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Datasheet for the decision of 12 October 2022

Case Number: T 1261/19 - 3.3.04

Application Number: 06707039.1

Publication Number: 1855720

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Language of the proceedings: EN

Title of invention:
Use of a modified poxvirus for the rapid induction of immunity against a poxvirus or other infectious agents

Patent Proprietor:
Bavarian Nordic A/S

Opponent:
Cupam Limited

Headword:
Smallpox vaccine/BAVARIAN NORDIC

Relevant legal provisions:
EPC Art. 107, 54(5), 56
RPBA Art. 12(4)

Keyword:
Admissibility of opponent's appeal (no)
Late-filed objection - admitted into the proceedings (no)
Main request - novelty (yes), inventive step (yes)

Decisions cited:
T 1569/11, T 1523/07, T 0509/04

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Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1261/19 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 12 October 2022

Appellant: (Patent Proprietor)	Bavarian Nordic A/S Hejreskovvej 10 A 3490 Kvistgaard (DK)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Respondent: (Opponent)	Cupam Limited 11 Darleydale close Sandhurst GU47 0YF (GB)
Representative:	McDonald, Beatrice McDonald Intellectual Property Limited 11 Darleydale Close Sandhurst Berkshire GU47 0YF (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 23 April 2019 revoking European patent No. 1855720 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	D. Luis Alves
	R. Romandini

Summary of Facts and Submissions

I. European patent No. 1 855 720, entitled "*Use of a modified poxvirus for the rapid induction of immunity against a poxvirus or other infectious agents*", was granted on European patent application No. 06 707 039.1, filed as an international application published as WO 2006/089690.

II. The patent was opposed on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), under Article 100(a) EPC, and on the grounds under Article 100(b) and (c) EPC.

III. The opposition division decided to revoke the patent. The opposition division held, *inter alia*, that the subject-matter of claim 1 of the main request (patent as granted) and of each of auxiliary requests 1 to 5 did not involve an inventive step (Article 56 EPC).

IV. Both the patent proprietor and the opponent filed appeals against this decision.

V. With their statement setting out the grounds of appeal, the patent proprietor filed claims according to a main request and auxiliary requests 1 to 4 (the main request being identical to auxiliary request 1 considered by the opposition division) and made submissions relating to inventive step. Furthermore, documents D9 to D14 were filed (subsequently renumbered D12 to D17). With two subsequent letters, the patent proprietor submitted further arguments and filed documents D20 and D21.

VI. With their statement setting out the grounds of appeal, the opponent contended that the claims of the main request considered by the opposition division lacked novelty. Further, documents D10 and D11 were filed. With a further letter, the opponent addressed the novelty and inventive step of the subject-matter set out in the claim sets filed on appeal by the patent proprietor. Further, documents D18 and D19 were filed.

VII. The board appointed oral proceedings and, in a communication pursuant to Article 15(1) RPBA, informed the parties of its preliminary opinion that, *inter alia*, the opponent's appeal was to be held inadmissible and the submissions made in their statement of grounds of appeal were to be deemed submissions of a respondent. Furthermore, the subject-matter of claim 1 of the main request was novel over the disclosure in document D4.

VIII. The oral proceedings before the board were held as scheduled. At the end of the oral proceedings the chair announced the board's decision.

IX. The main request consists of 14 claims. Claim 1 reads as follows:

"A Modified Vaccinia virus Ankara (MVA) for use in a method of immunizing an animal, including a human, to protect against smallpox infection within 2-7 days after immunization, wherein a protective immune response is generated against smallpox within 2-7 days after a single vaccination, and wherein the MVA is MVA-BN."

Claims 2 to 14 are dependent on claim 1.

