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Datasheet for the decision of 5 November 2014

Case Number: T 0283/11 - 3.3.08

Application Number: 01991753.3

Publication Number: 1335987

IPC: C12N15/863, C12N15/39, C12N7/04, A61K39/285, A61K48/00

Language of the proceedings: EN

Title of invention:
MODIFIED VACCINIA ANKARA VIRUS VARIANT

Patent Proprietor:
Bavarian Nordic A/S

Opponents:
Baxter Aktiengesellschaft
Acambis, Plc.
Acambis, Inc.
Innogenetics N.V.
Oxford Biomedica (UK) Limited
Sanofi Pasteur, Inc.
Emergent Product Development Germany GmbH
VIRBAC S.A.

Headword:
MVA-BN/Bavarian Nordic A/S

Relevant legal provisions:
EPC Art. 53(c), 54, 56, 83, 84, 108, 123(2), 123(3)
EPC R. 99
RPBA Art. 12(4), 13(1)

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

Decisions cited:
T 0156/84, T 1002/92, T 0464/94, T 1485/08, T 0593/09, T 0544/12

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

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Case Number: T 0283/11 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 5 November 2014

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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted on 7 December 2010 concerning maintenance of the European Patent No. 1335987 in amended form.

Composition of the Board:

Chairman M. Wieser
Members: B. Stolz
D. Rogers

Summary of Facts and Submissions

I. Appeals against the decision of the opposition division, dated 7 December 2010, whereby European patent No. 1 335 987 was maintained in amended form, were filed by opponent 1 (a joint legal entity of Baxter Aktiengesellschaft and Baxter Healthcare Corporation, referred to as appellant I) and opponent 7 (appellant II).

II. With its grounds of appeal, appellant I filed new documents D105, and D110 to D117 (numbering according to the consolidated list submitted by the patentee). Appellant II filed new documents D101 to D104, the same document D105 as appellant I, and documents D106 to D109 with its grounds of appeal.

III. In a communication, dated 10 May 2011, the board informed the parties of a possible issue concerning the admissibility of the appeal of appellant I.

IV. With letter dated 24 May 2011, appellant I provided its arguments as to why its appeal was admissible.

V. In a communication dated 9 June 2011, the board informed the parties of its preliminary opinion that the deficiencies in appellant I's notice of appeal concerning its name could be remedied, but that the final decision would be taken at the oral proceedings.

VI. In a further submission appellant I filed an experimental report, document D118.

VII. The patent proprietor (respondent) filed its response to the grounds of appeal and submitted new documents D119 to D147. It requested that the appeals be

dismissed or, in the alternative, the patent be maintained on the basis of one of auxiliary requests 1 to 15, all filed with its response.

VIII. In further submissions, appellant I filed further experimental reports as documents D148 and D149.

IX. The respondent submitted its comments on the latest submissions by appellant I and submitted new documents D150 to D152.

X. With a further submission appellant II filed new documents D153 to D163.

XI. The respondent submitted its comments on the submissions by appellant II and filed new documents D164 to D166.

XII. The parties were summoned to oral proceedings. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), annexed to the summons, informed them of the preliminary non-binding opinion of the board on some of the issues of the appeal proceedings.

XIII. Appellant I informed the board that it was not going to attend the oral proceedings.

XIV. The respondent submitted further arguments, a new main request and auxiliary requests 1 to 10, and document D167.

XV. Appellant II made further submissions.

XVI. Oral proceedings, held on 4 and 5 November 2014, were attended by appellant II and the respondent. In the

course of the proceedings, the respondent made previous auxiliary request 1 its new main request.

XVII. Independent claim 1 of the main request, (former auxiliary request 1), reads as follows:

1. Modified vaccinia virus Ankara strain MVA-BN deposited at the European Collection of Cell Cultures (ECACC), Salisbury (UK) under number V00083008 and derivatives thereof, wherein said Ankara strain MVA-BN or 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 human bone osteosarcoma cell line 143B, the human keratinocyte cell line HaCat and human cervix adenocarcinoma cell line HeLa and (ii) by a failure to replicate in vivo in severely immune compromised mice that are incapable of producing mature B and T cells.

Claims 2 to 6 define specific embodiments of the subject matter of claim 1. Claims 7 and 8 define pharmaceutical compositions and vaccines, respectively, comprising the virus of claims 1 to 6. Claim 9 defines specific embodiments of the subject matter of claims 7 and 8.

Independent claims 10 and 11 of the main request read:

10. MVA-BN or a derivative thereof according to any one of claims 1 to 6, the composition according to claim 7 or 9 or the vaccine according to claim 8 or 9 to affect, preferably induce, an

immunological response in a living animal, including a human.

11. MVA-BN or a derivative thereof according to anyone of claims 1 to 6, the composition according to claim 7 or 9 or the vaccine according to claim 8 or 9 for vaccination of a living animal, including a human, against a human pox virus disease.

Claims 12 to 32 define further compositions, methods, and kits comprising the virus, and uses of the virus, of claims 1 to 6.

XVIII. The following documents are cited in this decision:

D2: Hirsch et al. (1996), J. Virol. 70, 3741-3752

D3: WO97/02355

D4: VIVACS report

D16: WO 99/07869

D17: Drexler et al. (1999), Cancer Res. 59, 4955-4963

D18: Sutter & Moss (1992), PNAS USA 89, 10847-10851

D33: Drexler et al. (1998) J. Gen. Virol. 79, 347-352

D56: Declaration by Dr. Leonard Shultz

D61: Vollmar et al. (2006) Vaccine24, 2065-2070

D64: Pilcher et al. (1997), J. Cell Biology 137, 1445-1457

D65: Aragane et al. (1998) J. Cell Biology 140, 171-182

D66: Compilation of documents referring to the use of HaCat cells

D69: Wyatt et al. (1998), Virology 251, 334-342

D84: Suter et al. (2009), Vaccine 27, 7442-7450

D92: Declaration of P. Sharp

D93: Declaration of F.G. Falkner

D98: Declaration of W.D. Coston with exhibits 1-6

D99: Declaration B. Jacobs

D100: Declaration of D. Chanter

XIX. The arguments of appellant I, submitted in writing, as far as relevant for this decision, can be summarized as follows:

Admissibility of the appeal

The true intention when filing the notice of appeal was that the appellant/opponent should be the same joint legal entity as the opponent named in the notice of opposition. According to decision T 97/98 (OJ EPO 2002, 183), what mattered was the true intention when the appeal was filed and which could be derived from the notice of appeal. There was no transfer of the opposition from Baxter Healthcare S.A. to Baxter Healthcare Corporation.

Rule 80 EPC

The amendment in line 3 of claim 1 was not occasioned by a ground of opposition.

Article 53(c) EPC

Claims 10 and 11 were directed to the use of MVA-BN for medical treatment. The claim language was not in the proper format and did not comply with the requirements of Article 53(c) EPC.

Article 123(2) EPC

According to claim 1, the deposited strain had to possess the features defined in (i) and (ii). Viruses possessing this specific combination of features represented an undisclosed subgroup of all the viruses constituting the deposited heterogenous MVA isolate.

Article 123(3) EPC

Claim 1 required that the deposited strain **or** its derivatives possess the replication features (i) and (ii), thus effectively making them optional for the derivatives. To the extent that the claim encompassed derivatives of MVA-BN which did not possess both of features (i) and (ii), the protection conferred by the claim was extended when compared to the claims as granted.

Claim 1 was amended to characterize the severely immunocompromised mice as being incapable of producing mature B and T cells. This amendment broadened the scope of protection because the requirement for the virus to fail to replicate in mice had to be assessed

by reference to a group of mice that was more narrowly defined than the group of mice defined in the claims as granted.

Article 84 EPC

The amendment in line 3 of claim 1, requiring that the deposited strain **or** its derivatives possess the replication features (i) and (ii), rendered the claim unclear. The term "or" could be interpreted as rendering the features optional.

Article 83 EPC

The claimed virus had not been deposited according to the provisions of Rule 28 EPC 1973.

Moreover, according to document D115, the deposited virus did not show the properties defined by feature (ii) of claim 1. Detailed analysis of the data provided in document D71 revealed that MVA-BN showed amplification in HaCat cells for 6 out of 9 determinations. Document D73 showed furthermore that MVA-575 did not replicate in HaCat cells. If MVA-575 did not replicate in these cells but the claimed viruses did, the replication test in the HaCat cells could not be predictive for the improved attenuation. Since the patent did not show how a virus with the properties of features (i) and (ii) could be obtained, the same was true for the claimed derivatives.

Article 54 EPC

The term derivatives in claim 1 had to be interpreted broadly and encompassed strains having the same replication properties as MVA-BN without being

necessarily lineal descendants of the deposited strain MVA-BN. Consequently, claim 1 lacked novelty in view of any document disclosing strain MVA 575. The deposited strain was also not novel over strain MVA-F6 disclosed in prior art documents D1 to D3, D16 to D18, D21, D33 and D69. Documents D4 to D7 disclosed that the proprietor used the designations BN and F6 interchangeably which showed that the deposited strain and MVA-F6 were identical. At the structural level, document D69 showed complete identity of MVA-BN and prior art strain MVA 572. Regarding the functional features (i) and (ii) of claim 1, documents D4, D16, and D71 to D73 provided evidence that strain MVA-BN could not be distinguished from prior art strains MVA-F6, and MVA 575. Further evidence in support of this was available in documents D105, D110 to D118, D148 and D149.

Article 56 EPC

Document D18, disclosing strain MVA-F6, represented the closest prior art. There was no evidence on file supporting any alleged advantage of strain MVA-BN over prior art strains. MVA-F6 and MVA-BN were indistinguishable in terms of attenuation and immunogenicity and strain MVA-BN merely represented an obvious alternative to the prior art strain MVA-F6.

XX. The arguments of appellant II, as far as relevant for this decision, can be summarized as follows:

Admissibility of the main request

The main request could have been filed earlier and should not be admitted because it raised new issues under Article 123(2) and (3) EPC and Article 84 EPC.

Admissibility of new evidence

Documents D101, D102, D108, D112, D115, D118, D148 and D149 were filed to address issues raised in the decision under appeal. D101 and D102 addressed the issue of genetic identity between the prior art strains and strain MVA-BN, the remaining documents addressed issues in relation to severely immunocompromised mice incapable of producing mature B and T cells.

Rule 80 EPC

The amendment in line 3 of claim 1 was not occasioned by a ground of opposition.

Article 123(2) EPC

Due to the amendment in line 3 of claim 1, features (i) and (ii) were no longer exclusively used to characterize the derivatives of the deposited strain but were now also used to characterize the deposited strain itself. This rendered the functional features optional for either one of the deposited strain and the derivatives. As a consequence, the claim encompassed also strains not having the functional properties.

Further, the specific combination of features (i) and (ii) to characterize derivatives or the deposited strain was not directly and unambiguously derivable from the patent application as originally filed.

Article 123(3) EPC

Since the amendment in line 3 of claim 1 led to the inclusion of strains not having the functional

properties defined by features (i) and (ii), the scope of protection of the amended claim extended beyond the scope of protection of the claim as granted.

Due to the inclusion of previous claim 2 into claim 1, the scope of protection provided by claim 1 was extended. Claim 1 as granted defined the claimed viruses as incapable of replicating in any human cell line whereas claim 1 of the main request defined the claimed viruses as incapable of replicating in only three cell lines. The claim thus encompassed viruses incapable of replicating in the three specific cell lines, yet capable of replicating in other human cell lines.

Article 84 EPC

The amendment in line 3 of claim 1 led to unclarity because the word "or" in "wherein said Ankara strain MVA-BN or its derivatives are characterized by" could be interpreted in two ways, either in the sense of "and", i.e. cumulative, or in the sense of "wherein either the deposited strain or its derivatives", i.e. alternative.

Article 83 EPC

The deposit of the claimed virus did not meet the requirements of Rule 28 EPC 1973 (now Rule 31 EPC). The opposition division, when deciding not to admit this objection, considered only its timeliness. Instead it should have based its decision on the prima facie relevance of the objection.

Documents D115, D118 and D147 showed that the deposited virus did not have the properties of feature (ii).

A triple knockout mouse having the properties described in feature (ii) was not readily available and its reproduction required an undue amount of effort.

Derivatives of the deposited virus could not be readily obtained because the replication in HaCat cells was an unreliable indicator as shown by documents D71, D73, D99 and D100. According to document D71, MVA-BN was found to replicate in two out of three experiments. If geometric means of the cumulative data for MVA 575 were calculated from documents D71 to D73, the virus could not be distinguished from the claimed viruses. It was thus not possible to reliably distinguish the claimed subject matter from the prior art.

Article 54 EPC

Document D4 demonstrated that the deposited strain was actually labelled MVA-F6 when it was delivered to the depositary institution. Hence, the deposited strain was identical to the prior art strain MVA-F6. Documents D4 and D16 showed that the claimed strains had the same functional features (i) and (ii) as the strain MVA-F6. Moreover, the technical data on record (D84, D98) showed that the published sequences of MVA-BN and the prior art strains were identical. Additional evidence was submitted as documents D101 and D102. Documents D4 and D71 to D73 showed that strain MVA 575 had all the properties defined by feature (i). Evidence that the prior art strains had the properties of feature (ii) was presented in documents D112, D115, D118, D147 and D148.

Article 56 EPC

Strain MVA-F6 represented the closest prior art, and based on the evidence provided in documents D16 and D18, only differed from the claimed virus by its replication in HaCat and 143B cells. The problem to be solved had to be defined as the provision of a further safe virus. Since such a further virus could be obtained by routine measures, the claimed solution was obvious.

Document D18 disclosed MVA-F6 as a safe vaccine that could be used in high risk human patients. The results presented in documents D112, D115, D118, D147 and D148 showed that MVA-BN was neither more attenuated nor safer than the prior art strains MVA-F6 or MVA-575. Documents D156 to D158 provided further evidence that a derivative of MVA-575, namely MVA85A, was also safe and highly immunogenic as a single dose vaccine.

XXI. The arguments of the respondent, as far as relevant for this decision, can be summarized as follows:

Admissibility of the appeal of opponent 1 (Article 108 EPC and Rule 99 EPC)

This appeal should be held inadmissible. The opposition had been filed in the name of partially different business entities than those in the notice of appeal.

In general, opponent's and appellant's names had to be identical and correction of names was only allowable in the case of obvious errors in stating the names of appellants. The deficiency caused by the naming of "Baxter Healthcare Corporation" with an address in the USA did not qualify as being susceptible to remedy under Rule 101 EPC because this name represented a true legal entity. Evidence on file showed that Baxter

Healthcare Corporation existed and nothing on file could have signalled to third parties and in particular to the Patentee that the appeal should have been filed in the names of different business entities. Thus, one had to assume that a transfer of party status from the Swiss subsidiary to a US company had been the reason for the divergent naming. Such a transfer, however, was not timely announced to the EPO and supported by corresponding evidence.

Admissibility of the main request

The main request was originally filed with the response to appellants' grounds of appeal as auxiliary request VI. It addressed issues raised under Article 83 EPC, in particular in relation to severely immunocompromised mice.

Admissibility of new evidence

The issue of the suitability of SCID mice as test animals for feature (ii) had been discussed since 2007 when feature (ii) was amended to require a failure to replicate in severely immunocompromised mice incapable of producing B and T cells. Therefore, additional experimental data could have been filed earlier. In reply to appellants' filing of new evidence, the respondent had to file documents addressing the issues of SCID mice and AGR129 mice, new sequencing data, the correctness of the deposit of the virus, and data relating to MVA-M4 and MVA85A.

Rule 80 EPC

Line 3 of claim 1 was amended to overcome objections under Articles 83, 54 and 56 EPC against the deposited strain and against the derivatives.

Article 123(2) EPC

The combination of features of claim 1 was directly and unambiguously derivable from pages 7, 8 and 10 of the published international patent application WO 02/42480, which is identical to the application as filed.

From the wording of claim 1 it was clear that the functional features applied to the deposited strain as well as to the derivatives.

Article 123(3) EPC

Claim 1 resulted from the combination of claims 1, 2 and 3 as granted. There was no extension of the scope of protection provided by the patent.

Article 84 EPC

There was no ambiguity in the wording of claim 1 due to the amendment in line 3.

Article 53(c) EPC

Claims 10 and 11 were purpose limited product claims.

Article 83 EPC

Opponent VI raised an objection against the correctness of the deposit of the viral strain V0083008 for the first time on the day of the oral proceedings before the opposition division. The issue raised by the

opponent was very complex and rightfully not admitted by the opposition division.

The appellants did not provide any serious doubts substantiated by verifiable facts that the claimed derivatives could not be readily provided. The skilled person could readily perform the necessary tests to determine whether a virus had the properties of features (i) and (ii). This was demonstrated by the experiments described in the patent and by the reports on file (*e.g. D4, D71-73)*. Derivatives according to the claim could be readily derived from the deposited virus or from prior art MVA viruses such as MVA-572 or MVA-575.

Article 54 EPC

As shown by document D84, virus strains MVA-BN, MVA-572 and MVA-I721 were indistinguishable at the genetic level, yet they showed functional differences. For the comparison of the claimed viruses with the prior art viruses, functional comparisons were decisive. Table I and Example 2.1. of the patent showed functional differences between MVA-BN and MVA-575. MVA-575 replicated in at least one of the three human cell lines mentioned in claim 1. According to documents D33 and D69, the prior art strain MVA-F6 replicated in HeLa cells. The MVA-F6 strain used in document D4 was not a prior art strain. The data in document D4, showing identity between the prior art virus and MVA-BN, were in fact obtained several years after the filing date and with a virus that had been further passaged.

Article 56 EPC

D18 represented the closest prior art and disclosed virus MVA-F6. The technical problem had to be defined as the provision of an improved vaccinia virus for vaccination. The data in the patent and in document D61 demonstrated that this problem was solved. There was no suggestion in the prior art to use replication assays in HaCat cells and in immunocompromised mice unable to produce mature B and T cells in order to solve this problem.

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

XXIII. The Respondent requested to set aside the decision under appeal and to maintain the patent upon the basis of the claims of the Main Request filed on 5 November 2014 at the oral proceedings before the Board.

Reasons for the Decision

Article 108 EPC and Rule 99 EPC (Admissibility of appeal I)

1. Appellant I filed its appeal in the name of Baxter Aktiengesellschaft of Vienna and Baxter Healthcare Corporation, the latter with an address in Deerfield, Illinois, USA. The opposition had however been filed in the names of Baxter Aktiengesellschaft and Baxter Healthcare SA with addresses in Vienna and in Wallisellen, Switzerland, respectively.

2. Upon notification of this inconsistency by a communication of the board, the appellant requested correction of the defect according to Rule 101(2) EPC

and submitted that the true intention when filing the appeal had been that the appellant named in the appeal and the name of the opponent named in the notice of opposition should be the same. This could immediately be seen from the letter dated 15 April 2011 which accompanied the statement of grounds of appeal and which referred to "Appellant and Opponent 1". Furthermore, there had been no transfer of opposition between the two companies.

3. The case law of the boards concerning corrections under Rule 101(2) EPC provides that in the event of a deficiency as to the appellant's identity, the board must establish the true intention of the appellant on the basis of the information in the appeal or otherwise on file (cf. G 1/12, OJ EPO 2014, 11, A114, points 28 and 29).

4. In the present case the facts and evidence that assist in establishing the true intention of the appellant are that:

a) The representative is the same on appeal as during the opposition proceedings(cf. T 445/08 of 30 January 2012, point 5.4).

b) The notice of appeal refers to the appellant as "Appellant and Opponent O1" (cf. decision T 445/08, point 5.3(b).

c) Opponent O1 is a joint opponent consisting of two corporations, Baxter Aktiengesellschaft and Baxter Healthcare SA. In the notice of appeal the name of the first of these companies is correctly given and instead of Baxter Healthcare SA, the second firm is listed as Baxter Healthcare Corporation.

5. Proceedings before the EPO are conducted in accordance with the principle of free evaluation of evidence - see G 1/12 (supra, point 31). From the above facts and evidence, the errors made by the appellant's representative in the notice of appeal were to write "Corporation" instead of "SA" after "Baxter Healthcare", and to give the correct address of the wrong company. The board's evaluation of this evidence is that it was the intention of the appellant to file its notice of appeal in the names of Baxter Aktiengesellschaft and of Baxter Healthcare SA - collectively "Opponent O1". The board therefore finds that the above noted errors are correctable under Rule 101(2) EPC. As these errors have been corrected, the appeal is therefore admissible.

Admissibility of the Main request

6. In the decision under appeal, the opposition division decided to maintain the patent on the basis of the main request filed on 1 August 2007. This request formed the basis of respondent's main request, filed with its response to the grounds of appeal. The main request filed on 5 November 2014 differs from the previous main request by the combination of independent claim 1 with dependent claims 2 and 3, and the deletion of previous claim 4.

7. The main request was filed in response to the board's communication. The amendments do not add to the complexity of the case and do not raise any new issues. Exercising its discretion under Article 114(2) EPC in conjunction with Rule 13(1) of the Rules of Procedure of the Boards of Appeal (RPBA), the board decides to admit the main request into the proceedings.

Admissibility of new documents

8. At the end of the opposition proceedings, documents D1 to D100 were on file. With its grounds of appeal, appellant I refiled documents D105 and D110 which had not been admitted by the opposition division and filed new documents D111 to D117. Appellant II filed new documents D101 to D104, the same document D105 as appellant I, and documents D106 to D109 with its grounds of appeal.

These documents were introduced to counter arguments used by the opposition division in the appealed decision. Documents D101 to D103, and D109 address the issue of genetic identity between the prior art virus strains and the claimed strains. Arguments referring to the sequencing method used to assess genetic identity were new to the proceedings and and have never been presented before. Moreover, the documents provide and comment on summary conclusions but do not provide experimental details. Documents D104 to D107, D110, D111 and D117 provide additional information in relation to document D20 and its interpretation by the opposition division. Documents D112, D114 and D115 provide new experimental data and comments submitted in order to counter arguments used by the opposition division in its decision.

9. As a general rule, the boards of appeal, when exercising the discretion given to them under Article 114(2) EPC, tend to accept evidence submitted with the statement of grounds of appeal. In conjunction with this discretion, according to Rule 12(4) RPBA, the boards have the power not to admit evidence which could

have been presented or was not admitted in the first instance proceedings.

10. It is the Board's view, that in the present case, all of the documents D101 to D117 could have been presented in opposition proceedings. The documents referring to the results of a new sequencing approach for the comparison of viral strains were submitted as further evidence for genetic identity between the claimed strains and the prior art strains. The issue of genetic identity has been mentioned in the opposition briefs and was already addressed in points 1.2.2. and 1.2.3. of respondent's answer dated 1 August 2007. The majority of the further documents filed with the statements of grounds of appeal add technical information and experimental data in relation to the suitability of SCID mice for the assessment of feature (ii) of claim 1. In point 1.4 of its response of 1 August 2007, and again in point 2.8 of its submissions of 18 June 2008, the respondent had already noted that no evidence was on file to support the allegation that prior art viruses had the properties defined by feature (ii) of claim 1. Oral proceedings in opposition were held in October 2010. Yet appellant 1 filed its first experimental report and additional technical information regarding this issue only with its grounds of appeal in January 2011.

11. Appellant I was not present at the oral proceedings and could not be heard as to why it submitted its experimental evidence only with the grounds of appeal. Appellant II submitted that the evidence it provided was needed to counter arguments which the opposition division used to arrive at its decision.

12. The Board is aware that there might be situations where a party is confronted with fresh arguments submitted only late in opposition proceedings. This could be a reason for allowing further submissions in appeal proceedings. In the present case, however, the issues addressed by the new submissions had been raised from the beginning of the opposition proceedings in 2007. Moreover, the fact that the opposition division was not convinced by the evidence presented by the opponents in the first instance is not an invitation to file further (experimental) data.

13. The board decides therefore not to admit any of documents D101 to D117 into the procedure.

14. After the deadline for submitting the statement of grounds of appeal, appellant I filed further experimental reports, D118, D148 and D149. In order to support its arguments the respondent submitted new documents D119 to D147. Following these submissions, various rounds of further submissions by all parties followed, ending with the submission of document D166, (cf. items VI to XV, above).

15. All these additional documents were submitted to counter arguments based on the now non-admitted documents D101 to D117. The board, exercising its discretion under Article 114(2) EPC in conjunction with Rule 13(1) RPBA, therefore decides not to admit documents D118 to D166 into the procedure.

Article 53(c) EPC

16. Appellant I interpreted claims 10 and 11 (cf. item XVII, above) as defining unallowable methods of medical treatment.

17. According to Article 53(c) EPC, second half-sentence, **products** for use in methods for the treatment of the human or animal body are not among the subject matter excluded from patentability. Since claims 10 and 11 are product claims, appellant I's objection is without merit.

Rule 80 EPC

18. The appellants submitted that the amendment in line 3 of claim 1, linking the deposited strain to functional features(i) and (ii), was not occasioned by a ground of opposition.

19. In point 8.5 of its opposition brief, dated 28 September 2006, appellant II argued that the deposited strain of claim 1 was genetically indistinguishable from certain prior art MVA strains and lacked therefore novelty. In response to this objection, the patent proprietor amended line 3 to define the deposited strain as possessing the same functional properties as the claimed derivatives. This amendment is therefore clearly occasioned by a ground of opposition.

Article 84 EPC

20. Both appellants raised a clarity objection against the amendment in line 3 of claim 1 concerning the interpretation of the feature "wherein said Ankara strain MVA-BN **or** its derivatives are characterised" (emphasis added by the board) by (i) and (ii). According to the appellants' interpretation, the wording implies that at least one of **either** the Ankara strain MVA-BN **or** its derivatives possess the properties

(i) and (ii). In other words, the characterizing features becomes optional.

21. The board is not convinced by this argument because the feature in question specifies the properties of the strain deposited under "number V00083008 and derivatives thereof" as mentioned in the preceding lines. The claim defines said strains further as those "wherein said Ankara strain MVA-BN or its derivatives are characterised" by (i) and (ii). Read in this context, the "at least one of either - or" interpretation does not make sense.

22. Appellant I also raised an objection that the amended claim was unclear because it required that the deposited strain had the characterizing properties (i) and (ii) whereas the deposited strain, according to [0025] of the patent, was characterized as having at least one of four properties listed there.

23. According to Article 84 EPC, the claims shall be clear and shall define the matter for which protection is sought. As is apparent from the appellant's arguments in respect of novelty and sufficiency of disclosure, they had no difficulties in establishing the meaning of claim 1 with regard to the required properties of the deposited strain. The board therefore considers that the claims meet the requirements of Article 84 EPC.

Article 123(2) EPC

24. Based on the interpretation that at least one of either the deposited virus or the derivatives are characterized by features (i) and (ii), and that the claim therefore encompassed derivatives without any functional restrictions, the appellants submitted that

claim 1 encompassed subject matter which was neither disclosed in the patent application nor within the scope of the claims as granted.

25. As a consequence of its decision on clarity (see point (21) above), the board rejects this argument.

26. Throughout the proceedings, it was argued that the deposited virus was not genetically homogeneous but a mixture of genetically heterogenous viral subpopulations. Both appellants raised the objection that the amendment linking the deposited strain to features (i) and (ii) represented an undisclosed combination of features, defining effectively a previously undisclosed subgroup of viruses within the deposited isolate. They submitted also that the specific combination of features (i) and (ii) was not disclosed in the application as filed.

27. According to page 7, lines 7 to 12, of the patent application, *"Viruses having the same replication characteristics than* [sic] *the deposited virus are viruses that replicate with similar amplification ratios than the deposited strain in CEF cells and the cell lines BHK, HeLa, HaCat and 143B and that show a similar replication in vivo as determined in the AGR129 mouse model (see below)."* The subsequent paragraph states that "*the vaccinia strains according to the present invention, in particular MVA-BN and its derivatives are characterized by a failure to replicate in vivo*" which "*can preferably be determined in mice that are incapable of producing mature B and T cells. An example for such mice is the transgenic mouse model AGR129*". In the same paragraph, on page 8, it is stated that "*Instead of the AGR 129 mice any other mouse strain can be used that is incapable of producing*

mature B and T cells and as such is severely immune compromised."

28. The specific combination of features (i) and (ii) is therefore directly and unambiguously derivable from pages 7 and 8 of the patent application. Moreover, since "*viruses having the same replication characteristics than* [sic] *the deposited virus*" (page 7, line 7) are characterized by this combination of features, it follows that the deposited virus can be characterized by this combination of features.

Article 123(3) EPC

29. The subject matter of claim 1 results from the combination of independent claim 1 as granted with dependent claim 2, referring to claim 1, and dependent claim 3, in turn referring to claims 1 and 2, both as granted. As Article 123(3) EPC requires that "The European patent", including the claims as granted in their entirety, "may not be amended in such a way as to extend the protection it confers", the appellants' objection in this respect is moot.

Article 83 EPC

30. According to points 59 to 61 of the minutes of the oral proceedings before the opposition division, an objection relating to the correctness of the deposit of the strain MVA-BN was raised by opponent 6 for the first time at the oral proceedings. Exercising its discretion under Article 114(2) EPC, the opposition division did not admit this objection into the opposition proceedings.

31. Point 9.1 of the decision under appeal merely states: "*Sufficiency of disclosure of the deposited MVA-BN was not contested.*" The decision does not contain any reasoning why the opposition division refused to admit the objection raised by opponent 6.

32. In the absence of such a reasoning, the board is not in a position to decide whether or not the opposition division has exercised its discretion in an appropriate way. It is therefore necessary for the board to put itself in the place of the opposition division and to decide whether or not it would have exercised such discretion in the same way as the opposition division did (cf. e.g. Headnote 2 of decision T 544/12 of 22 November 2013).

33. Referring to decisions T 1002/92 of 6 July 1994, T 156/84 of 9 April 1987 and T 1485/08 of 20 December 2012, appellant II submitted that the substance of this objection was so highly relevant that the opposition division was wrong not to admit it.

34. The facts underlying the cited cases are as follows: No oral proceedings were held in the opposition proceedings giving rise to appeal T 156/84 and the issue to be decided was whether the opposition division, deciding not to admit a document for the sole reason that it was filed after the nine month opposition period, exercised it discretion correctly. In the case underlying decision T 1002/92, almost two years passed between the submission of a non-admitted document and the issuance of the decision by the opposition division. In decision T 1485/08, the opposition division decided not to admit the late filing (i.e. on the day of the oral proceedings) of an English translation of an evidently highly relevant

Korean patent which had been filed in a timely fashion with the grounds of opposition.

35. According to point 3.3.of the Reasons of decision T 1002/92, the consideration of the relevance is the principal factor governing the exceptional admissibility of late-filed new facts, evidence and related arguments in proceedings before the Opposition Divisions.

36. A principal factor cannot, however, be, on its own, the decisive factor since otherwise, Article 114(2) EPC, giving an opposition division the discretionary power to admit or not to admit late filed facts, evidence and arguments, would be redundant.

37. In the present case, the objection was only raised on the day of the oral proceedings, despite the fact that the subject matter of claim 1, the deposited strain, had not changed from the beginning of the opposition proceedings. The board sees no reason why this objection could not have been raised earlier.

38. Taking into account the particular facts of the case, the board decides that, had it been in the position of the opposition division, it would have exercised the discretion under Article 114(2) EPC in the same way as the opposition division. The objection under Article 83 EPC relating to the deposit of MVA-BN deposited at the ECACC under number V00083008 is therefore not admitted.

39. Appellant II submitted that severely immune compromised mice incapable of producing mature B and T cells were not readily available and could not be obtained without undue burden because their production required three consecutive knock-outs in the mouse genome.

Consequently, MVA virus could not be tested for the property defined by feature (ii) of claim 1.

40. In points 6 and 7 of document D56, Dr. Leonard Shultz, an expert from the Jackson Laboratory, an internationally recognized source and supply facility for mutant mice, declares that mice with the required properties were available and could be reproduced from publically available mice carrying the individual mutations.

41. In the absence of any evidence to the contrary, appellant II's argument relating to the availability of mice, incapable of producing mature B and T cells, must fail.

42. Appellant II furthermore submitted that the replication test in HaCat cells was so unreliable that it was useless for the establishment of the presence of feature (i) in an MVA virus. It referred to documents D71 and D72 which showed no replication of MVA prior art strains 575 and 572 in HeLa cells, but replication in HaCat cells. On the contrary, document D73 showed no replication of the prior art strains in HaCat cells but replication in HeLa cells.

43. Document D73 is the only document on file reporting results upon replication in HaCat and HeLa cells of prior art viruses which are inconsistent with the results presented in the patent, and the results presented in documents D4, D71 and D72. As the results presented in these other documents are consistent in this respect, it seems possible that the divergent data reported in document D73 result from an accidental swapping of cell lines or results. For this reason, the board gives little weight to this document.

44. The evidence on file shows furthermore (documents D4, D71-73), that the parties did not have any problem to perform the tests for the comparison of the claimed viruses with the prior art viruses. While there was a debate about the significance of the results, the board has no doubts that the required tests could be readily performed and put the skilled person in a position to identify (without undue burden) the technical measures necessary to solve the problem underlying the patent at issue (cf. Headnote of decision T 593/09 of 20 December 2011).

45. The main request therefore meets the requirements of Article 83 EPC.

Article 54 EPC

46. Both appellants submitted that the prior art MVA strains MVA575 and MVA-F6(580) anticipated the subject matter of claim 1.

47. The three digit suffix used to designate MVA viruses specifies the number of times the virus has been passaged in CEF (chicken embryo fibroblast) cells. Comprehensive summaries of the family history of MVA strains are on file for instance as Exhibit 1 attached to document D59 and on page 28 of Exhibit 2 attached to document D98. They show that MVA-F6(580) was obtained from predecessor strain MVA572 after 6 passages and 3 plaque purifications. MVA 575 was independently derived from intermediate isolate MVA574.

The MVA-BN strain used for the tests of the present patent has the passage number 583, and the deposited strain has the passage number 586.

48. The respondent considered it doubtful whether MVA-F6(580) was indeed publicly available. It submitted that it never had access to MVA-F6(580) for comparative tests but did not provide any further evidence.

49. MVA-F6(580) was described in prior art documents D2, D3, D17, D18 and D33 as established by cross references in document D3 to documents D18 and D2 (cf. page 19, 1st paragraph), and by cross references in document D33 to document D18. The strain is furthermore described in document D69. These documents do not provide evidence of whether and how often the strain was further passaged. However, documents D2, D18, D33 and D69 are peer reviewed scientific publications published in well known journals which in general require that the described material is made available. In view of the evidence on file and in the absence of any evidence that MVA-F6(580) was not available to the public, the board rejects respondent's argument and decides that MVA-F6(580) belonged to the state of the art.

50. The parties did not dispute that the strain MVA-BN of claim 1 is identical, at the genetic level, with prior art strains MVA-F6(580) and MVA575.

According to the respondent, the claimed virus and the prior art viruses were however not genetically homogeneous isolates but represented in fact polyclonal mixtures of genetically distinct subpopulations. Depending on the prevalence of specific subpopulations, the isolates had distinguishable replication phenotypes.

51. It remains therefore to be established whether the viruses of claim 1, both, the deposited polyclonal

isolate and its derivatives, and prior art strains MVA-F6(580) and MVA575 share the same replication properties.

52. Table 1 of the patent, documents D4 and D71 to D73 provide comparative experimental data. The results of the different sets of experiments do not give a consistent picture of the replicative properties of the viruses tested, and the parties have submitted arguments as to why the data provided by these documents support their respective cases.

53. According to [0010] of the patent in suit, replication of a virus is expressed as the ratio of virus produced by infected cells and the amount of virus used to infect the cells, with a ratio of less than 1 indicating a lack of reproductive replication.

54. This ratio is to a certain extent dependent upon the experimental conditions, for instance upon the multiplicity of infection, the status of the cells used, the type and amount of medium used and the temperature maintained during infection (cf. point 58 of document D99).

It is within the nature of tests performed with living cells, that the results obtained show a certain variability if an experiment is repeated. For this reason, the results of multiple experiments performed in parallel at the same place and time are analysed with statistical tools and it makes no sense to base comparisons of the viruses on a comparison of isolated data points.

55. If the ratio of output to input is clearly above 1000, as shown for the replication of all viral isolates in

CEF cells in all experimental reports on file, the variability of the assay conditions is of minor importance. If, on the other hand, the output to input ratio, as shown for the replication in HaCat and HeLa cells, is close to 1, the influence of the assay conditions may not be negligible.

56. The board does therefore not accept appellant II's argument that the statistical analysis of a data set obtained by combining the data from Table 1 of the patent with those of documents D71 to D73 demonstrates with reasonable certainty that the prior art virus MVA575 meets the requirements of feature (i) of claim 1. The data disclosed in these documents were obtained in experiments carried out independently. Moreover, the result of this analysis depends significantly on the data from document D73 which, contrary to all other data sets, shows an output to input ratio close to zero for MVA575 replicated in HaCat cells.

57. Novelty has to be established on the basis of certainty about the replication properties of the prior art viruses. In other words, only if replication data are consistent throughout the experimental reports on file, can the board accept this evidence as a true feature of a viral isolate.

58. Leaving aside document D73 for the reasons indicated in point 43 above, MVA575 consistently showed replication rates in HeLa and 143B cells of clearly below 1 (cf. Table 1 of the patent, Tables 1 to 3 of document D4, Table 5 of document D71, Table 6 of document D72). The board, considering the data on file, is therefore convinced that MVA575 does not replicate in HeLa or 143B cells.

The data for the replication of MVA575 in HaCat cells, on the other hand, are as follows: clearly above 1 in Table 5 of document D71 and in Table 6 of document D72, marginally above 1 in Table 1 of the patent, and clearly below 1 in only one out of two experiments (and the averaged result of the two experiments) reported in document D4. On the basis of these results, the board decides that it has not been established with certainty that prior art virus MVA575 has a replication ratio of below 1 in HaCat cells.

59. Documents D2, D3, D17, D18, D33 and D69 disclose MVA F6(580) but do not provide any data about the replication of the viral isolate in HaCat cells.

Document D4 is the only document providing results of a direct comparison of the replication of MVA-BN and MVA F6 in HaCat cells. The experiments were performed about 4 years after the filing date of the patent in suit. They show no replication of MVA-F6 in HeLa, 143B and HaCat cells.

60. The respondent submitted that the MVA-F6 isolate which was tested in document D4 had been derived from the prior art isolate MVA-F6(580) by three further rounds of passaging in CEF cells, and was therefore different from MVA-F6(580). It should be designated MVA-F6(583). Since the viral isolate designated MVA-F6(580) was polyclonal in nature, the further passaging had most likely changed its polyclonal composition and hence the replication properties of MVA-F6(583). Document D4 could therefore not be relied upon to establish the replication properties of MVA-F6(580).

61. Karl Heller, the expert who was supervising the experiments described in document D4, confirms in

declaration D91 that the original MVA-F6(580) has been passaged three more times. The parties did not dispute that it is normal practice to titrate and passage viral isolates. To address the argument that the subclonal composition of MVA-F6 would have changed during three rounds of passaging, expert declarations (D92, D93) commenting on the likelihood of such changes were submitted. The experts consider it unlikely that the passaging of MVA-F6(580) on CEF cells would have changed the subclonal composition. The expert of document D91 "*believe[s] that the results obtained with MVA-F6 (passage 583) are indicative of the results that would have been obtained had MVA-F6 (passage 580) been used instead*" (point 10). In point 9 of document D93, the expert stated that "*I believe that the MVA-F6 (passage 583) tested by VIVACS GmBH [document D4] would have the same replication characteristics as MVA-F6 (passage 580)*".

62. The board thus finds itself in a situation where it has to decide on the basis of contradicting opinions and arguments provided by the parties. However, it is not justifiable to decide whether a document is prejudicial to novelty on the basis of a mere probability that it discloses all the features of the patent. If a patent is revoked, or a request is held unallowable, for lack of novelty, the board has to be certain, taking into consideration all the facts and arguments put forward during the proceedings, that its decision is justified (cf. point 16 of decision T 464/94 of 21 Mai 1997).

63. In view of the fact, that the experimental report D4 is the only document providing a comparison between the claimed virus and MVA-F6 and that the interpretation of its results is plausibly contested, the board decides that the evidence on file is insufficient to conclude

that MVA-F6(580) has the replicative properties specified in part (i) of claim 1.

64. Since neither the prior art isolate MVA575 nor MVA-F6(580) has all the necessary replicative properties in HeLa, 143B and HaCat cells, there is no need to examine their replicative properties in severely immune compromised mice according to feature (ii) of claim 1.

65. The board decides that the main request is novel (Article 54 EPC).

Article 56 EPC

66. The closest prior art is represented by document D18, disclosing MVA-F6(580) and its replication properties in HeLa and CEF cells.

67. In the light of this disclosure, the technical problem underlying the patent is the provision of an improved MVA isolate.

68. According to Table 1 of the patent, viral isolate MVA-BN is more attenuated than prior art viruses MVA575, MVA-HLR and MVA-Vero because it does not replicate in HaCat cells and it replicates least in the human cell lines tested. According to [0092] and Figure 11 of the patent, MVA-BN induced significantly higher antibody titers when used in a preboost/boost regime than any of the prior art viruses, MVA-572, Elstree or Wyeth when used either alone or in combination.

69. Appellant II submitted that the relevant comparison for demonstrating an improvement should have been with MVA-F6(580).

70. In the absence of any evidence to the contrary, the board accepts respondent's argument that the improvement reported for MVA-BN in [0092] is linked to the improved attenuation demonstrated in human cell cultures (cf. Table 1). In the absence of convincing evidence that MVA-F6(580) has the same replicative properties in HaCat cells as MVA-BN, the board sees no need to examine the replicative properties of MVA-F6(580) in severely immune compromised mice in order to arrive at the conclusion, that MVA-F6(580) is not as attenuated as MVA-BN.

71. The board thus concludes that not only the deposited isolate MVA-BN with accession number V00083008 but also the derivatives according to claim 1, with the required replicative properties in the human cell lines and in immune compromised mice, solve the underlying technical problem.

72. It remains to be examined whether this solution involves an inventive step.

73. Appellant II's main arguments as to why the claimed solution lacked an inventive step were based on the fact that document D18 described MVA-F6(580) as a generally safe virus, and that merely propagating this virus further would, without the use of any inventive skill, result in alternative viruses with all the properties defined in claim 1.

74. As discussed above, on the basis of the available evidence, the board does not arrive at the conclusion that MVA-F6(580) has all the properties required by claim 1.

75. The claimed viruses do not replicate in HaCat cells (cf. [0014] of the patent), HeLa cells or 143B cells, and as explained in point 70 above, the board considers this combination of features as a hallmark of the improved MVA isolates.

The assessment of inventive step depends therefore on the answer to the question whether document D18, either alone or in combination with any other document, rendered the selection of viral isolates not replicating in HaCat cells obvious.

76. According to document D28, the HaCat cell line was established in 1988, and its repeated use for various purposes has been described (cf. documents D64 to D66). It was however not used to test the replicative properties of MVA isolates.

77. The replication properties of MVA isolates in a number of human cell lines have been assayed. Document D20 describes replication assays in human HEK293, HeLa and SW839 cell lines (Table 1). Table 1 of document D33 describes replication assays in human HEK293, HeLa, SK 29 MEL 1, LC 5; 85HG66, U138, C 8166, HUT 78 and SY 9287 cell lines. Document D60 describes replication properties in human MRC-5, 143B, HeLa and FS-2 cell lines. Document D70 discloses replication assays in human HeLa, AG1523 and 143B cell lines (page 16, Materials and Methods). None of these documents describes or suggests in any way the use of HaCat cells.

78. While it may have been obvious to propagate MVA-F6(580), the board finds nothing in the prior art that would have suggested the use of HaCat cells to identify viral isolates with improved properties.

79. The main request therefore meets the requirements of Article 56 EPC.

Adaptation of the description

80. At the oral proceedings, the respondent submitted amended pages 2, 2a, and 3 to 18 of the description to bring it in line with the main request. The board is satisfied that this has been done.

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 maintain the patent as amended in the following version:

   Description: Pages 2, 2a, and 3 to 18, received during the oral proceedings before the Board on 5 November 2014.

   Claims: Nos. 1-32 of the Main Request received during the oral proceedings before the Board on 5 November 2014.

   Drawings: Figures 1-11 of the patent specification as granted.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated