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Datasheet for the decision of 21 September 2021

Case Number: T 0250/16 - 3.3.04

Application Number: 08854338.4

Publication Number: 2211901

IPC: A61K39/145

Language of the proceedings: EN

Title of invention:
Vaccination with multiple clades of H5 influenza A virus

Patent Proprietor:
Seqirus UK Limited

Opponent:
GlaxoSmithKline Biologicals SA

Headword:
Adjuvanted priming influenza vaccine/SEQIRUS

Relevant legal provisions:
EPC Art. 54, 56
RPBA Art. 13

Keyword:
Main request - novelty (yes), inventive step (yes)
Late-filed argument - admitted (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

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 0250/16 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 21 September 2021

Appellant: (Patent Proprietor)	Seqirus UK Limited Point Level 3, 29 Market Street Maidenhead, Berkshire SL6 8AA (GB)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondent: (Opponent)	GlaxoSmithKline Biologicals SA Rue de l'Institut 89 1330 Rixensart (BE)
Representative:	West, Heloise GlaxoSmithKline Global Patents (CN925.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 26 November 2015 revoking European patent No. 2211901 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	R. Morawetz
Members:	D. Luis Alves
	P. de Heij

Summary of Facts and Submissions

I. The appeal by the patent proprietor (appellant) concerns the decision of the opposition division to revoke European patent No. 2 211 901, entitled "Vaccination with multiple clades of H5 influenza A virus".

II. An opposition had been filed invoking the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), under Article 100(a) EPC, as well as the grounds under Article 100(b) and (c) EPC.

III. The decision under appeal dealt with sets of claims of a main request and of auxiliary requests 1 to 8. The opposition division held, *inter alia*, that the subject-matter according to the main request and auxiliary requests 1 to 7 did not involve an inventive step (Article 56 EPC) whereas auxiliary request 8 related to subject-matter extending beyond the content of the application as filed (Article 123(2) EPC).

IV. With the statement setting out the grounds of appeal, the appellant filed sets of claims of a main request and of auxiliary requests 1 to 8, all identical to those underlying the decision under appeal.

V. With the reply to the statement setting out the grounds of appeal the opponent (respondent) made submissions concerning priority, added-matter, novelty and inventive step.

VI. With a further letter dated 2 January 2017, the appellant filed arguments and sets of claims of auxiliary requests 9 to 24.

Claims 1 to 4 of auxiliary request 23 (later to become the main request, see section IX.) read:

"1. An immunogenic composition comprising hemagglutinin antigen from a first clade of H5 influenza A virus, for use in a method for immunizing a subject against influenza virus comprising steps of (i) administering to the subject the immunogenic composition comprising hemagglutinin antigen from the first clade of H5 influenza A virus, and later (ii) administering to the subject an immunogenic composition comprising hemagglutinin antigen from a second clade of H5 influenza A virus, wherein the first and second clades are different from each other, and wherein the composition comprising the first clade antigen is adjuvanted and the composition comprising the second clade antigen is adjuvanted.

2. An immunogenic composition comprising hemagglutinin antigen from a second clade of H5 influenza A virus, for use in a method for immunizing a subject against influenza virus comprising steps of (i) administering to the subject an immunogenic composition comprising hemagglutinin antigen from a first clade of H5 influenza A virus, and later (ii) administering to the subject the immunogenic composition comprising hemagglutinin antigen from the second clade of H5 influenza A virus, wherein the first and second clades are different, and wherein the composition comprising the first clade antigen is adjuvanted and the composition comprising the second clade antigen is adjuvanted.

3. The immunogenic composition of claim 1 or claim 2, where:
• the first clade is clade 1 and the second clade is clade 2.
• the first clade is clade 2 and the second clade is clade 1.
• the first clade is clade 1 and the second clade is not clade 2.
• the first clade is clade 2 and the second clade is not clade 1.

4. The immunogenic composition of any preceding claim, wherein at least one of the immunogenic compositions is a split virion virus."

VII. By letter of 7 October 2019, the board summoned the parties to oral proceedings. In a communication pursuant to Article 15(1) RPBA, the board informed the parties of its preliminary opinion. The board noted, *inter alia*, that document D5 was relied on by the respondent only in the context of lack of novelty and that this document would, even in case of a valid claim by the patent in suit to the earliest priority date, be comprised in the state of the art according to Article 54(3) EPC. Therefore, a decision on the right of priority seemed irrelevant. Subsequently, the oral proceedings were postponed on one occasion and were eventually held by videoconference.

VIII. The appellant and the respondent replied to the board's communication by letters dated 10 March 2021 and 20 August 2021 respectively.

IX. The oral proceedings took place by videoconference with the agreement of both parties.

During the oral proceedings, the appellant made auxiliary request 23 their main request.

At the end of the oral proceedings, the chair announced the board's decision.

X. The following documents are referred to in the present decision:

D1: Nolan *et al.*, IDSA Symposium Abstract LB-4, 13 October 2016.

D3: European Centre for Disease Prevention and Control (ECDC) Technical Report, Expert Advisory Groups on human H5N1 vaccines, August 2007.

D5: WO2008/009309

D8: Li *et al.*, Chang Gung Med J 30(4), July-August 2007, pages 294-304.

D11: Leroux-Roels *et al.*, Lancet 370, August 2007, pages 580-589.

D12: Stephenson, Expert Rev. Vaccines 4(2), 2005, pages 151-155.

D13: WO2006/100110

D17: Stephenson *et al.*, Vaccine 21, 2003, pages 1687-1693.

D19: WO2007/130330

D21: Stephenson *et al.*, N Engl J Med 359, 15, 9 October 2008, pages 1631-1633 and Supplementary Appendix.

XI. The appellant's arguments relevant to the present decision can be summarised as follows:

Admittance of the main request into the appeal proceedings

The respondent's request for the main request not to be admitted was too late, as this claim request had been filed years earlier. It differed from auxiliary request 6 underlying the decision under appeal and filed together with the statement of grounds of appeal, only on account of the deletion of claims 5 to 15. Under the provisions of the RPBA 2007 the request should be admitted. Furthermore, the request addressed outstanding issues, because none of the objections as to lack of novelty raised by the respondent applied to the claimed subject-matter.

Novelty (Article 54 EPC)

Novelty in view of the disclosure in document D5 was challenged for the first time at the oral proceedings. Therefore, this objection should not be admitted into the appeal proceedings.

Document D5 did not disclose the subject-matter of claims 1 and 2 for two reasons. Firstly, the passage on page 92, lines 15 to 30, did not disclose specifically that, in the heterologous prime-boost scheme, the strains used in first and second vaccinations belonged to different clades. Such an embodiment was not directly and unambiguously derivable from the document,

because at least one other reasonable interpretation of the passage was possible. Secondly, in order to arrive at the combination of adjuvanted compositions and strains belonging to different clades, as required by the claims, it was necessary to make two selections: the selection of heterologous prime-boost from the passage on page 92 and the additional selection of adjuvanted composition from the passage on page 9 or on page 38.

Inventive step (Article 56 EPC)
Document D1 as the closest prior art

The claimed subject-matter differed from the vaccination scheme disclosed in document D1 in that the priming vaccine contained an adjuvant.

The effect of this difference was a more rapid immune response to the boosting vaccination, in particular more rapid cross-protection. This was shown in the patent in table I and paragraph [0149]. It could also be seen from document D21, figure 1, panels A and B, as well as from a comparison of the immune response at days 7 and 14, as shown respectively in panels C and D, and the figure in the appendix. Table I of the patent showed, for example, that at day 15 the percentage of patients with hemagglutinin inhibition (HI) titre ≥40 was 90% for the patient group having received adjuvanted priming (group 1), whereas it was 60% for the patient group having received non-adjuvanted priming (group 2). The patent also showed wide cross-protection at day 7 for the patient group 1 whereas 14 days were required for patient group 2. The Committee for Proprietary Medicinal Products (CPMP) criteria for assessing vaccine efficacy were: seroprotection at least 60%, seroconversion at least

40% and increase in geometric mean titre (GMT) of at least 2.5-fold (paragraph [0128] of the patent). The relevance of quickly attaining protection was emphasised in the patent in paragraph [0148].

A comparison with the immunisation scheme disclosed in document D1 was not possible. Therefore, the respondent's argument that such a comparison showed the absence of an improvement in immune response was not correct. The appropriate comparison was between vaccination schemes differing only in the presence of adjuvant, as was the case between groups 1 and 2 in the patent.

The respondent did not provide any reasoning as to why the effect observed could not be extrapolated to other vaccines as claimed. There was no evidence that other adjuvants would not achieve the same effect. Decision T 1797/09 was referred to in this context. In addition, there was nothing in the patent itself pointing to clades or other aspects being of significance to the rapidity of cross-protection.

The respondent's line of argument relating to the methodology of the clinical study, concerning comparability of groups 1 and 2 of the patent in view of varying amount of antigen and additional priming dose, as well as to size of the groups, should not be admitted into the appeal proceedings, as it was put forward at the oral proceedings for the first time.

In any event, this line of argument was contradicted by the authors of document D21, stating on page 1632, right-hand column, that neither the number of doses nor the amount of antigen had any effect on the outcome of the study, and showing on the same page, left-hand

column, that the results were statistically significant.

In view of the technical effect, the objective technical problem was the provision of an improved vaccination scheme which induces cross-protection in response to a boosting vaccine more rapidly.

None of the cited documents D3, D11, D12 or D17 addressed a faster immune response. None of the documents disclosed an effect of adjuvant in the priming vaccine on the immune response to the boosting vaccine. It was contested that the skilled person would expect a faster immune response with the boosting vaccine due to memory B cells resulting from the priming vaccine. The patent reported in paragraph [0149] that no difference in memory B cells was observed between patient groups 1 and 2, at baseline before boosting vaccine. It was unknown how long immunological memory persisted (see document D3, page 13, last paragraph).

Document D5 as the closest prior art

An objection based on this document as the closest prior art should not be admitted into the appeal proceedings.

XII. The respondent's arguments relevant to the present decision can be summarised as follows:

Admittance of the main request into the appeal proceedings

The admittance of a claim request could be challenged at any stage of the proceedings. The request was late

filed and did not resolve the outstanding issues. No justification was presented for the late filing. The objections were known from the decision of the opposition division.

Novelty (Article 54 EPC)

The objection as to lack of novelty in view of the disclosure in document D5 should be admitted under the RPBA 2007 because the claim request at issue had been filed late.

The subject-matter of claims 1 and 2 was disclosed in this document. The passage on page 92, lines 15 to 30, referred to the example preceding it. Therefore, the specific strains used in the example had to be implicitly read into this passage. Thus, the passage disclosed a heterologous prime-boost vaccination scheme using strains belonging to different clades, as required by the claims. Furthermore, adjuvanted compositions were disclosed on page 9, line 2, as well as on page 38, line 4. Different passages of one document could be combined, provided that there were no reasons not to do so. In this context, reference was made to decision T 332/87.

Inventive step (Article 56 EPC)
Document D1 as the closest prior art

The difference between the subject-matter of claims 1 and 2 and the disclosure in document D1 was the presence of an adjuvant in the priming composition.

No technical effect of this difference could be acknowledged, for three main reasons:

Firstly, the available clinical data did not show a stronger immune response with adjuvanted priming, because the patient groups 1 and 2 were not directly comparable and the patient number was too small to draw conclusions. Indeed, each patient group consisted of 12 patients only, as could be seen from document D21, third page of the appendix. As to the comparability of the groups, it could be seen from documents D21 and D17 that not all patients received the same priming dose or number of doses, some having received an additional priming dose at 16 months, which significantly increased the immune response (see document D17). Therefore, it was not known whether differences existed between the groups in terms of the dose and amount of antigen. As to the point in time of raising this objection, reference was made to the reply to the appeal, page 70, paragraph 5, concerning the number of patients.

Secondly, the clinical data in the patent did not show a broader cross-protection. Moreover, any effect based on paragraph [0149] was not present at the priority date claimed by the patent, because a corresponding paragraph was not present in the document from which priority was claimed. Also, document D21 did not show broader cross-protection – a comparison between panels C and D in figure 1 showed no difference between the adjuvanted and non-adjuvanted groups.

Thirdly, the results did not show an effect on the rapidity of the immune response: it could be seen from table I of the patent that the maximum level of immune response was reached at day 15 for both patient groups. This was confirmed in document D21, figure 1, panels A and B.

Furthermore, the patent did not show a direct comparison with the immunisation protocol in the closest prior art disclosed in document D1. Therefore, no technical effect over that disclosure could be acknowledged.

Moreover, it was not credible that any alleged technical effect would be present for the whole scope of the claims. Extrapolations were required in relation to clades, dose, type of adjuvant, number of priming and boosting doses and the form of antigen. As regards the latter, document D3 stated that it could impart a substantial difference.

In view of the above, the objective technical problem was the provision of an alternative immunogenic composition for use in an immunising method.

Even when taking into account the alleged technical effects in the formulation of the objective technical problem, the claimed solution was obvious.

An adjuvant had an effect on the quantity and quality of the immune response. It was already known from document D3 that the presence of adjuvant in a vaccine composition led to broader cross-protection (see points 4.2, 4.9 and page 12, second sentence). Documents D11 and D12 also disclosed an effect of adjuvant on cross-protection. Upon administration of the boosting vaccine the reaction was faster because the organism had previously been exposed to the antigen. Document D3 explained that priming produced immunological memory (see point 5.4, third and fifth paragraphs). The skilled person would expect the immune response to be faster.

An effect of adjuvant in the priming vaccine on the immune response to the boosting vaccine was already known from document D17. This could be recognised from a comparison of the rows in Table 1, showing the antibody titres at baseline as well as after boosting vaccine, in the presence and absence of adjuvant in the priming vaccine. Thus, a stronger response to the priming vaccine led to a stronger response to the boosting vaccine. The skilled person would also expect the immune response to the boosting vaccine to be faster. It was known that adjuvant led to a long-lasting immune response due to memory B cells as well as memory T cells (with respect to CD4+ T cells, see document D13, page 84).

Document D5 as the closest prior art

The appellant relied on paragraph [0149] of the patent for the presence of a technical effect. However, this paragraph was not part of the document from which priority was claimed. Since the priority date could not be validly claimed, document D5 was comprised in the state of the art for the purposes of Article 56 EPC.

The objection to lack of inventive step based on document D5 as representing the closest prior art was raised in response to the board's finding at the oral proceedings that the subject-matter claimed was novel over this disclosure.

XIII. The appellant requested as their main request that the decision under appeal be set aside and the patent be maintained on the basis of the claims filed as auxiliary request 23 by letter dated 2 January 2017.

The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal complies with the requirements specified in Articles 106 to 108 and Rule 99 EPC and is admissible.

Main request
Admittance into the appeal proceedings

2. This claim request was filed with the appellant's letter dated 2 January 2017 (see section VI.) and thus after their statement of grounds of appeal. The parties were notified of the initial summons to oral proceedings before the entry into force of the Rules of Procedure of the Boards of Appeal in the version of 2020. Thus, pursuant to Article 25(3) RPBA 2020, admittance of this claim request is governed by Article 13 RPBA 2007.

3. The request represents an amendment to the respondent's case within the meaning of Article 13(1) RPBA 2007. Therefore, it lies within the board's discretion to admit it, or not admit it, into the appeal proceedings. This discretion is to be exercised in view of, *inter alia*, the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.

4. The request differs from auxiliary request 6, considered by the opposition division in the decision under appeal and filed with the statement of grounds of appeal, in that claims 5 to 15 have been deleted.

5. The request thus consists of a simplification by deletion of claims. There is thus no new subject-matter

which could add to the complexity of the case. It is noted that the admittance of auxiliary request 6 was not contested by the respondent.

6. The respondent argued that no justification had been presented for the timing of the filing, i.e. later than with the statement of grounds of appeal. However, exercising its discretion, the board finds that the simplification introduced by this request in combination with the time that was available to the respondent and the board to consider it justifies its admission in the present case. Thus, neither the state of the proceedings nor the need for procedural economy speak in this case against admitting the request. The respondent further asserted that the request did not solve all outstanding issues. However, the board considers that the request addresses the sole issue of lack of novelty in view of documents D8 and D19 raised with respect to the set of claims of the previous auxiliary request 6.

In the reply to the board's communication under Article 15(1) RPBA, the respondent had argued that the present claim request should not be admitted on account of lack of convergence. This objection must be rejected for the reason alone that the present claim request clearly is convergent as compared to the main request, filed with the statement of grounds of appeal.

Novelty (Article 54 EPC) - Claims 1 and 2

7. The only objection under Article 54 EPC applying to this claim request is based on the disclosure in document D5. It was raised for the first time at the oral proceedings before the board.

8. The admittance of this objection was contested by the appellant. However, in view of the board's conclusion on the issue of novelty (see below), there is no need for the board to give reasons for considering this objection in substance.

9. It was undisputed that document D5 is comprised in the state of the art according to Article 54(3) EPC. It concerns vaccination during an influenza A pandemic and discloses vaccination schemes involving the administration of a priming and a boosting vaccine, which may contain antigen from the same strain (homologous boosting) or may differ in that the antigen is derived from variant or drift strains of the same influenza A virus subtype (heterologous boosting) (see page 9, second and third paragraphs, page 19, first full paragraph, page 33, third paragraph, and page 92, lines 15 to 39). Throughout the document the concept of heterologous boosting is illustrated with reference to a priming vaccine comprising antigen from an H5N1 Vietnam strain and a boosting vaccine comprising antigen from an H5N1 Indonesia strain.

10. The passage on page 92, lines 15 to 30, is immediately preceded by a discussion of the results of the clinical trial (example IV). The parties were in disagreement as to whether the strains used in that example were implicitly to be read into this passage in place of "Vietnam strain" and "Indonesia strain". This is of relevance insofar as the strains used in example IV belong to different clades, as required by claims 1 and 2 of the main request.

11. However, claims 1 and 2 further require that both compositions should be adjuvanted. At the oral proceedings the respondent argued that this feature is

disclosed in document D5, page 9, line 2, as well as page 38, line 4, and that different passages of a document can be combined, provided that the skilled person has no reasons not to do so.

12. The passage on page 9 reads: "*In a specific embodiment, the composition used for the revaccination may be unadjuvanted or may contain an adjuvant, in particular an oil-in-water adjuvant.*" The passage on page 38 reads: "*In one aspect of the present invention, the adjuvanted immunogenic composition for the first administration may be given intramuscularly, and the boosting composition, either adjuvanted or not, may be administered through a different route, for example intradermal, subcutaneous or intranasal.*" Thus, the presence of adjuvant in the boosting composition is one of two possible embodiments. The board is not convinced that the skilled person would derive, directly and unambiguously, from these passages that the embodiment to be applied to the concepts on page 92, and specifically to the concept concerning heterologous boosting, was the adjuvanted boosting composition. To arrive at the combination as claimed, two selections are necessary from the cited passages: the selection of the adjuvanted boosting composition, from adjuvanted and non-adjuvanted, and the selection of heterologous boosting, from homologous and heterologous boosting. Thus, irrespective of the contested reading of the passage on page 92 (see point 10.), the board could not find a direct and unambiguous disclosure of the combined features of the claimed vaccination scheme in document D5.

13. In conclusion, the subject-matter of claims 1 and 2 is novel over the disclosure in document D5.

Inventive step (Article 56 EPC)

14. Claim 1 is directed to a first composition for use in a vaccination scheme in which a second composition is administered at a later point in time, the compositions containing hemagglutinin antigen from a clade of H5 influenza A virus, wherein the clade in the first composition differs from that in the second composition and wherein both compositions comprise adjuvant. Claim 2 is directed to a second composition for the same use as defined in claim 1 (see section VI.).

Document D1 as the closest prior art

15. It was common ground between the parties that, for the assessment of inventive step, document D1 could be taken to represent the closest prior art.

16. This document discloses the concept of prime-boost vaccination in the context of preparation for a pandemic. The concept thus involves a first, pre-pandemic vaccination, with a composition comprising antigen derived from a first strain, and a second, pandemic vaccination, with a composition comprising antigen derived from the strain causing the pandemic. In the study modelling this concept, individuals first received two doses of a composition containing antigen from an influenza A H5N1 clade 3 strain (priming). Eight years later, they received a single dose containing antigen from an influenza A H5N1 clade 1 strain (boosting). The results reported in this document show, at 28 days after boosting, for the primed individuals, a higher geometric mean titre (GMT) of serum antibody measured by hemagglutinin inhibition (HAI), as well as higher response in terms of a 4-fold increase in antibody titre and in terms of a titre at

least 1:40. The authors conclude that priming can result in significant immune responses to an antigenically variant strain of H5N1 influenza virus.

Objective technical problem

17. It was also common ground between the parties that the difference between the claimed subject-matter and the vaccination scheme disclosed in document D1 lies in the presence of adjuvant in the priming composition.

18. There was, however, disagreement as to the technical effect of this difference. In this context the board notes that the appellant requested to not admit the respondent's line of argument based on the methodology of the study. However, in view of the board's conclusion on the issue of inventive step (see below), there is no need for the board to give reasons for considering this line of argument in substance.

19. Whereas the appellant submitted that a faster cross-protection was achieved after administration of the boosting composition, the respondent argued that no improvement could be acknowledged in terms of a stronger or faster immune response. Specifically, as regards a faster immune response, both the patent, in table I, as well as document D21, in Figure 1, panels A and B, showed that the maximum level of immune response was achieved at the same point in time for the adjuvanted and non-adjuvanted groups in the study.

20. The parties directed the board to table I and paragraph [0149] of the patent and to Figure 1 of document D21. Table I shows the results of the "Human study I", in which patients received a boosting vaccine prepared with a strain belonging to influenza A H5N1

clade 1 (see page 34 and following). The priming vaccine had been prepared from a strain belonging to clade 0 and included an adjuvant (patient group 1, results in column G1) or no adjuvant (patient group 2, results in column G2). The board agrees with the respondent that, from table I, it can be seen that the maximum response in terms of percentage of patients with HI titre ≥40 (seroprotection), as well as those with seroconversion, is seen at day 15. However, as argued by the appellant, the table also shows that seroprotection is reached earlier for patient group 1, i.e. the group having received the adjuvanted priming composition. Indeed, taking the percentage of patients with HI titre ≥40, which can be considered to be the parameter that correlates best with protection (see paragraph [0145]), the table shows higher values for group 1 already at day 8 and also at day 15 than for group 2. This effect is further supported in paragraph [0149] of the patent, which reports a more rapid cross-protection for patient group 1, against all clades tested. In that context, cross-protection is the induction of protective antibody responses against viruses that are antigenically distinct from the virus used in the priming vaccine (see e.g. paragraphs [0144], [0146] and [0149] of the patent).

21. Thus, the board concludes that the results reported in the patent support that a faster cross-protective immune response can be attributed to the distinguishing feature.

22. The respondent, however, disputed the results in paragraph [0149] of the patent. Two main reasons were put forward: the paragraph was absent from the document from which priority was claimed; and the patient groups were not comparable and were of a small size.

23. The first reason given is irrelevant in the present assessment, because all documents cited in the context of obviousness, i.e. D3, D11, D12 and D17, were published before the earliest priority date claimed by the patent. Also, document D21 was relied on as technical evidence only.

24. The respondent referred to document D21 to contest the results as reported in paragraph [0149] of the patent. However, as submitted by the appellant, document D21 states that neither the differences pointed out by the respondent, namely the varying amount of antigen and the additional earlier booster, nor the size of the study groups affected the significance of the results (see page 1632, paragraph bridging the two columns). Therefore, the data shown in document D21 do not support the respondent's case.

25. The issue of whether a broader protection can be seen from a comparison of panels C and D of Figure 1 in document D21 does not play a role here. The claim does not require protection against every clade tested, but even a detailed look at this figure does not show the absence of protection. Panel B shows the results of testing with a clade 2.2 strain, which thus belongs to a clade that is different from those used in the priming and in the boosting composition. Also in this case the response is superior for the patient group having received adjuvanted priming. A comparison between panels C and D reveals a higher percentage of patients with a protective titre of 1:40 at day 7 in panel C (at least 80%, for all clades tested, adjuvanted priming) than in panel D (below 60%, for all clades tested, non-adjuvanted priming).

26. In conclusion, contrary to the respondent's submissions, the board finds nothing in document D21 that would contradict the results reported in the patent. On the contrary, the data in document D21 (e.g. panels C and D in Figure 1) support the appellant's case.

27. The respondent contested that any effect could be correlated with the difference with respect to the prior art. They argued that no direct comparison could be made between the results in the patent and those in document D1. Contrary to the respondent's submission, the board holds a comparison of the results in the patent with those in a different clinical study, such as disclosed in document D1, to be neither possible nor required in order to demonstrate an effect attributable to the distinguishing feature. It suffices that comparative tests convincingly show that the effect has its origin in the distinguishing feature and, in the case at hand, this is the presence of adjuvant in the priming composition. This is the case with patient groups 1 and 2 of "Human study I" of the patent, as discussed in points 20. and 24. above.

28. The respondent further argued that an effect observed in the study of the patent cannot be extrapolated to the whole scope of the subject-matter as claimed, which is not restricted to the same virus clades, adjuvant, dose, number of doses or form of antigen.

29. On the basis of the results reported in Table I and paragraph [0149] of the patent, the board has no reason to assume that there would not be faster cross-protection if the priming or boosting composition contained a different clade from that used in the study. It is noted that the effect of faster

cross-protection is reported in paragraph [0149] for all clades tested. Document D3, relied on by the respondent, discloses that sub-unit, split-virion and whole virus vaccines differ in the need for adjuvant in order to induce a cross-reactive immune response. However, it is silent on the effect of the adjuvant on the rapidity of this response. No further evidence or line of argument was put forward by the respondent to support the assertion that a given adjuvant or form of antigen would affect the rapidity of the immune response resulting from the adjuvanted priming.

30. In view of the above considerations, the board agrees with the appellant that the objective technical problem can be formulated as the provision of an improved vaccination scheme which induces cross-protection in response to a boosting vaccine more rapidly.

Obviousness

31. The question that remains to be addressed is whether the skilled person would in an obvious way solve the objective technical problem by including adjuvant in the priming composition.

32. The respondent argued that the skilled person was motivated to use an adjuvant in the priming composition because they knew that the effect observed when the boosting vaccination is administered is merely a result of the level of immune response achieved with the priming vaccination. With an adjuvanted priming vaccination, they argued, the skilled person would expect a rapid immune response to the boosting vaccination because the immune system had previously been exposed to the antigen. The board does not find this line of argument persuasive because it rests on

the assumption that the immune system is exposed to the same antigen by the priming and the boosting compositions. However, according to the vaccination scheme disclosed in document D1 (see point 16. above) and also according to the claimed vaccination scheme, the antigens used in the priming and the boosting compositions are different.

33. The disclosures in documents D3, D11 and D12, insofar as they disclose that the presence of an adjuvant in a first immunogenic composition has an effect on the immune response to that composition, do not provide the skilled person with any information on the immune response to a later administered immunogenic composition comprising an antigenically distinct immunogen and much less on the rapidity of that response.

34. Document D3 was referred to by the respondent in the context of rapidity of the immune response, but fails to address this point. The passages cited read as follows: "*However, even without detectable levels of serum antibodies, there may be some immunological memory that could reduce illness severity or even offer protection in the event of a subsequent challenge by a pandemic virus.*" (point 5.4, third paragraph), and "*There are insufficient data about the duration of immunological memory (Goji et al, 2006), but from first principles an assumption can be made that priming will produce some degree of immune memory and is likely to be worthwhile. The question will remain difficult to answer until the immune correlates of protection are better understood. In addition to affecting the quality of the immune response, adjuvant also appears to prolong its duration.*" (point 5.4, fifth paragraph).

35. As regards document D17, the board notes that it was not argued that the document discloses a faster immune response to a boosting composition in correlation with presence of adjuvant in a priming composition. Instead, it was argued that it discloses a stronger immune response and that the skilled person would have expected the immune response to be faster. The argument was made with reference to Table 1, more specifically with reference to what can be inferred when comparing the results shown in various rows in the table.

36. Table 1 of document D17 shows seroconversion after vaccination with adjuvanted (first, third and fifth columns) or non-adjuvanted (second, fourth and sixth columns) H5N3 vaccine, in individuals primed 16 months earlier with a H5N3 vaccine. The board considers that, comparing the results for day 0 versus day 21, it can be recognised that a higher seroconversion was achieved with the vaccination with adjuvanted vaccine. However, from the table as well as from the text of document D17, the comparison of adjuvanted versus non-adjuvanted vaccine appears to refer to the boosting vaccine (see section 3.1). This means that, even if the same vaccine formulation was used in the boosting as in the priming vaccine, it is not possible to draw conclusions as to the effect of adjuvant in the priming vaccine, because the groups differ additionally in the presence of adjuvant in the boosting vaccine. In any event, no passage of the document was cited which mentions the effect asserted as being disclosed by the respondent. In view of the above, the board is not convinced that the skilled person seeking to provide an improved vaccination scheme which induces cross-protection in response to a boosting vaccine more rapidly would have recognised, without hindsight, in document D17 a pointer to the claimed solution. Indeed,

the document neither links a stronger immune response after the boosting to the presence of adjuvant in the priming vaccine nor mentions a faster immune response.

37. Finally, at the oral proceedings the respondent relied in this context on a passage of document D13, page 84, section IV.5, first sentence, disclosing memory T cells in response to adjuvanted versus non-adjuvanted influenza vaccines. Irrespective of whether this disclosure can be considered to represent common general knowledge, it does not support the respondent's argument, because it does not relate to an effect on cross-reactivity achieved with a subsequent boosting vaccination.

38. The board has not been referred to any evidence describing an effect of the use of an adjuvant in an immunogenic composition on the timeline of the immune response to a later administered antigenically distinct immunogen.

39. The board concludes that starting from the disclosure in document D1 the skilled person would not arrive in an obvious manner at the claimed vaccination scheme.

40. Therefore, the subject-matter of claim 1 involves an inventive step (Article 56 EPC). The same conclusion applies equally to the subject-matter of independent claim 2 and dependent claims 3 and 4.

Document D5 as the closest prior art

Admittance of an objection as to lack of inventive step raised at the oral proceedings

41. This line of attack was put forward at the oral proceedings before the board. In the case at hand, the provisions of Article 13(3) RPBA 2007 apply (see point 2. above). They stipulate that amendments sought to be made after oral proceedings have been arranged are not to be admitted if they raise issues which the board or the other party cannot reasonably be expected to deal with without adjournment of the oral proceedings. The board finds that this is the situation here. Indeed, no assessment of the technical effect, objective technical problem or obviousness in view of document D5 had ever been put forward in the written proceedings (see also section above VII.). The board thus came to the conclusion that the issues to be dealt with would have required an adjournment of the oral proceedings and decided not to admit the objection into the appeal proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent with claims 1 to 4 of the main request, filed as auxiliary request 23 with the letter dated 2 January 2017, and a description to be adapted thereto.

The Registrar: The Chair:

A. Chavinier-Tomsic R. Morawetz

Decision electronically authenticated