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

D4: EP 1 335 987 B1

D7: Lodish, H. *et al.*, "Molecular Cell Biology", 3rd edn., New York: Scientific American Books, 1995, page 1305

D10: Roitt, I. *et al.*, "Immunology", 4th edn., 1996, pages 1.11, 16.5 and 19.5

D11: Declaration of Dr Tom Evans

D12: Frey, S.E. *et al.*, JAMA 289 (24), 2003, pages 3295-3299

D13: Fenner, F. et al., "Smallpox and its Eradication", WHO, 1988, pages 146-163 and 587

D14: Janeway, C.A, *et al.*, "Immunobiology", 5th edn., Garland Publishing, 2001, pages 412-423

D18: EP 1 975 558 B1

D19: Blanchard, P. *et al.*, Vaccine 21, 2003, pages 4565-4574

XI. The patent proprietor's arguments, as far as relevant to this decision, may be summarised as follows.

Admissibility of the opponent's appeal

The opponent was not adversely affected by the opposition division's decision to revoke the patent. Under Article 107 EPC, the right to appeal was limited

to parties adversely affected by a decision. Therefore, the opponent's appeal should be rejected as inadmissible. This conclusion found support in decision T 1569/11.

Main request

Clarity (Article 84 EPC)
Admittance of the objection into the appeal proceedings

Claim 1 of this request was identical to claim 1 of auxiliary request 1 considered by the opposition division. The decision under appeal stated that there were no objections to the clarity of the claims according to auxiliary request 1. Furthermore, no such objections had been mentioned in the opponent's statement of grounds of appeal. Thus, the objection under Article 84 EPC should not be admitted into the appeal proceedings.

Novelty (Article 54 EPC)

Document D4 did not provide a direct and unambiguous disclosure of either of the features "protective immune response within 2-7 days" and "single vaccination".

It was part of the common general knowledge in the field of smallpox vaccination that a protective immune response occurred at the earliest 10 days after immunization (see documents D12 and D13). This field-specific knowledge was more relevant to the claimed subject-matter than disclosures relating to immunology in general as represented by documents D7, D10 and D14.

Therefore, the two above-mentioned features did not result from reading document D4 in conjunction with the skilled person's common general knowledge.

The established case law supported the novelty of the claimed subject-matter with respect to the disclosure in document D4. According to decision G 2/88 of the Enlarged Board of Appeal, what is inherent in the prior art cannot destroy the novelty of a use claim (see reasons 10, 10.1 and 10.2). This principle also applied to claims directed to a product for a medical use, as could be taken from decision T 694/16. In the case in hand, the effect of a protective immune response against smallpox within 2 to 7 days of a single vaccination remained hidden in document D4. In fact, the challenge experiments reported in this document were carried out only 2 weeks post-second vaccination, corresponding to 5 weeks post-first vaccination.

Inventive step (Article 56 EPC)

The patent disclosed a new mechanism by which the primary immune response generated against MVA-BN was protective against smallpox infection (see paragraphs [0034] and [0035]).

The claimed MVA-BN for use in immunization differed from that disclosed in document D4 on account of the mechanism of action, a protective immune response within 2 to 7 days and a protective immune response after a single vaccination.

The objective technical problem was to be formulated as the provision of a further clinical use of MVA-BN.

Documents D7, D10 and D14 related to general immunology. The common general knowledge relevant to the claimed vaccine was in fact represented by documents dealing with smallpox vaccines, such as documents D12 and D13.

Document D12 disclosed that neutralizing antibodies at the relevant levels were not present until 12 to 15 days after immunization and that in naive individuals the viral shedding reached a maximum at 14 days (see Figure 3, Figure 2 and page 3298, middle column). Document D13 disclosed that antibodies were not detected until more than 10 days after immunization and that vaccination consisted of a prime-boost regime (see page 158, right-hand column and page 587). Thus, in the technical field of poxvirus it was common general knowledge that neutralizing antibodies were present only 10 to 15 days after immunization.

The teaching in these documents was not to be disregarded in view of later developments in smallpox vaccination. In fact, no such developments had occurred, as confirmed by the fact that the more recent document D4 also disclosed a prime-boost vaccination regime. Document D4 did not disclose single vaccination with the MVA-BN strain, or a vaccine that was effective in less time than prior-art vaccines. Instead, the document concerned improvements to the safety of vaccination against smallpox (see paragraph [0007]).

