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Datasheet for the decision of 6 September 2024

Case Number: T 1803/23 - 3.3.08

Application Number: 16736134.4

Publication Number: 3320101

IPC: C12N15/864, A61K48/00

Language of the proceedings: EN

Title of invention:
Methods and pharmaceutical compositions for expressing a polynucleotide of interest in the peripheral nervous system of a subject

Patent Proprietor:
INSERM (Institut National de la Santé et de la Recherche Médicale)
Université Paris-Saclay
Commissariat à l'énergie atomique et aux énergies alternatives
Assistance Publique-Hôpitaux de Paris (APHP)
Université de Montpellier

Opponent:
Strawman Limited

Headword:
expression in the peripheral nervous system/INSERM

Relevant legal provisions:
EPC Art. 56
RPBA 2020 Art. 13(2)

Keyword:
Late filed evidence - admitted (no)
Inventive step - (no)

Decisions cited:
T 0355/97, T 1213/03, T 1210/05, T 1097/09, T 1797/09, T 0862/11, T 0534/13

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

Case Number: T 1803/23 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 6 September 2024

Appellant: (Opponent)	STRAWMAN LIMITED Orchard Lea Horns Lane Combe Witney, Oxfordshire OX29 8NH (GB)
Representative:	Longland, Emma Louise Venner Shipley LLP 406 Science Park Milton Road Cambridge CB4 0WW (GB)
Respondent: (Patent Proprietor 1)	INSERM (Institut National de la Santé et de la Recherche Médicale) 101, rue de Tolbiac 75013 Paris (FR)
Respondent: (Patent Proprietor 2)	Université Paris-Saclay Bâtiment Bréguet 3, rue Joliot Curie 91190 Gif-sur-Yvette (FR)
Respondent: (Patent Proprietor 3)	Commissariat à l'énergie atomique et aux énergies alternatives Bâtiment "Le Ponant D" 25 rue Leblanc 75015 Paris (FR)
Respondent: (Patent Proprietor 4)	Assistance Publique-Hôpitaux de Paris (APHP) 3, avenue Victoria 75004 Paris (FR)

Respondent: (Patent Proprietor 5)	Université de Montpellier 163, rue Auguste Broussonnet 34090 Montpellier (FR)
Representative:	Icosa 83 avenue Denfert-Rochereau 75014 Paris (FR)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 31 July 2023 concerning maintenance of the European Patent No. 3320101 in amended form**

Composition of the Board:

Chair	T. Sommerfeld
Members:	B. Claes
	A. Bacchin

Summary of Facts and Submissions

I. European patent No. 3 320 101 entitled "*Methods and pharmaceutical compositions for expressing a polynucleotide of interest in the peripheral nervous system of a subject*" was granted in respect of European patent application No. 16 736 134.4, filed as an international patent application published as WO 2017/005806 (application as filed).

II. The appeal lodged by the opponent (appellant) lies from the opposition division's interlocutory decision that the patent with the set of claims of the main request (filed on 23 September 2022) and the invention to which it relates met the requirements of the EPC.

III. With the grounds of appeal, the appellant submitted that the decision under appeal was wrong, *inter alia*, in finding that the subject-matter of claim 1 as granted involved an inventive step (Article 56 EPC).

IV. With the reply to the appeal, the patent proprietors (respondents) maintained the main request and submitted one auxiliary request (auxiliary request 1).

Claim 1 of the main request reads as follows:

"1. An AAV9 vector containing a polynucleotide of interest for use in a method of treatment of a peripheral demyelinating disease by selectively expressing the polynucleotide of interest in myelinating Schwann cells in the peripheral nervous system in a subject in need thereof, wherein the method comprises a step of transducing myelinating Schwann

cells in a peripheral nerve of the subject with said AAV9 vector containing the polynucleotide of interest, wherein the polynucleotide of interest is operatively linked to a promoter sequence and wherein the administration of the vector is done by direct injection into the nerve."

Claim 1 of auxiliary request 1 is identical to claim 1 of the main request, except for the information being inserted that the vector is administered by "direct intrasciatic injection into the nerve" (emphasis added by the board).

V. The parties were summoned to oral proceedings and subsequently the board issued a communication pursuant to Article 15(1) RPBA providing the board's preliminary appreciation of substantive and legal matters concerning the appeal. The board expressed concerns in respect of inventive step in particular.

VI. The respondents made further submissions under cover of a letter dated 19 July 2024 and, subsequently, the appellant replied to this submission.

VII. At the beginning of the oral proceedings the respondents submitted a new experimental report (ER).

VIII. The following documents are referred to in the decision:

D1: Homs J. *et al.*, Gene Therapy (2011), pages 1-9

D2: Hoyng S.A. *et al.*, Gene Therapy (2015), pages 1-14

D3: US 2013/0039888 A1

D10: WO 2015/031392 A1

ER: "Intrasciatic injection on adult mice and teasing analysis"

IX. The parties' submissions and arguments on appeal, insofar as they are relevant for the decision, are taken into consideration in the reasons for the decision of the board below.

X. The parties' requests relevant for the decision of the board were as follows:

The appellant requested that the decision under appeal be set aside and amended such that the patent be revoked. The appellant further requested that the respondents' submissions of 19 July 2024 and the new experimental data, filed at the beginning of the oral proceedings, not be admitted.

The respondents requested that the appeal be dismissed (main request), or, alternatively, that the decision under appeal be set aside and that the patent be maintained with the set of claims of auxiliary request 1, filed with the reply to the appeal.

The respondents also requested that the new experimental data, filed at the beginning of the oral proceedings, be admitted. The respondents further requested that a new objection concerning the therapeutic effect of the vector, according to point 65 of the grounds of appeal, not be admitted and considered in the appeal proceedings. The respondents also requested that, in the event that the board should consider that comparative data are required, that the

burden of proof be reversed to the detriment of the opponent.

Reasons for the Decision

Main request - claim 1 - the claimed invention

1. The patent relates to peripheral neuropathy gene therapy. Specific transduction of non-neuronal cell types in the peripheral nervous system, in particular of Schwann cells, is of great interest for the treatment of demyelinating diseases. Specific cell targeting can be achieved by using viral adeno-associated vectors (AAV), which can enter a particular cell type through its specific receptor. The patent discloses a strong transduction rate of myelinated Schwann cells upon intrasciatic injection of the AAV9 vector in mice and non-human primates with good diffusion of the vector (see the patent, paragraphs [0002] to [0004]).

2. A particular AAV serotype, i.e. AAV9, is claimed in this context, which carries a gene of interest for use in a method for treatment of a peripheral demyelinating disease by selectively expressing the polynucleotide of interest in myelinating Schwann cells. The claim requires the treatment to comprise the direct injection of the AAV9 vector into a peripheral nerve and the transduction of myelinating Schwann cells in the nerve.

Admittance of experimental report (ER) (Article 13(2) RPBA)

3. At the beginning of the oral proceedings before the board, the respondents submitted a new experimental report (ER) entitled "Intrasciatic injection on adult

mice and teasing analysis" and requested that the report be admitted into the appeal proceedings (see sections VII. and X.). The board decided not to take the new ER into account in the appeal proceedings for the following reasons.

4. The respondents did not contest that the submission of the ER constituted an amendment to their appeal case after the notification of a communication under Article 15(1) RPBA, which, in principle, is not taken into account by the board (Article 13(2) RPBA); however, they submitted that there were exceptional circumstances, justified with cogent reasons, which would justify admitting the ER according to Article 13(2) RPBA.

5. According to the respondents, the board's very communication under Article 15(1) RPBA had provided the reason for submitting the additional experimental data, since it gave rise to the need for comparative experiments with the closest prior art for the first time in the context of inventive step, and therefore shifted the burden of proof to the respondents. It was not apparent from the earlier proceedings that such comparative data were required to acknowledge the formulation of the objective technical problem as being that of providing an *improved* AAV therapy for the treatment of peripheral demyelinating diseases. It was established in the case law of the Boards of Appeal, in the context of whether or not a technical effect is obtained, that the benefit of the doubt lay with the patent proprietor, and the burden was on the party contesting inventive step (opponent) to provide comparative data if necessary. The fact that the board requested comparative data thus represented exceptional circumstances which justified the admittance of the ER,

providing the requested comparison between the vectors AAV8 and AAV9, for reasons of equality of treatment of the parties. In addition, in its communication under Article 15(1) RPBA, the board based the opinion on inventive step on document D1 in combination with the common general knowledge, which was also a new aspect if compared with the opposition proceedings.

6. The board does not share this view. The sequence and detail of the parties' submissions in the opposition proceedings and the written part of the appeal proceedings prior to the issuance of the board's communication pursuant to Article 15(1) RPBA demonstrate that the respondents had reason to file evidence of an improved therapeutic effect earlier in the proceedings.

6.1 Even in the notice of opposition the opponent had submitted that document D1, representing the closest prior art, disclosed that the AAV8 vector targets Schwann cells when administered by intrasciatic injection (see point 23) and that, based on the (sole) difference between the disclosure in document D1 (AAV8 vector) and claim 1 as granted (AAV9 vector), the objective technical problem should be formulated as that of providing an *alternative* AAV therapy for treating conditions associated with peripheral nerve myelination (see point 26).

6.2 In the reply, the patent proprietors agreed with the difference identified by the opponent and asserted that the technical effect of this difference was that the AAV9 vector enabled selective expression of a polynucleotide of interest in myelinating Schwann cells in the peripheral nervous system. Accordingly, the objective technical problem was that of providing an

improved vector capable of selectively expressing a polynucleotide of interest in myelinating Schwann cells in the peripheral nervous system (see the reply to the notice of opposition, bottom of page 7 to top of page 8).

6.3 In its preliminary opinion, the opposition division endorsed the identified difference and the technical effect of it as asserted by the patent proprietors, i.e. AAV9 selectively transduced myelinating Schwann cells (points 9.3 and 9.4 of the preliminary opinion). The opposition division formulated the objective technical problem, similarly to that submitted by the patent proprietors, as that of providing an *improved* vector for treating conditions associated with peripheral nerve myelination (peripheral demyelinating disease).

6.4 During the oral proceedings in opposition, the opponent submitted that document D1 taught selective expression in myelinating Schwann cells which could only have been due to transduction of myelinating Schwann cells by AAV8. In the same way as AAV9, the AAV8 vector thus equally selectively transduced myelinating Schwann cells (see minutes of the oral proceedings, point 26).

6.5 In the decision under appeal, the opponent's new argument was dismissed, holding that document D1 did "*not disclose, in a direct and unambiguous way, that the transduction with AAV8 results in selective expression in myelinating Schwann cells. In consequence, this feature of selective expression of the polynucleotide of interest in myelinating Schwann cells provides for a further difference from D1*" (see point 18.3, last two sentences). Consequently, the opposition division continued to base the formulation

of the technical problem on the technical effect of selective expression of the AAV9 in myelinating Schwann cells in the peripheral nervous system, i.e. that of providing an *improved* AAV therapy for treating peripheral demyelinating disease.

6.6 On appeal, the appellant reiterated that the objective technical problem was not to provide an *improved* AAV therapy (see point 60 of the statement of grounds of appeal). In fact, the skilled person understood document D1 as teaching that AAV8 targets (myelinating) Schwann cells (*ibid.* point 62) and, although the burden was on the patent proprietors to provide evidence for their allegation that the preference/selectivity of AAV9 for myelinating Schwann cells was not also provided by AAV8 as the alleged technical effect, they had failed to do so (*ibid.* point 64). Consequently, the patent only provided an *alternative* AAV therapy (*ibid.* point 68).

6.7 In reply, the respondents submitted that document D1 did not disclose that the analysed Schwann cells were myelinating Schwann cells, non-myelinating Schwann cells, or a mixture of both (see first paragraph of point 4.4.1.2 of the reply to the statement of grounds of appeal); in fact, D1 did not report on the existence of the two classes of Schwann cells and accordingly did not distinguish between the two classes in the experiments (*ibid.* page 21, sixth and seventh paragraphs). Hence, D1 did not disclose that AAV8 transduced myelinating Schwann cells and not non-myelinating Schwann cells, or only transduced them poorly (*ibid.* page 21, eighth and ninth paragraphs). In conclusion, the respondents accordingly concluded that "[a] fortiori, *D1 does not teach that myelinating Schwann cells are selectively transduced with their*

AAV8 vector in comparison to non-myelinating Schwann cells" (*ibid.* page 22, first paragraph). Since the patent demonstrated that AAV9 almost exclusively transduced myelinating Schwann cells, the technical effect of the difference between the disclosure in document D1 and the claim was that the AAV9 vector made it possible to selectively express a polynucleotide of interest in myelinating Schwann cells in the peripheral nervous system (*ibid.* page 22, third and fourth paragraphs). According to the respondents, the objective technical problem was thus that of providing an *improved* vector for treating a peripheral demyelinating disease (*ibid.* point 4.4.2).

7. It can be understood from points 6.1 and 6.4 above that, throughout the opposition proceedings, the appellant argued that the objective technical problem was to provide an *alternative* AAV therapy, and has rejected a problem in terms of an *improved* AAV therapy, as maintained by the respondents and the opposition division, because the effect of an improved AAV therapy, as maintained by the respondent, did not appear justified in view of the disclosure in the patent. Also on appeal, the appellant has explicitly submitted that there was no evidence available that the preference/selectivity of AAV9 for myelinating Schwann cells was not also provided by AAV8 (see point 6.6 above) and that the patent therefore only provided an *alternative* AAV therapy.

8. Neither during the opposition proceedings nor in the reply to the appeal (see point 4.7 above) have the respondents submitted such evidence. Instead, they maintained that, because document D1 did not disclose a myelinating Schwann cell selectivity for AAV8, the AAV9 therapy in the claim was improved as compared with the

administration of AAV8 in terms of preference of AAV9 for transducing myelinating Schwann cells.

9. In the communication under Article 15(1) RPBA (see section V.) the board agreed with the appellant, and referred to the general principles established in the case law of the Boards of Appeal that alleged advantages to which the patent proprietor merely refers, without offering sufficient evidence to support the comparison with the closest prior art, cannot be taken into consideration in determining the problem underlying the invention and therefore in assessing inventive step (see Case Law of the Boards of Appeal, 10th edition 2022, referred to in the following as Case Law, I.D.4.3.1 and I.D.4.3.2). Therefore, in order to acknowledge that the AAV9 therapy in the claim constituted an *improved* AAV therapy as compared with the administration of AAV8 in document D1, an appropriate comparison with the closest prior art had to be available which convincingly demonstrated that an alleged technical effect was achieved, i.e., in this case, the technical effect of more selective transduction of AAV9 over AAV8 in myelinating Schwann cells as compared with non-myelinating Schwann cells in the peripheral nervous system. No such evidence was available, however. The board thus agreed with the appellant that the objective technical problem could not appropriately concern an improvement, but had to be formulated as that of providing an *alternative* AAV therapy for treating peripheral demyelinating disease (see also point 18 below).

10. Obviously, therefore, the board's communication under Article 15(1) RPBA was not the first time the need for appropriate comparative data in order to acknowledge an improvement over the closest prior art was raised, as

alleged by the respondents. Therefore, such data could and in fact should have been submitted in the respondents' reply to the appeal at the latest.

11. Also when filing the submission dated 19 July 2024 (see section VI.) the respondents neither submitted nor announced the submission of comparative data, but instead questioned that such data were required in the case in hand (see page 2, framed text) and held that the problem formulated on the basis of the improvement "*should be considered to be solved by the claimed invention since there are no reasons to assume the contrary*" (see page 3, point 1, first paragraph). Furthermore, it was argued that, in the event that the opponent "*disputes the existence of an inventive step, it bears the burden of proof in this respect at first and second instance*" (see page 3, point 2).

12. The board concurs with the respondents that generally each party bears the burden of proof for the facts it alleges; however, it is an established principle in the case law of the Boards of Appeal (see e.g. decisions T 355/97, point 2.5.1 of the Reasons; T 1213/03, point 2.2 of the Reasons; T 1097/09, point 2.3.3 of the Reasons; as well as Case Law, I.D.4.3.1) that if the patent proprietor alleges that the claimed invention provides a given technical effect - an improvement - over the prior art, then the burden of proof for that fact rests upon that party. In the absence of any data confirming the alleged improvement, such an effect cannot be taken into account in the formulation of the technical problem.

13. Nevertheless, the respondents have referred to a number of decisions of the Boards of Appeal (e.g. T 1797/09, point 2.7 of the Reasons; T 862/11, points 6.5 and 6.6

of the Reasons) holding that, as long as the claimed solution was plausibly or credibly solved, it was up to the opponent to submit comparative tests in support of its assertions that an improvement was implausible owing to the lack of evidence; however, in the case in hand, the available data in Example 2 of the patent only allow for the conclusion that the AAV9 vector selectively transduced myelinating Schwann cells as compared with non-myelinating Schwann cells; as regards this selective transduction by AAV9 in comparison with AAV8, no concrete data are available, as was also argued by the appellant. Accordingly, the board considers that a case cannot be made that the claimed solution plausibly or credibly solves the objective technical "improvement" problem of AAV9 over AAV8. The principles referred to by the respondents, and recalled by the cited case law, are not applicable to the present case and therefore cannot justify reversing the burden of proof to the appellant for submitting comparative data demonstrating that the improvement is not achieved, as was requested by the respondents.

14. With regard to the above considerations, comparative data are required in the present case in order to conclude that the claimed subject-matter solves the objective technical problem in terms of an improved AAV therapy, and such data should have been filed with the respondent's reply to the appeal at the latest. The board thus has not seen cogent reasons from the respondents that there are exceptional circumstances for submitting the ER on the comparative data only at the very last moment in the opposition appeal proceedings, i.e. the oral proceedings (Article 13(2) EPC). The board has accordingly not taken the ER into account in coming to its decision on inventive step.

Inventive step (Article 56 EPC)

Closest prior art

15. It was undisputed that the disclosure in document D1 represents the closest prior art for the purpose of assessing whether the claimed subject-matter involves an inventive step following the problem-solution approach.

16. Document D1 discloses the targeting of Schwann cells via intrasciatic injection of AAV8 as a gene-therapy strategy for peripheral myelin disorders (see e.g. the title and abstract, lines 10 and 11). It demonstrates that "*AAV8 mostly infects Schwann cells ... when injected into the sciatic nerve of mice*" and "*that AAV8-driven expression of ciliary neurotrophic factor (CNTF) by mouse Schwann cells increases the expression of myelin protein and improves regeneration of injured sciatic nerve shortly after in vivo transduction*" (see page 1, right-hand column, lines 14 to 20). D1 concludes that "*we provide evidence that intranerve administration of AAV8 is a useful tool for local and specific Schwann cell transduction, and it proves to be efficient for stimulating expression of genes involved in peripheral nerve myelination and regeneration in the injured mouse nerve*." (see page 7, right-hand column, lines 11 to 15).

Differences, technical effect and objective technical problem

17. As concerns the difference(s) between the claimed subject-matter and the disclosure in document D1, it was equally undisputed that one difference was that an AAV9 serotype vector was claimed instead of the AAV8 vector disclosed in document D1. The parties were,

however, in dispute as to whether this was the only technical difference.

18. In the context of the disclosure of the patent, the board understands "selective expression" in the feature "by selectively expressing the polynucleotide of interest in myelinating Schwann cells" in claim 1 as a function of the particular transduction tropism of the particular AAV9 serotype claimed and not as a function of the expression of the particular gene of interest in the vector. Both the opposition division and the respondents on appeal had the same understanding (see decision under appeal, point 14.3, and the reply to the appeal, point 4.1.3.1).

19. The opposition division was satisfied that the claimed AAV9 vector enabled the selective expression of a polynucleotide of interest in *myelinating* Schwann cells. Document D1, however, failed to directly and unambiguously disclose that AAV8 transduction resulted in the selective expression in *myelinating* Schwann cells and, consequently, the feature of selective expression of the polypeptide of interest in myelinating Schwann cells constituted a further technical difference (see decision under appeal, point 18.3). Accordingly, these two identified differences resulted *"in the technical effect of selective expression in myelinating Schwann cells in the peripheral nervous system"* and therefore "*the objective technical problem should be defined as the provision of an improved AAV therapy for treating peripheral demyelinating disease*", thereby thus implicitly dismissing the objective technical problem formulated by the opponent in terms of an *alternative* AAV therapy based only on the difference of the use of AAV9 over AAV8 (see point 18.4 of the decision under appeal).

20. On appeal, the appellant submitted that, even if it was accepted that the transduction by AAV8 and expression took place in non-myelinating Schwann cells in the transduction experiments disclosed in document D1, as was argued by the respondents on appeal, i.e. that it could not be distinguished which Schwann cells were transduced, the objective technical problem still did not need to be formulated in terms of an improvement. Indeed, in that case, no evidence was available that demonstrated that the preference of AAV9 for myelinating Schwann cells was not also exhibited by AAV8 according to document D1, and the onus was on the respondents to provide evidence of an improvement by AAV9 over AAV8. At best, the patent provided evidence that AAV9 transduced myelinating Schwann cells more than other cell types in normal sciatic nerves. There was, however, no evidence to suggest that AAV9 would constitute an improvement in this respect over AAV8 (see grounds of appeal, paragraphs (64) to (66)).

21. The respondents, however, argued that Examples 1 to 4 demonstrated that AAV9 made it possible to selectively express a polynucleotide of interest in myelinating Schwann cells in the peripheral nervous system and thus that the claimed subject-matter solved the technical problem in terms of an improvement. According to the respondents, the burden was on the appellant to provide grounds and evidence that this was not the case, certainly when grounds to assume the contrary were absent. The fact that AAV8 could supposedly also have a preference for myelinating Schwann cells was neither disclosed in document D1 nor based on evidence. Consequently, the problem to be solved should not be reformulated and should be maintained as that of

providing an improved vector therapy for treating a peripheral demyelinating disease.

22. The board agrees with the respondents that it is established case law of the Boards of Appeal that, in general, in proceedings before the EPO each party bears the burden of proof for the facts it alleges. The board also agrees that, in principle, it is not sufficient for an opponent to attack a granted patent based on an unsubstantiated assertion and that at least evidence has to be provided that raises doubts that the problem is solved by the claimed invention (see decisions T 534/13, points 4.2 and 4.3 of the Reasons; T 862/11, points 6.5.4 and 6.6 of the Reasons; and T 1210/05, point 2.3.3 of the Reasons, cited by the respondents in this respect).

23. However, the situation underlying the case in hand is not a situation in which it is the opponent (appellant) alleging a fact, but rather a situation in which the appellant corroborates a fact that the respondents themselves have submitted as being a given, namely, the functionality of AAV9 that it transduces myelinating Schwann cells more than other cell types in normal sciatic nerves and thus allows for selective expression in myelinating Schwann cells in the peripheral nervous system. The board can also agree with the respondents that Examples 1 to 4 support such a fact.

24. In the context of the assessment of inventive step, the operative allegation of fact which needs to be proven is that the claimed AAV9 vector constitutes an *improvement* over the AAV8 vector as disclosed in document D1 and thus justifies the formulation of the objective technical problem in terms of such an improvement. An "improvement" inherently implies a

comparison of one product or process with another, such that it is convincingly demonstrated that the improvement originates from the feature(s) distinguishing the invention from the closest prior art. The "improvement" argument was submitted by the respondents, hence the respondents bear the burden of proof. In the absence of concrete *indicia* rendering the particular improvement of AAV9 over AAV8 credible and in the absence of the demonstration of such improvement, the allegation of fact does not go beyond an unsubstantiated assertion. In the case in hand, the board thus agrees with the appellant that, under the given circumstances, the burden of proof is on the respondents to prove, or at least render credible, the allegation of fact. It is undisputed that such proof or *indicia* are not available from the patent or further citations.

25. Consequently, the objective technical problem to be solved by the claimed subject-matter cannot appropriately be formulated as in point 18.4 of the decision under appeal and endorsed by respondents (see point 4.4.2 on page 22 of the reply to the appeal). On the contrary, the board agrees with the appellant's submission (see point 68 of the grounds of appeal) that it has to be formulated as that of providing an *alternative* AAV therapy for treating peripheral demyelinating disease.

Obviousness

26. With regard to the objective technical problem as formulated above, it needs to be established whether the skilled person would reasonably have expected an AAV9-based vector to constitute an alternative to the AAV8-based vector disclosed in document D1, which, upon

Schwann cell transduction, makes it possible to promote axonal regeneration and myelin protein overexpression in an injured sciatic nerve, a well-known model of peripheral nerve regeneration.

27. The disclosures in document D1 itself, but also in document D2, for example, teach that it was not unusual in the technical field to repeat experiments with vectors derived from different AAV serotypes. Furthermore, AAV9-based vectors were known in the art to transduce Schwann cells in neural tissue (see, for example, document D2, table 3; document D3, paragraphs [0018] and [0022]; document D10, paragraph [0035]). The board accordingly agrees with the appellant that, when seeking an alternative vector to AAV8 in the experiments in D1 that enables targeting of Schwann cells and increases their expression of myelin, the skilled person would try the AAV9 serotype, either as part of a study assessing each of the AAV serotypes in turn or by considering its documented association with the transduction of Schwann cells with a reasonable expectation of similar results to those disclosed for AAV8 in document D1. The board accordingly concludes that the claimed AAV9 vector constituted an arbitrary choice of an obvious alternative to AAV8. Such a choice is obvious to the skilled person.

28. The respondents' arguments on obviousness, in the context of the objective technical problem formulated in terms of an alternative on appeal, are not convincing. Indeed, the respondents have solely based their arguments on the fact that it was unknown and unexpected to the skilled person that an AAV9-based vector was capable of *selectively* expressing a polynucleotide of interest in *myelinating Schwann cells*

in the peripheral nervous system and that this surprising property, which had the advantage of avoiding side effects and loss of vector and polynucleotide upon transduction of non-relevant cell types, was described for the first time in the patent.

29. However, as formulated in point 26. above, what needs to be established in the case in hand is whether the skilled person would have reasonably expected an AAV9-based vector to constitute an alternative to the AAV8-based vector disclosed in document D1 in terms of transduction of Schwann cells and promoting axonal regeneration and myelin protein overexpression in an injured sciatic nerve, and the board has answered this in the affirmative (see point 27.). In the context of the current assessment, contrary to the position of the opposition division (see decision under appeal, point 18.6.14) and of the respondents, the newly discovered property of AAV9-based vectors referred to by the respondents amounts to a so-called "bonus effect", which, even if surprising in scale, inevitably follows from the use of an obvious measure and is obtained by the skilled person without any inventive effort. It has been established in the case law of the Boards of Appeal that, under such circumstances, a bonus effect cannot substantiate inventive step (see Case Law, I.D.10.8).

30. In view of the above considerations, the subject-matter of claim 1 is obvious to the skilled person and thus fails to involve an inventive step (Article 56 EPC).

Auxiliary request 1 - claim 1

31. In claim 1 of this request, the feature "direct injection into the nerve" has been further specified as "direct *intrasciatic* injection into the nerve".

32. Since the experiments disclosed in document D1 concern intrasciatic injections, the conclusion on inventive step of the subject-matter of claim 1 of the main request applies, *mutatis mutandis*, to this claim.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated