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Datasheet for the decision of 23 November 2010

Case Number: T 0456/09 - 3.3.08

Application Number: 00108872.3

Publication Number: 1026253

IPC: C12N 15/87

Language of the proceedings: EN

Title of invention:
Expression of exogenous polynucleotide sequences in a vertebrate

Patentees:
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Opponents:
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Aventis Pharma S.A.
PowderMed Limited
TRANSGENE S.A.
Oxxon Therapeutics Ltd.

Headword:
Polynucleotide transfection/VICAL

Relevant legal provisions:
EPC Art. 76(1), 123(2)

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main request - added subject-matter (no)"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0456/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 23 November 2010

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 19 December 2008 revoking European patent No. 1026253 pursuant to Article 101(2),(3)(b) EPC.**

Composition of the Board:

Chairman: L. Galligani
Members: P. Julià
J. Geschwind

Summary of Facts and Submissions

I. European patent no. 1 026 253 was granted on the basis of European divisional patent application no. 00 108 872.3 which had been filed on 21 March 1990 in accordance with Article 76 EPC on the basis of the earlier European patent applications nos. 90 905 276.3 and 96 104 264.5 published, respectively, as EP 0 465 529 (International patent application WO 90/11092) and EP 0 737 750. The patent was granted with 14 claims, wherein claims 1 and 8 read as follows:

"1. Use of a polynucleotide coding for a polypeptide in the manufacture of a medicament for therapy or immunization of a vertebrate, which polynucleotide is a DNA plasmid or mRNA, wherein the medicament contains **just** said polynucleotide in a pharmaceutically acceptable, injectable carrier, which carrier is liquid, for administration of said polypeptide to cells of the vertebrate by injection of the medicament into the vertebrate, whereby the DNA plasmid or mRNA is incorporated into cells of the vertebrate and provides transitory expression of the encoded polypeptide, to produce a therapeutic or immunogenic effect."

"8. A composition containing **just** a polynucleotide coding for a polypeptide in a pharmaceutically acceptable, injectable carrier, which carrier is liquid, which polynucleotide is a DNA plasmid or mRNA, for use in a method of therapy or immunisation in a vertebrate by administration of said polypeptide to cells of the vertebrate by injection of the composition into the vertebrate, whereby the DNA plasmid or mRNA is incorporated into cells of the vertebrate and provides

transitory expression of the encoded polypeptide, to produce a therapeutic or immunogenic effect."
(bold-type characters added by the board)

Claims 2 to 7 and claims 9 to 14 were specific embodiments of claims 1 and 8, respectively. Claims 2 and 9 characterized the vertebrate as being a mammal and claims 6 and 13 defined the polynucleotide as a DNA plasmid.

II. Eight oppositions were filed against the granted patent on the grounds as set forth in Articles 100(a),(b) and (c) EPC. The opposition division considered the main request and the auxiliary requests 1 to 7 then on file not to fulfil the requirements of Articles 76(1) and 123(2) EPC and, accordingly, revoked the patent.

III. A notice of appeal and a statement setting out the grounds of appeal were filed by the patentees (appellants), who maintained also all claim requests before the opposition division.

IV. Written submissions were filed by opponents 01, 04 and 05 (respondents I, IV and V, respectively) in reply to appellants' grounds of appeal.

V. The board issued a summons to oral proceedings to which a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) was attached. In that communication the parties were informed of the board's preliminary, non-binding views on the issues to be discussed at the upcoming oral proceedings.

VI. The appellants and opponent 02 (respondent II) replied to the board's communication and submitted arguments regarding the opposition ground under Article 100(c) EPC. The appellants filed three versions of a new main request (versions A, B and C), withdrew auxiliary requests 4 to 7 and filed a "Declaration of Dr Sullivan" dated 21 October 2010.

VII. Oral proceedings took place on 23 November 2010 in the presence of only respondents V and VIII (opponents 05 and 08). All other parties had informed the board of their intention not to attend these proceedings.

VIII. Claims 1 and 7 of the **main request version A** read as granted claims 1 and 8, respectively, except for the substitution of the term "*vertebrate*" by "*mammal*" (cf. point I *supra*). Claims 2 to 6 and 8 to 9 were specific embodiments of claims 1 and 7 and read as granted claims 3 to 7 and claims 10 to 14, respectively.

IX. The arguments presented in writing by the appellants, insofar as they are relevant to the present decision, may be summarized as follows:

Articles 76 and 123(2) EPC
The features "just said polynucleotide" and "just a polynucleotide"

The disclosure of a patent application had to be construed with a mind willing to understand. Within the content of a patent application, it was possible to find a variety of inventions and embodiments thereof. Indeed this was the present case, wherein the application as filed and the earlier applications

disclosed several inventions and their embodiments. As a result thereof, the definition given in the application as filed and in the earlier applications for "*a naked polynucleotide*" was not decisive to the question of whether the subject-matter of the main request was directly and unambiguously derivable from these application documents.

The definition of "*a naked polynucleotide*" found in the description of the application as filed and in that of the earlier applications listed two types of exclusions, namely i) any delivery vehicle that could facilitate the uptake of a polynucleotide into a cell and ii) any material promoting cell transfection. This definition of "*a naked polynucleotide*" was broader than that of "*just a polynucleotide*", i.e. a polynucleotide alone in an inert liquid carrier. Indeed, the feature "*just a polynucleotide*" provided a narrower embodiment than that provided by "*a naked polynucleotide*". Within the subject-matter defined as "*a naked polynucleotide*" remained an embodiment which only employed "*just a polynucleotide*" in a liquid carrier as set out in the claims. This was, in fact, the narrowest embodiment of the invention, given that the addition of any non-inert ingredient to the medicament or to the pharmaceutical composition brought these products immediately outside the scope of the claims.

The examples of the application as filed and those of the earlier applications showed that "*just a polynucleotide*" in a (pharmaceutically acceptable, injectable) liquid carrier - and not associated with any transfection promoting material - could enter cells *in vivo* and be expressed therein. Paragraphs [0044] and

[0049] of the description of the application as filed and the corresponding paragraphs of the earlier applications also provided a formal basis for the feature "*just a polynucleotide*" in a (pharmaceutically acceptable, injectable) liquid carrier, i.e. a polynucleotide alone without liposomes and without any other active material. Other interpretations, such as those put forward by the opposition division and the respondents, were contrary to the plain meaning of "*just a polynucleotide*".

The feature "mammal"

It was implicit throughout the whole disclosure that the invention related to the treatment of mammals as well. The components set out for use in therapy were designed for expression in mammalian cells, in particular those used in transient gene therapy which were explicitly described as being functionally active in mammalian cells. The description of the application as filed and that of the earlier applications explicitly stated that the methods and applications described therein could be implemented in all vertebrate systems, comprising mammalian and avian species, as well as fish.

X. The arguments of the respondents, insofar as they are relevant to the present decision, may be summarized as follows:

Admissibility of the declaration of Dr Sullivan

Although filed within the time limit set in the board's communication under Article 15(1) RPBA, the declaration

of Dr Sullivan was late filed at the present stage of the appeal proceedings. The technical issues addressed in that declaration were under discussion from the beginning of the opposition proceedings. Thus, the declaration of Dr Sullivan was not a direct reply to new issues raised only in the board's communication but could have been filed at an earlier stage of the proceedings. Dr Sullivan's partiality was evident from his important position at the patentees' company and thus, his declaration had no probative value. Moreover, the declaration addressed the technical issues under discussion in very general terms and without reference to any prior art document. Dr Sullivan's affirmations and statements were thus not supported by any technical evidence.

Articles 76(1) and 123(2) EPC
The features "just said polynucleotide" and "just a polynucleotide"

The application as filed and the earlier applications disclosed two alternative methods for the introduction of DNA or RNA into vertebrate cells. Whereas one method contemplated the use of liposomes, the other method excluded their use as well as the use of other material promoting transfection, such as viral sequences. In that method, the polynucleotide introduced into the cells was constantly and consistently characterized as a "*naked polynucleotide*" which, according to the definition found in the description of the application as filed and of the earlier applications, was to be free from any delivery vehicle facilitating the entry into the cell. A "*naked polynucleotide*" was defined as being free of viral sequences, particularly viral

particles carrying genetic information, and free from any material promoting transfection, such as liposomal formulations. However, none of the limitations or exclusions found in the application as filed or in the earlier applications for a "*naked polynucleotide*" was contemplated in the main request.

First, the expression "*just a polynucleotide*" could not be equated to "*a naked polynucleotide*". The term "*just*" did not provide any limitation whatsoever with regard to the sequence of the polynucleotide which could thus include sequences, such as viral sequences or sequences facilitating a first (or even a second) uptake of polynucleotides into host cells, that were explicitly excluded in the definition given to the term "*naked*" found in the application as filed and in the earlier applications. The deletion of that term led to the result that the polynucleotide addressed in the claims was no longer characterized by the definition associated with "*a naked polynucleotide*" provided by the application as filed and the earlier applications.

Second, the main request specified that the polynucleotide was not used in isolation but in a pharmaceutically acceptable, injectable carrier which was characterized as being a mere liquid carrier. A liquid carrier, however, did not exclude the presence of transfection promoting agents, such as viral sequences or liposome suspensions, which were yet clearly excluded from "*a naked polynucleotide*" as defined in the application as filed and in the earlier applications. Thus, the subject-matter of the main request went beyond the original content of the

application as filed and that of the earlier applications.

Third, the term "*just*" was found only once in the whole description of the application as filed and in that of the earlier applications. Indeed, it was found - only and exclusively - in the context of immunisation but not in therapy. In that specific context, the term "*just*" excluded the presence of liposomes. This exclusion could not, however, be extrapolated to the main request, in which that term was used out of context and was not associated with any of the limitations contemplated in the application as filed and in the earlier applications.

Fourth, for the assessment of Article 123(2) EPC, it was necessary to clearly define the subject-matter falling within the claims. The term "*just*" had been differently interpreted by the appellants during the prosecution of the patent-in-suit. On the one hand, it had been equated to the term "*naked*", both being equivalent and having the same meaning. On the other hand, it had been described as providing a narrower definition than that of a "*naked polynucleotide*" and representing therefore the narrowest embodiment of the patent-in-suit. In the context of the claims, these different interpretations of the term "*just*" only showed that the claims included subject-matter extending beyond that of the original disclosure of the application as filed and that of the earlier applications, in which all polynucleotides were clearly limited to "*naked polynucleotides*".

The feature "mammal"

According to the established case law, the requirements of Articles 123(2) and 76(1) EPC were very strict and, for a feature to have a support, it had to be directly and unambiguously derivable from the application as filed and be found in the earlier applications. In the application as filed and in the earlier applications, the feature "*mammal*" was only mentioned in the context of immunisation. Although the application documents referred to certain uses in relation to human and veterinary therapy, the exemplified uses with "*mice*" and "*humans*" could not support an intermediate generalization to "*mammals*" in general for therapy. The reference to "*mammalian*" was found in the application as filed and in the earlier applications only when comparing the immune systems of all vertebrates, which was said to be in all vertebrates very similar. However, there was no similar reference in the context of therapy. Indeed, a successful therapeutic treatment for fish (vertebrate) did not imply that it had also to be effective in a mammalian animal (vertebrate).

The combination of features

The combination of features characterizing the claimed medical use was not unambiguously and directly derivable from the application as filed nor found in the earlier applications. The application documents disclosed all sorts of alternative medical uses under two broad concepts, namely i) pharmaceutical products and medical uses based on "*a naked polynucleotide*" and ii) the use of liposomes to introduce polynucleotide sequences into vertebrate cells. However, there was no

disclosure of the specific combination of features as found in claims 1 and 7 of the main request, which could only be derived by selection from several lists. The application documents did not disclose the specific combination but merely listed possible alternative medical uses (therapy or immunization, naked polynucleotide or polynucleotide with liposomes, different administration forms, nature and type of carrier, etc.). An arbitrary selection of members from all those lists could not be unambiguously and directly supported by these lists as such.

XI. The appellants (patentees) requested in writing that the decision under appeal be set aside and the case be remitted to the first instance for further prosecution based on the main request either in the version A, B or C as filed on 22 October 2010.

XII. The respondents (opponents) requested that the appeal be dismissed. Furthermore, they requested during the oral proceedings that the declaration of Dr Sullivan provided by the appellants with letter of 22 October 2010 not be admitted into the proceedings.

Reasons for the Decision

Admissibility of the declaration of Dr Sullivan

1. The declaration of Dr Sullivan was filed by the appellants in reply to the communication of the board pursuant to Article 15(1) RPBA and within the time limit set by the board in that communication. It addresses an issue raised by the board, namely whether,

in the context of the claims, a polynucleotide coding for a viral sequence carrying the genetic information to facilitate entry into a cell would be technically meaningful. The board also noted in that communication that there appeared to be no evidence on file to support the existence of such a polynucleotide.

2. The declaration of Dr Sullivan can only be seen as a direct reply to the question raised in the board's communication and which was identified therein as an important question in the present appeal proceedings. In this declaration, it is *inter alia* stated that there are no reported viral nucleic acid sequences that, as part of a polynucleotide, can act as a delivery vehicle to facilitate entry of a polynucleotide into a cell. In the board's view, the fact that there is no reference to a prior art document to support the statements made in that declaration cannot diminish its probative value. Negative results or the absence of positive results do not usually result in a scientific publication.

3. In *inter partes* cases counterevidence may well be provided by one party in order to show that the statements made by another party are incorrect or tainted with subjectivity. In the present case, nothing has been put forward by the respondents to throw into doubt the statements made in Dr Sullivan's declaration. If, as hinted by the respondents at the appeal oral proceedings, a quick search of the prior art had already retrieved several prior art documents showing that Dr Sullivan's statements were wrong, this documentary evidence should have been filed as soon as possible, giving the board the possibility to exercise its discretion under Article 13(1) RPBA to decide on

its admissibility in appeal proceedings. Moreover, if, as stated by the respondents, the issues raised in the board's communication were under discussion from the beginning of the opposition proceedings, evidence should already be on file to show that Dr Sullivan's statements were incorrect. In the absence of such evidence, the board sees no reason to doubt on Dr Sullivan's statements.

4. Thus, the declaration of Dr Sullivan is admitted into the appeal proceedings.

Main request version A
Articles 76(1) and 123(2) EPC

5. The description of the application as filed and those of the parent and the grandparent applications are identical (all references are made to pages and paragraphs of the published version of these applications). No differences have been identified except for the formulae given on page 17 of the application as filed and on pages 16 and 17 of the parent application, which both differ from those found on page 46 of the grandparent application. However, these formulas illustrate only several liposome-forming materials and they have no bearing to the subject-matter claimed in the main request. Thus, the requirements of Articles 76(1) and 123(2) EPC are treated together when reference is made to the descriptions of these application documents.

6. In the decision under appeal, the opposition division decided that the requests then under consideration did not fulfil the requirements of Articles 76(1) and 123(2)

EPC because it did not see, in the application as filed and in the earlier applications, a support for two features, namely i) the broad meaning of the wording "*just said polynucleotide*" and "*just a polynucleotide*" in claims 1 and 7 and ii) the term "*mammal*" in general. The respondents further contest a support for the combination of the specific features contemplated in claims 1 and 7 (cf. point X *supra*).

The features "just said polynucleotide" and "just a polynucleotide"

7. The description of the application as filed and that of the earlier applications disclose two different methods for delivering a polynucleotide into a vertebrate cell. Whereas one method contemplates the use of the polynucleotide with liposomes, the other method does not contemplate the presence of liposomes but only the "*naked polynucleotide*". The application documents also refer to "*Transient Gene Therapy*" (TGT) and to "*DNA and mRNA Vaccines*" (cf. pages 8 and 13, respectively, of the application as filed) and formulations for both uses are defined as "*Therapeutic Formulations*" in general (cf. page 15 of the application as filed). Indeed, immunisation might well be seen as a preventive therapy.

8. According to the appellants, its main request intends to limit the claimed subject-matter - only and exclusively - to the method that contemplates the use of the polynucleotide without liposomes (cf. point IX *supra*). In fact, when reading claim 1 of the main request, the medicament for therapy or immunisation of a mammal is defined as containing "*just said*

polynucleotide in a pharmaceutically acceptable, injectable carrier, which carrier is liquid", wherein the polynucleotide has been previously defined as being "*a DNA plasmid or mRNA*" (cf. point VIII *supra*). In the context of the claim and from a mere lexical standpoint, the board understands the term "*just*" to be equivalent to the term "*only*", i.e. the medicament is defined as containing "*only*" the polynucleotide in a carrier or, in other words, the polynucleotide "*alone*" in a carrier.

9. This is also in line with the meaning given to the term "*just*" in the description of the application as filed and in that of the earlier applications. Although the term is found only once in the whole description and in the context of immunisation, the term "*just*" directly opposed to the sentence "*without the liposome*", namely "*... the method may be practiced without the liposome, utilizing **just** the polynucleotide in an injectable carrier ...*" (cf. page 6, paragraph [0049], lines 53 to 54 of the application as filed), is understood as being equivalent to "*only*", i.e. the method may be practiced utilizing "*only*" the polynucleotide in a carrier or, in other words, the polynucleotide "*alone*" in a carrier - without liposomes.

10. There is ample support in the application as filed and in the earlier applications for such a method and not only a mere formal support. The examples of all the application documents describe the administration and introduction of a polynucleotide (DNA plasmid or mRNA) in a (pharmaceutically acceptable, injectable) liquid carrier into (rat, mice, human) mammal cells without using liposomes, i.e. "*just the polynucleotide*" in a

carrier or, in other words, the polynucleotide "*alone*" in a carrier - without liposomes.

11. Nevertheless, it is argued by the respondents that the polynucleotides disclosed in the application as filed and in the earlier applications are all "*naked polynucleotides*", whereas those of the main request are not "*naked*" and therefore, they do not contemplate any of the limitations associated to a "*naked polynucleotide*" as defined in the application documents (cf. page 7, paragraph [0052] of the application as filed). For those broader polynucleotides, there is, in the respondent's view, no support in the application as filed or in the earlier applications (cf. point X *supra*).

12. According to the application as filed and to the earlier applications, "*... polynucleotide sequences are naked in the sense that they are free from any delivery vehicle that can act to facilitate entry into the cell ... free of viral sequences, particularly any viral particles which may carry genetic information ... free from, or naked with respect to, any material which promotes transfection ...* " (cf. page 7, paragraph [0052] of the application as filed). Whereas the board agrees that none of these limitations is associated with the polynucleotides of claims 1 and 7 in the main request, the board does not share the conclusions drawn by the respondents from this fact.

13. First, and for the purpose of clarification, the board does not consider the above limitations to exclude the presence of viral polynucleotide sequences in a "*naked polynucleotide*". This strict interpretation is totally

in contradiction with the disclosure of the application as filed and that of the earlier applications which explicitly refer to the possible use of viral polynucleotide sequences, such as promoters, origins of replication, etc (cf. *inter alia* page 8, paragraph [0059] and page 13, paragraph [0099] of the application as filed). The board understands the above limitations only to exclude the presence of a delivery vehicle, or a material promoting transfection, from a "*naked polynucleotide*", be it from a virus (such as viral particles) or from any other source (such as liposomal formulations, precipitating agents, etc.), nothing more and nothing less.

14. Second, the polynucleotide of claims 1 and 7 coding for a polypeptide, and which upon transitory expression in the transfected mammalian cell produces a therapeutic or immunogenic effect, could be envisaged to be itself a delivery vehicle or to contain in itself - as part of the polynucleotide sequence - an additional nucleotide sequence, in particular a viral nucleotide sequence, which is a delivery vehicle or a material promoting transfection. However, according to the declaration of Dr Sullivan "*... there are no reported viral nucleic acid sequences that as part of a polynucleotide could act as a delivery vehicle to facilitate entry of the polynucleotide into the cell ...*" (cf. pages 3 and 4, points 8 and 10, respectively, and page 5, point 14 of the declaration of Dr Sullivan) and therefore, such a polynucleotide is technically not meaningful. There is no evidence on file to contradict the declaration of Dr Sullivan nor have the respondents drawn the attention of the board to any prior art document contradicting the statements made in that declaration (cf. point 3

supra). Thus, the above interpretation of claims 1 and 7 is to be disregarded and the question whether or not it has a support in the application as filed or in the earlier applications is not anymore relevant.

15. Third, several of the readings of claims 1 and 7 put forward by the respondents are considered not to be appropriate and, in any case, not relevant (cf. point X *supra*).

15.1 It has been argued that the polynucleotide of claims 1 and 7 could also carry genetic information (such as encoding viral particles), which upon introduction and expression in a transfected cell, may facilitate, in a second step, the uptake into other cells. This interpretation requires, however, a first uptake and introduction of the polynucleotide into a host cell, the production of the encoded polypeptide, export of that polypeptide from the host cell and interaction of the encoded polypeptide with (other?) polynucleotides to facilitate their uptake and introduction into other host cells. No evidence has been provided to support such a, in the board's view, far-fetched interpretation, in particular to show that the technical requirements involved in a method as suggested were all known and available to the skilled person. Moreover, it is also arguable whether, in such a method, the polynucleotide and the encoded polypeptide can be considered to produce "*a therapeutic or immunogenic effect*" as required in claims 1 and 7. All in all, the board cannot follow this interpretation.

15.2 Claims 1 and 7 have also been read as including several polynucleotides. This interpretation is in

contradiction with the board's understanding of the term "*just*" explained in points 8 and 9 *supra*. It is noted, nevertheless, that the presence of "*additional polynucleotides*" together with a "*naked polynucleotide*" encoding a therapeutic polypeptide or peptide is also contemplated in the application as filed and in the earlier applications (cf. *inter alia* page 12, paragraph [0098] of the application as filed).

15.3 It has also been argued that the definition of the carrier as being a "*liquid carrier*" does not exclude the presence of material promoting transfection, such as precipitating agents or liposomes (cf. point X *supra*). Should this be the case, the subject-matter of the main request would then embrace the two methods disclosed in the application as filed and in the earlier applications for delivering a polynucleotide into a vertebrate cell, i.e. the polynucleotide with liposomes or without liposomes, depending on whether the liquid carrier contains liposomes or not (cf. point 7 *supra*). Both methods are, however, supported by the application as filed and the earlier applications and, in that case, the respondents' interpretation would only show the appellants' failure to limit the claimed subject-matter to a single method as intended.

16. It is noted that some of the above interpretations and the objections correspondingly raised do not appear to relate to Articles 76(1) and 123(2) EPC but, by their nature, to be more related to Article 84 EPC, which is not a ground of opposition. Moreover, in view of the fact that, except for the substitution of the term "*vertebrate*" by "*mammal*" (cf. point VIII *supra*), claims 1 and 7 of the main request are identical to granted

claims 1 and 8, it is questionable whether objections raised for lack of clarity might be allowable nor have they been formally raised by the respondents. Should these interpretations, nevertheless, be considered relevant, which the board is far from suggesting here, they might well have consequences when the requirements of other articles of the EPC are assessed.

The feature "mammal"

17. The features "*mammal*" and "*mammalian cells*" are explicitly found in claim 1 of the application as filed which read "*use of a polynucleotide which directs synthesis of a therapeutic polypeptide in* ***mammalian*** *cells, in the preparation of medicament; wherein said polynucleotide, when introduced in vivo directly into a tissue of a* ***mammal*** *....*" (bold-type characters by the board). Thus, the requirements of Article 123(2) EPC for these features are fulfilled. It remains, however, to assess the requirements of Article 76(1) EPC, since the claims of the earlier applications were different from those of the application as filed.

18. Under the heading "*DNA and mRNA Vaccines*" of the application as filed and of the earlier applications reference is made to the similarity of the immune systems of all vertebrates and "*mammalian*" are explicitly cited therein (cf. page 13, paragraph [0104 of the application as filed). A formal support for immunisation of "*mammals*" is acknowledged by the respondents but a support for the combination of "*mammals*" and therapy is contested (cf. point X *supra*). The board does not share, however, the respondents' view and considers that a formal support for this

combination is found in the application as filed and in the earlier applications.

19. First, treatments by immunisation might be considered to be a particular type of (preventive) therapy. Indeed, under the heading "*Transient Gene Therapy*", references are found in the application as filed and in the earlier applications to "*immunization strategies*" (cf. page 9, paragraph [0073] of the application as filed) for which, as seen above, "*mammalian*" are considered. Second, under the same heading, reference is also made to the possible delivery of the polynucleotide to the interstitial space of tissues of the animal body, wherein the "*uterus*" is explicitly included among several other tissues (cf. page 9, paragraph [0070] of the application as filed). Third, when the possible presence of additional sequences and elements - to be used in conjunction with the polynucleotide (gene of interest) - is discussed, reference is explicitly made to these elements as being "*functionally active in mammalian cells*" (cf. page 12, paragraph [0098] and page 13, paragraph [0099] of the application as filed). Fourth, the application as filed and the earlier applications explicitly acknowledge that, beyond the therapies described, the method of the invention can also be used in "*... animal stock to increase production of milk in dairy cattle ...*" (cf. page 13, paragraph [0102] of the application as filed). Fifth and last, most of the vertebrates, if not all, cited in the application as filed and in the earlier applications under the heading "*Transient Gene Therapy*" as well as those exemplified in all these documents are "*mammals*" (mice, rat and human).

20. In view of all the above considerations, the board is of the view that the skilled person when reading the application as filed and the earlier applications as a whole would have considered the use of the disclosed methods for therapeutic purposes in mammals. A support for that combination is thus directly and unambiguously derivable from all these application documents, even though in an implicit manner (Articles 76(1) and 123(2) EPC).

Combination of features

21. The application as filed and the earlier applications disclose two different methods for delivering a polynucleotide into a vertebrate cell (cf. point 7 *supra*). They also describe in more detail how to perform that delivery as well as appropriate means and suitable elements to carry it out. These disclosures are not lists of possible alternatives but they are described in the application as filed and in the earlier applications, when reading their description as a whole, as possible embodiments contemplated - in an explicit manner - for each of the two disclosed methods. The subject-matter claimed in the main request cannot be seen as a selection, let alone an arbitrary one, but only as a limitation to an embodiment already described in the original disclosure.

22. The board sees no reason to depart from the findings of the opposition division on that issue and considers the contested combination of features to have a formal support in the application as filed and in the earlier application documents.

Conclusion on Articles 76(1) and 123(2) EPC

23. In view of the foregoing considerations, the board considers that the main request fulfils the requirements of Articles 76(1) and 123(2) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution on the basis of the main request version A filed on 22 October 2010.

The Registrar: The Chairman:

A. Wolinski L. Galligani