in suit therefore sufficiently discloses the subject-matter of claim 1. Appellant II submitted no objections in relation to sufficiency of disclosure for the subject-matter of claims 2 to 9 of the patent in suit. Also the board has none either. Hence, the sole claim request meets the requirements of Article 83 EPC.

Novelty

27. Claim 1 (see section IX above) is drafted in the so-called "second medical use" format. Pursuant to established case law, a disclosure in the prior art can anticipate the subject-matter of such a claim only if it discloses the product referred to in the claim (here the deposited MVA-BN or derivatives thereof defined by the functional properties of features (i) and (ii)) for the claimed therapeutic application (in this case the initiated or accelerated maturation of the immune system correlated with an increase in the number of dendritic and their precursor cells) in the same patient group (here neonatal animals) (see Case Law of the Boards of Appeal, 8th edition 2016 (hereinafter "CLBA"), I.C.7.2.4.). The disclosure in the prior art, moreover, only anticipates claimed subject-matter if the latter is directly and unambiguously derivable from the disclosure, including any features implicit to a person skilled in the art. In this context an implicit disclosure means a disclosure which the person skilled

in the art would objectively consider as necessarily implied in the explicit content (see CLBA, I.C.4.3.).

28. In the appeal proceedings, appellant II has solely maintained that the subject-matter of claim 1 lacked novelty over the disclosure in document D8.

29. Document D8 discloses *inter alia* that a vaccination of baby mice which are half a day old, *i.e.* of neonatals, with a native MVA575 isolate protects the animals from a lethal infection of vesicular stomatitis virus (VSV) by means of the so-called "*paramunity*" (see Title, abstract, page 330, Table 1 and column 1, third paragraph and figure 1). The document reports that the paramunity-mediated protection is achieved by the "*optimal regulation*" of the innate, *i.e.* antigen-unspecific response of the immune system and a simultaneously increased activity of cellular components accompanied by an increased release of cytokines (see page 329, column 2, last paragraph to page 330, column 1, line 4) and discloses that: "*The nonspecific parts of the complex immune system are closely interwoven with the specific parts, which means that the specific immune system is likewise optimized*" by the paramune effects of MVA (see page 330, column 1, first paragraph).

30. The board concludes that, the skilled person would derive from the above passages in document D8 that MVA575 activates by means of "paramunity" the antigen-unspecific and the antigen-specific response of the immune system which protects neonatal mice against an infection of VSV.

31. It was common ground between the parties that neonatal animals have an immature immune system characterised by

an insufficient antigen-specific immune response and that a mature, *i.e.* fully functional immune system comprises an antigen-unspecific and an antigen-specific response. For the immune system to become fully functional, therefore, only the latter response requires a maturation since the unspecific response is innate and therefore fully functional from birth (see paragraph [0009] of the patent in suit). Accordingly, since document D8 teaches that the MVA575-mediated paramunity optimises the antigen-specific response of the immune system, a maturation of the immune system in the neonatal animals has been necessarily induced by MVA575. The board is therefore satisfied that an initiated maturation of the immune system in neonatal mice is a feature of the MVA575-mediated paramunity disclosed in document D8 which is objectively to be considered as implicit by the skilled person. This feature can thus not provide novelty to the subject-matter of claim 1.

32. Appellant II did not dispute that MVA575 was not identical to the deposited MVA-BN isolate referred to in claim 1, but submitted that the MVA575 strain disclosed in document D8 anticipated the "derivatives" of the deposited MVA-BN strains referred to in claim 1 since native MVA575 had the same replication properties defined in features (i) and (ii) of claim 1.

33. It therefore needs to be assessed whether the native MVA575 isolate does indeed have the replication properties defined in features (i) and (ii) of claim 1.

34. The board notes that documents D1 and D4 to D6 all disclose comparative experimental data in relation to the deposited MVA-BN isolate and native MVA575 replication in a variety of human cell lines, including

HaCat cells (see feature (i) of claim 1). As outlined in point 22 above, the patent in suit defines "reproductive replication" in HaCat cells as the output to input ratio of virus after infection, wherein a ratio of below 1 indicates a lack of reproductive replication according to feature (i) of claim 1.

35. An analysis of the experimental data disclosed in documents D1, D4 and D5 reveals that the replication ratio of the native MVA575 strain in HaCat cells is above 1 in Table 1 on page 57 of document D1, above 1 in Table 5 of document D4 and above 1 in Table 6 of document D5. Accordingly, the data demonstrate that MVA575 reproductively replicates in HaCat cells.

36. Document D6 on the contrary reports results of native MVA575 replication having a ratio below 1, thereby indicating that the virus does not reproductively replicate in HaCat cells (see Table on page 11). Reasons why the data disclosed in document D6 diverge from those disclosed in documents D1, D4 and D5 (see point 34 above) were not provided by the parties.

37. Therefore, in view of the partially contradicting data disclosed in documents D1 and D4 to D6, the board does not consider it as established with certainty that the native MVA575 strain has a replication ratio below 1 in HaCat cells, *i.e.* does not reproductively replicate in HaCat cells as required in feature (i) of claim 1. Therefore, the board concludes that the native MVA575 strain is not a derivative of MVA-BN as defined in claim 1 and that the subject-matter of claim 1 is novel over the disclosure of document D8. The same applies to the subject-matter of claims 2 to 9 which are all dependent thereon. Hence, the sole request meets the requirements of Article 54 EPC.

Inventive step

Closest prior art

38. 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.

39. The parties agreed that the disclosure of document D8 represents the closest prior art and the board sees no reason to differ.

40. Document D8 discloses that the administration of native MVA575 isolates protects neonatal mice against viral infection by means of paramunity (see point 28 above). Moreover, since paramunity activates the unspecific immune response which optimises the antigen-specific response requiring a previous maturation of the immune system, the board arrived at the conclusion that the administration of MVA575 implicitly initiates the maturation of the immune system in neonatal animals (see point 30 above).

Technical problem and solution

41. It has not been established that MVA-BN and derivatives thereof according to claim 1 and native MVA575 strains have the same replication properties in at least HaCat cells (see point 36 above).

42. Appellant I submitted that MVA-BN mediated the maturation of the immune system, resulting in long-term protection in neonatal animals, whereas MVA575 induced

only short-term immunity, since paramunity did not induce any such maturation.

43. The board concludes however, as outlined in point 39 above, that the induction of the maturation of the immune system is an implicit feature of MVA575-mediated paramunity resulting in the protection of neonatal mice against viral infection. Moreover, appellant I has not submitted any comparative experimental data disclosing advantageous properties of MVA-BN or derivatives thereof according to claim 1 *vis-à-vis* MVA575 in the induction or acceleration of the maturation of the immune system of neonatal animals, and nor are such properties derivable from the experimental data disclosed in the patent in suit.

44. Accordingly, since no such advantageous properties can be acknowledged *vis-à-vis* the closest prior art, the technical problem to be solved is formulated as the provision of alternative MVA strains for use in the induction of the maturation of the immune system in neonatal animals.

45. The board is satisfied that this technical problem is solved by the subject-matter of claim 1 in view of the experimental data disclosed in examples 1 and 2 of the patent in suit.

Obviousness

46. It remains to be assessed whether or not the skilled person starting from the use of MVA575 for the induction of the maturation of the immune system in neonates as disclosed in document D8 and faced with the technical problem defined above, would modify the teaching of document D8 either in view of that document

alone or in combination with other prior art teaching to arrive at the claimed subject-matter in an obvious manner.

47. Document D8 discloses only inactivated MVA575 isolates as possible alternatives to the use of native MVA575 for the induction of the maturation of the immune system in neonatal mice (see page 329, column 2, second paragraph and figure 1 on page 331). Due to their inactivation, however, the MVA575 viruses are no longer able to abortively infect neonatal animals as referred to in claim 1. Further native MVA isolates are not suggested in document D8. Accordingly, the subject-matter of claim 1 cannot be considered obvious in the light of the teaching of document D8 alone.

48. Appellant II submitted that the MVA-F6 strain was commonly known in the prior art and would therefore be considered by the skilled person as an alternative to the use of MVA575. Moreover, since MVA-F6 and MVA-BN were closely related and in fact even indistinguishable in relation to the functional properties defined by features (i) and (ii) of claim 1 - as shown by documents D61, D62 and declaration D64, the latter in reference to document D21 - the skilled person would have arrived at the subject-matter of claim 1 in an obvious manner.

49. The board notes that it was undisputed by the parties that MVA-F6 was known in the prior art and related to MVA-BN (see document D19, page 11, last paragraph to page 12, first paragraph) and that therefore the skilled person could have used it as an alternative to MVA575. However - for MVA-F6 to be a solution to the technical problem defined above - it must be shown to have the replication properties defined in claim 1.

50. Document D64 (as expert declaration), reports that MVA-F6, also known as MVA-580, is an MVA isolate obtained from the strain MVA-572 after three rounds of plaque purification (see point 49a on page 16). The MVA-F6 was then further passaged six times in chicken embryonic fibroblast (CEF) cells to generate the deposited MVA-BN strain referred to in claim 1 (see points 49b to 49f on pages 16 and 17). In this context, the declaration notes that the further passaging of MVA-F6 to generate MVA-BN in CEF cells could have resulted in mutations in the viral genome of MVA-BN, *i.e.* the MVA-F6 and MVA-BN virus populations could be heterogeneous (see point 50 on page 17). The document further refers to document D4 (see point 89), *i.e.* document D21 in the present proceedings, and states that the data of document D21 reveal that MVA-F6 like MVA-BN does not reproductively replicate in HaCat cells.

51. The board notes in this context, that it was uncontested by the parties that document D21 did not test the replication properties of MVA-F6 *per se* but that of an MVA-F6 strain which has been passaged for three more times in CEF cells. As pointed out above (see point 50), the further passaging of MVA strains in CEF cells might result in heterogenous virus populations. Furthermore, data comparing the replication properties of MVA-BN and MVA-F6 in HaCat cells have not been submitted by appellant II. Accordingly, the board concludes that document D64 in conjunction with the disclosure in document D21 does not establish with certainty that MVA-BN and MVA-F6 are in fact identical, in particular in terms of their replication properties in HaCat cells.

52. Furthermore, the board notes that the other documents D61 and D62 also do not establish that MVA-F6 has the

same replication properties as MVA-BN in HaCat cells because the documents mention the replication of MVA strains in several cell lines but not in HaCat cells (see documents D61, Table 1; D62, page 1035, column 2, first paragraph).

53. In view of these considerations, the board concludes that there is no evidence on file that the MVA-F6 strain has the same replication properties as MVA-BN or derivatives thereof as defined in claim 1. Accordingly, even if the skilled person could have used MVA-F6 instead of MVA575 as an alternative to the claimed therapeutic application, he would not have arrived at the subject-matter according to claim 1. The board therefore concludes that the subject-matter of claim 1 is not obvious for the skilled person having regard to the state of the art. The same applies to the subject-matter of claims 2 to 9 which depend thereon. The sole claim request therefore meets the requirements of Article 56 EPC.

Adaptation of the description

54. During the oral proceedings, appellant I submitted amended pages 3, 3a and 4 to 15 of the description to bring it in line with the sole request. Appellant II had no objections to the amended pages and the board too is satisfied that these amendments are appropriate and necessary to render the description consistent with the set of claims of the sole request and comply with the requirements of Article 84 EPC and Rule 80 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in amended form with

   - the claims of the sole request pending at the end of the oral proceedings before the board,
   - a description with pages 3, 3a and 4 to 15 as filed during the oral proceedings, and
   - the figures of the patent as granted.

The Registrar: The Chairman:

P. Cremona B. Claes

Decision electronically authenticated