Document D7 disclosed a 1 000-fold difference in the antibody levels generated in the primary and secondary immune responses, and the primary immune response was not considered sufficient for protection (see Figure 27-11). Document D10 disclosed that the time frame of an immune response varied according to the

route of administration and the type of vaccine, with live vaccines being more effective than killed vaccines (see page 19.5, right-hand column). Figure 1.19 did disclose an increase and decrease in antibody levels but did not disclose the extent of the primary immune response.

The disclosure in document D4 did not provide an incentive to test the immune response to MVA-BN as early as 2 to 7 days after immunization. The challenge experiment was only carried out 5 weeks after immunization. Figure 11 showed negligible antibody levels 2 weeks after immunization. A primary immune response could not be equated with a protective immune response. For the skilled person, the antibody levels shown were not indicative of a protective immune response. Paragraph [0092] concerned sufficient levels for a protective immune response but did not disclose any difference in the speed of the immune response. It concluded that two vaccinations were useful. The fact that the antibody levels were analysed weekly did not provide any incentive for an analysis at an earlier point in time either. Paragraph [0052] did refer to a "single shot" but in the context of the challenge model in Example 2.1., with application of a prime-boost vaccination. Therefore, no incentive could be derived from this paragraph of document D4 either.

There was no document in the proceedings disclosing that a primary immune response was protective.

Furthermore, in view of the common general knowledge that protection against smallpox infection occurred at the earliest 10 to 14 days after immunization, the skilled person had no reasonable expectation of

succeeding in providing a protective immune response 2 to 7 days after immunization.

XII. The opponent's arguments, as far as relevant to this decision, may be summarised as follows:

Admissibility of the opponent's appeal

The appeal should be held admissible. In any event, the opponent's submissions in the statement of grounds of appeal should be considered in the appeal (see decision T 1569/11, reasons 1.3).

Main request

Clarity (Article 84 EPC)
Admittance of the objection into the appeal proceedings

The objection under Article 84 EPC was not raised in the opposition proceedings because the discussion on what was then auxiliary request 1 (main request in the appeal proceedings) started very late in the day at the oral proceedings.

Novelty (Article 54 EPC)

The opposition division had not correctly applied decisions G 2/88 and G 6/88 of the Enlarged Board of Appeal and had not taken into account the skilled person's common general knowledge when reading document D4.

Moreover, it was established case law that a prior-art disclosure also included features which for the skilled person were implicit in what was explicitly disclosed.

It was part of the common general knowledge that, upon immunization, a primary immune response was measurable within 2 to 5 days, reaching a peak within 7 days (see documents D7, Figure 27.11; D10, Figures 1.19, 16.8 and 19.10; D11, paragraph 7, first sentence; D14, Figure 10.31). The immune response was protective as early as 4 to 96 hours after antigen exposure (see document D14, page 420, lines 15 to 18).

Document D4 disclosed that MVA was capable of inducing a protective immune response against smallpox and that the MVA-BN strain showed higher immunogenicity than other MVA strains. Reading this with their common general knowledge, the skilled person would have inferred that immunization with the MVA-BN strain would generate a protective immune response within 2 to 7 days.

Thus, the technical feature "to protect against smallpox infection within 2-7 days after immunization" in claim 1 was disclosed in document D4 when read with the skilled person's common general knowledge.

According to the principles set out in decisions G 2/88 and G 6/88 of the Enlarged Board of Appeal, for the claimed use to be novel the technical effect it relied on had to be novel. Therefore, in the case in hand the claimed use was not novel.

Furthermore, according to the case law of the boards of appeal dealing with claims to a medical use based on a technical effect, the claimed use represented a further medical indication as compared with a prior-art disclosure only if that technical effect was both new and inventive over said disclosure (see T 509/04). In the case in hand, the technical effect "protective

immune response against smallpox within 2-7 days after a single vaccination" was disclosed in document D4, for the reasons given above.

According to the case law of the boards of appeal dealing with claims directed to a second medical use based on a group of patients, the claimed use was only novel if the group of patients was novel. However, in the case in hand the patients in claim 1 did not differ from those disclosed in document D4.

Inventive step (Article 56 EPC)

The patent (see paragraphs [0034] and [0035]) did not support the alleged new mechanism of immune protection, nor was there any other evidence of such a mechanism.

Document D4 showed a statistically significant increase in immune response with the MVA-BN strain compared with the prior-art MVA strain (see antibody levels 2 weeks after immunization, Figure 11). The MVA-BN strain was surprisingly better in terms of the "speed and magnitude" of the immune response (see paragraph [0092]). It generated a 1 000-fold increase in antibody levels even before the boost vaccination (see Figures 2 and 6).

Thus, document D4 disclosed that an immune response could be seen after one vaccination. All that was missing was the demonstration of a protective immune response at early stages after this vaccination.

The technical effect associated with this difference was "a protective immune response to smallpox within 2 to 7 days of one immunization".

The objective technical problem was "to provide an additional method of providing a protective immune response by MVA-BN".

In view of the common general knowledge, the skilled person would have had a reasonable expectation that with MVA-BN an improved immune response would be generated as early as 2 to 5 days after immunization. The only question that remained in view of the disclosure in document D4 was whether that response was protective.

Documents D7, D10, D11 and D14 represented said common general knowledge. Furthermore, document D14 disclosed that specific immune responses, T cells and memory cells were present as early as 96 hours after immunization (see Figure 10.31).

Documents D12 and D13, relating to vaccination against smallpox, were superseded by the more recent document D4. They referred to studies that had been carried out many years previously – and not with MVA-BN.

Document D4 gave the skilled person the incentive to test the immune response to MVA-BN at earlier points in time. Furthermore, document D4 explicitly suggested single vaccination (see paragraphs [0052] and [0096]).

In view of the common general knowledge the skilled person had a reasonable expectation of success. It was irrelevant for the question of obviousness whether the prior art disclosed a given antibody level at an earlier point in time. All that was relevant was whether the measured immune response was protective and

how early it was protective. To answer these questions the skilled person would carry out a challenge study.

XIII. The patent proprietor (appellant) requested (i) that the decision under appeal be set aside and the patent be maintained in amended form on the basis of the set of claims of the main request or, alternatively, of auxiliary requests 1 to 4, all filed with the statement of grounds of appeal; and (ii) that the opponent's appeal be held inadmissible.

The opponent (respondent) requested (i) that the opposition division's decision "be amended" and that the patent be revoked; (ii) that the claims according to the main request and auxiliary requests filed with the patent proprietor's statement of grounds of appeal be held unallowable; and (iii) that the statement of grounds of appeal and documents D10 and D11 be admitted into the appeal proceedings in the event that the board held the opponent's appeal inadmissible.

Reasons for the Decision

Admissibility of the opponent's appeal

1. Pursuant to Article 107 EPC, any party to proceedings adversely affected by a decision may appeal. By contrast, any other parties to the proceedings, i.e. parties not affected by the decision, shall be parties to the appeal proceedings as of right. Since the opposition division's decision was to revoke the patent, the opponent is not considered to be adversely affected. The opponent did not explain the way in which they were adversely affected by the decision. Indeed,

the opponent's statement setting out the grounds of appeal contains only the following request:
"*The patent was revoked by the Opposition Division in its Decision of 23 April 2019. The Opponent requests that this Decision be amended and that the patent be revoked in its entirety as lacking novelty under Article 54 EPC.*"

2. In decision T 1569/11, cited by the opponent in this context, the opponents' appeal was held inadmissible because the opponents were seeking to challenge not the decision to revoke the patent but rather its reasons (see reasons 1.2). Thus, the cited decision does not support the opponent's case.

3. Accordingly, the opponent's appeal is rejected as inadmissible for lack of compliance with the requirements of Article 107 EPC.

Admissibility of the opponent's submissions made with their statement of grounds of appeal

4. The opponent's request for the submissions made in their statement of grounds of appeal to be admitted into the appeal proceedings is allowable and these submissions were considered in the appeal as submissions of a respondent. Furthermore, the board concurs with the opponent that the board in decision T 1569/11, in a similar situation, held that the submissions made by the opponents in their statements of grounds of appeal were to be considered submissions by respondents, despite holding their appeals inadmissible (see reasons 1.3).

Main request - claim 1

Clarity (Article 84 EPC)
Admittance of the objection into the appeal proceedings

5. With the reply to the appeal the opponent raised objections for lack of clarity. Specifically, they argued that the meaning of the feature "after a single vaccination" in claim 1 was not clear.

6. Claim 1 is identical to claim 1 of auxiliary request 1 considered in the decision under appeal. Paragraph 21 of the decision states that no objections under Article 84 EPC were raised.

7. The board notes that the claim request at issue was filed two months prior to the oral proceedings before the opposition division. The board considers that the objection could and should have been filed in the opposition proceedings. Accordingly, the board decides to hold this objection inadmissible (Article 12(4) RPBA 2007).

Claim construction

8. Claim 1 is drafted as a purpose-limited product claim according to Article 54(5) EPC. The claim relates to MVA-BN (modified vaccinia virus Ankara BN). The defined purpose is the use in a method of immunizing an animal to generate a protective immune response against smallpox infection within 2 to 7 days after a single vaccination. In the board's view the feature "within 2-7 days" is a technical feature of the purpose defined in the claim. As regards the expression "after a single vaccination", the board is of the view that in claim 1 the protective response generated within 2 to 7 days

after vaccination does not refer to a response after vaccination by a boost vaccine in a prime-boost regime. Instead it refers to the immune response that is generated after one administration of the vaccine.

Novelty

9. The opponent contested the opposition division's decision that the subject-matter of claim 1 was not disclosed in document D4.

10. According to established case law of the boards of appeal, the claimed subject-matter lacks novelty if it is directly and unambiguously derivable from the state of the art, including any features implicit to the skilled person. In this context, implicit disclosure is that which a skilled person would objectively consider as necessarily implied in the explicit content (see e.g. decision T 1523/07, reasons 2.4).

11. Document D4 concerns vaccinia virus Ankara strains for enhancing safety and improving vaccination regimes against smallpox infection (see paragraph [0007]). It discloses that the MVA-BN strain is safer and more immunogenic that other MVA strains (see paragraphs [0018] and [0031]). In a challenge experiment 2 weeks after a prime-boost vaccination with MVA-BN, the prime and boost vaccination being spaced 3 weeks apart, MVA-BN elicited the same level of protection as a DNA prime-MVA boost vaccination (see paragraph [0019] and Example 2.2.2.). Thus, contrary to prior-art MVA strains, the same level of protection was obtained in a prime-boost vaccination with MVA-BN as in DNA prime-MVA boost vaccination.

12. It was undisputed that this document did not contain any explicit disclosure of MVA-BN eliciting a protective immune response as early as 7 days after immunization. The opponent argued, however, that there was an implicit disclosure of this feature. In this context the opponent referred to the skilled person's common general knowledge as represented by documents D7, D10, D11 and D14, arguing that all the features in claim 1 were provided in document D4 when it was read with said common general knowledge.

13. Accordingly, the question in the case in hand is whether this feature is implicitly disclosed in the sense that it is necessarily implied by what is explicitly disclosed in document D4.

14. The opponent submitted that it belonged to the common general knowledge, as represented by the above-cited documents, that a primary immune response was measurable within 2 to 5 days of immunization.

15. However, the claim requires a protective immune response. For this reason alone, the opponent's argument cannot succeed.

16. The opponent further argued that document D14 discloses that an immune response is protective as early as 4 to 96 hours after antigen exposure.

17. Document D14 refers to three phases of the immune response, classified as immediate (0 to 4 hours), early (4 to 96 hours) and late (after 96 hours) (see Figure 10.31). In the first two phases innate immunity is involved, the early phase contributing to the initiation of adaptive immunity (see figure legend). An adaptive immune response takes several days to develop

(see page 420, lines 4 and 5). These two passages leave the board in no doubt that, in document D14, adaptive immune response does not correspond to the "early phase" but is instead classified within the "late phase".

The opponent argued that, according to Figure 10.31, column entitled "late phase", there is already immunological memory at 96 hours post-exposure, and thus immunological protection.

However, the figure states after 96 hours. Thus, in the board's view it remains undefined whether and when there is a protective immune response. The passage in lines 15 to 18 of the same page does not depart from this: "*An effective adaptive immune response leads to a state of protective immunity. This state consists of the presence of effector cells and molecules produced in the initial response, and immunological memory.*" This passage thus characterises the state of protective immunity as involving effector cells and molecules produced in the initial response, plus immunological memory, without any disclosure of the point in time for immunological memory. The subsequent passage provides considerations on the mechanism of immunological memory without any reference to its timeline. In fact, if the common general knowledge were, as asserted by the opponent, that a protective immune response is present as early as 96 hours after antigen exposure and that this knowledge is generally applicable to any antigen, then no prime-boost regime would be necessary for any vaccination and protection against exposure would already be present 96 hours post-vaccination.

18. The opponent's arguments referring to the principles set out in decisions G 2/88 and G 6/88 of the Enlarged

Board of Appeal relied on the technical feature "to protect against smallpox infection within 2-7 days after immunization" being disclosed in document D4. In view of the board's conclusion above, this argument is moot. The same applies to the opponent's argument relying on decision T 509/04, for the same reason.

19. Moreover, decision T 509/04 confirms, in the context of a claim in the form of a composition or product for the manufacture of a medicament for a given therapeutic application, that even if a technical effect may have inherently taken place when carrying out what has previously been made available to the public, the claimed invention is nevertheless novel if attaining the technical effect has not been previously made available to the public (see reasons 6).

20. The parties' submissions on case law relating to patient subgroups do not seem pertinent to the interpretation of this feature, which defines the therapeutic use of the MVA-BN vaccine, not the patients.

Inventive step (Article 56 EPC)

Closest prior art and objective technical problem

21. The disclosure in document D4 was considered to represent the closest prior art. The content of this document is summarised in point 11. above.

22. The subject-matter of claim 1 differs from this disclosure at least in that a protective immune response to smallpox is generated within 2 to 7 days after a single vaccination.

23. The objective technical problem may be formulated as the provision of a further use of MVA-BN in eliciting a protective immune response against smallpox, in agreement with the parties. It was not contested that the patent shows that this problem is solved.

Obviousness

24. At issue in the case in hand is whether the skilled person, in view of their common general knowledge and the disclosure in document D4, would have measured the immune response to MVA-BN at earlier points in time than disclosed in document D4, in the expectation of solving the above-posed problem.

25. To answer this question it is necessary to first establish what was part of the common general knowledge in the relevant field. The parties cited documents D7 and D10 to D14 in this context.

25.1 As stated under point 14. above in the context of novelty, documents D7, D10 and D11 were cited to demonstrate that a primary immune response being generated within 2 to 5 days of immunization was part of the common general knowledge. Since this point was not disputed, the contents of these documents need not be discussed further.

25.2 There was, however, disagreement as to whether it was part of the common general knowledge that a protective immune response is generated within 1 week of immunization. Document D14 was cited in this context. In point 17. above, the board concluded, in the context of novelty, that the content of this document does not support the argument that this was common general knowledge.

25.3 Documents D7, D10 and D14 are excerpts of immunology textbooks. They concern general principles of immunology and do not specifically address immune responses in the context of smallpox vaccination. Document D11 is a declaration submitted by the opponent. The relevant part of the declaration cited in this context is point 7, which also refers to general principles of immunology. By contrast, documents D12 and D13 concern vaccination against smallpox. The board therefore considers these disclosures to be more relevant for establishing what was part of the common general knowledge in the technical field of smallpox vaccination.

25.4 Document D12 is concerned with the immune response to smallpox in individuals vaccinated with different doses of the vaccine Dryvax of Wyeth Laboratories (see title and page 3295, left-hand column, last paragraph, and page 3296, middle column, second paragraph). The kinetics of the antibody response was quantified by neutralization assay. The level of neutralizing antibodies is depicted at five points in time: day 0 (vaccination), day 3 to 5, day 6 to 8, day 12 to 15 and day 26 to 30. At 6 to 8 days after vaccination the level is still no different from that at day 0. The first point in time for which increased levels are shown is at 12 to 15 days after vaccination (see Figure 3A). Therefore, this document leads to the conclusion that no neutralizing antibodies could be detected 6 to 8 days after vaccination and that such antibodies were present at 12 to 15 days.

Document D13 also deals with the immune response in smallpox vaccination and discloses that no antibodies were detected up to the 10th day post-vaccination (see

page 158, right-hand column, second paragraph, second sentence).

From these disclosures the board concludes that there was no evidence of neutralizing antibodies to vaccinia virus at any point in time before 10 days post-vaccination.

25.5 While document D13 was published in 1988, document D12 was published in 2003 and concerns a study carried out in 2002 (see page 3296, left-hand column, first paragraph), so the mere fact that these documents report on studies with a vaccine developed much earlier than the publication date of document D4 does not, as argued by the opponent, disqualify the disclosures from reflecting the common general knowledge. In fact, the examples in document D4 use the vaccine studied in document D12 for comparison with MVA-BN. In the board's view this demonstrates that the skilled person would not disregard information obtained with this vaccine for being outdated.

25.6 In view of the foregoing, the opponent's submissions fail to convince the board that there was a reasonable expectation of providing MVA-BN for eliciting a protective immune response against smallpox within 2 to 7 days of a single immunization.

26. The opponent further argued that, from the immune response observed in Figures 2, 6 and 11 of document D4, the skilled person had a reasonable expectation that there was a protective immune response. The skilled person would test whether this was the case by carrying out a challenge experiment.

26.1 The board does not find this argument persuasive. Firstly, the board notes that this argument does not lead to the conclusion that a protective immune response would be present as early as 7 days after immunization, as required by claim 1. The possibility of a protective immune response being generated within 7 days of immunization was not part of the common general knowledge either (see point 25.4 above). Secondly, document D4 equally discloses the presence of an immune response to immunization with MVA-572. Following this line of reasoning would lead to the conclusion that the skilled person equally expected MVA-572 to elicit protection against smallpox within 7 days of immunization.

26.2 According to the opponent, since the antibody level was significantly increased with MVA-BN compared with MVA-572, there was an expectation that the immune response was protective. The board does not find this argument convincing. Apart from the fact that Figure 11 shows antibody levels 2 weeks after immunization whereas the claim requires protection within 7 days at the latest, no information can be drawn from that figure as to the extent of the increase relative to MVA-572. Furthermore, it is not apparent what level of increase in antibody levels would lead to the expectation of a protective level, nor is there any evidence on file in this regard.

26.3 Document D4 discloses that MVA-BN is more immunogenic than MVA-572. Nevertheless, it consistently discloses that prime-boost vaccination is necessary and that a protective immune response is not expected until weeks after the boost vaccination (see page 4, lines 11, 12 and 24 to 28; page 5, lines 19 to 21; page 12, lines 39 to 42; Example 2.2.2.). In the board's view, the

results shown in Figure 11 do not depart from this general teaching. The figure shows antibody titres after MVA-BN vaccination in a prime-boost regime, as indicated by "MVA-BN: MVA-BN" in the figure legend. The conclusions presented in paragraph [0092] are based on the results shown in Figure 11 and include the statement "[...] *vaccinations with MVA-BN significantly enhanced the speed and magnitude of the antibody response* [...]". In the board's view, the correct interpretation of this statement should not be inconsistent with the results shown in the figure or with the general teaching in the document. Thus, this statement does not indicate to the board that there might be a protective immune response at a point in time earlier than 2 weeks.

26.4 Figures 2 and 6 were cited to show an improved immune response generated by MVA-BN versus a prior-art MVA strain, and a 1 000-fold increase in antibody levels even before boost vaccination, respectively.

26.5 Figure 2 depicts the virus titre in ovaries of mice, as a function of the vaccination dose, 4 days post-challenge. As explained in the corresponding Example 2, the experiments were designed to compare MVA-BN with other MVA strains, at various doses (see paragraphs [0086] and [0091]). For this a lethal vaccinia challenge model was used. Vaccination followed a prime-boost regime, with prime and boost spaced 3 weeks apart (see page 12, lines 6 and 7). Challenge followed 2 weeks after the boost. Mice vaccinated with 2 immunizations of either MVA-BN or MVA-575 were completely protected; the efficacy of the strains differed at low doses, with MVA-BN being more potent (see conclusions reported in paragraphs [0089] and [0090]).

In view of both the point in time of the challenge, i.e. 5 weeks after the prime vaccination, and the prime-boost regime, this figure does not indicate to the board that the immune response could be protective as early as 7 days after a single vaccination.

26.6 Figure 6 depicts antibody titres against MVA in immune-compromised monkeys receiving MVA-BN. As explained in Example 2.2.3., the aim was to investigate the impact of three vaccinations with MVA-BN, in a Rhesus monkey challenged with simian immunodeficiency virus (SIV) at week 22 post-prime vaccination. A boost vaccination was delivered at 8 weeks, as indicated by the symbol V2 in Figure 6 (see also page 13, lines 49 and 50). The figure shows antibody titres after the first vaccination for a point in time between V1 and V2. As far as can be recognised from the figure, this corresponds to a time between 2 and 4 weeks after prime vaccination.

Thus, this figure does not show the point in time at which the 1 000-fold increase was measured. Irrespective of the foregoing, for the reasons set out in point 26.2 above the board holds that an increase in antibody titres is not *per se* indicative of protection with a single vaccination as early as 7 days after vaccination.

27. Lastly, the board is not convinced that document D4 already discloses or suggests a single immunization with MVA-BN. Paragraphs [0052] and [0096] were cited in this respect.

27.1 Paragraph [0052] mentions "a vaccine shot". The full sentence reads: "*It has been found by the inventors*

that already a vaccine shot containing an effective dose of only 10^2 $TCID_{50}$ (tissue culture infections dose) of the virus according to the present invention is sufficient to induce complete immunity against a wild type vaccinia virus challenge in mice." The opponent asserted that this passage disclosed a single immunization. However, from the paragraph as a whole it becomes clear that the quoted sentence concerns the amount of virus in a shot rather than the number of shots. This is apparent from the sentences that immediately follow, which state that highly attenuated strains such as MVA-BN were expected to be less immunogenic because of the lower amount of epitopes, and that accordingly it had been surprising that the amount used was nevertheless protective - see page 8, lines 1 to 4, which reads: "*This amount of antigen, carried by the viral particles, was not considered sufficient for induction of a potent immune response. However, the virus according to the invention stimulates even with a very low effective dose of only 10^2 $TCID_{50}$ a potent* [...]". Furthermore, the sentence in question refers to findings in document D4 relating to a dose of 10^2 $TCID_{50}$ in a virus challenge in mice. This dose corresponds to the experiments in Example 2.1. and thus refers to the prime-boost vaccination carried out in that example (see paragraphs [0088] and [0089]).

27.2 The passage at issue in paragraph [0096] reads: "*[...] there was no significant difference in the numbers of CTLs induced to the three epitopes when one immunisation of MVA-BN (10^7 $TCID_{50}$) was used, indicating that a secondary immunisation with MVA-BN did not significantly boost CTL responses.*" The board notes that this passage does not indicate the time of

the measurement, so it does not disclose how early these CTL levels were present.

28. Document D18 is the patent in the case on which decision T 1021/11 is based. Document D19 is document D1 cited in that case. The opponent filed documents D18 and D19 to counter the patent proprietor's argument that decision T 1021/11 was relevant to the case in hand. According to the opponent, the factual situation is so distinct that this decision should not be considered in this case. Since decision T 1021/11 was irrelevant to the board's decision in the case in hand, documents D18 and D19 do not need to be considered any further.

29. In light of the above considerations, the board concludes that the subject-matter of claim 1 of the main request was not obvious with regard to the cited prior art. The same applies to claims 2 to 14, all of which refer back to claim 1.

Order

For these reasons it is decided that:

1. The opponent's appeal is rejected as inadmissible.

2. The decision under appeal is set aside.

3. The case is remitted to the opposition division with the order to maintain the patent on the basis of the following documents: claims 1 to 14 of the main request as filed with the statement of grounds of appeal and

description pages and drawings of the patent as granted.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated