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TOPIC: O00 Obviousness

SUJET: O00 Évidence

Application No. : 2,514,781

Demande n^{o} 2 514 781

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,514,781 having been rejected under subsection 30(3) of the *Patent Rules* (SOR/96-423) as they read immediately before October 30, 2019, has been reviewed in accordance with paragraph 199(3)(c) of the *Patent Rules* (SOR/2019-251). The recommendation of the Patent Appeal Board and the decision of the Commissioner are to refuse the application.

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INTRODUCTION

[1] This recommendation concerns the review of rejected patent application number 2,514,781 which is entitled "Methods of Gene Therapy for Treating Disorders of the Ear by Administering a Vector Encoding an Atonal-associated Factor" and owned by GenVec, Inc.

[2] The application stands rejected on the ground of obviousness, i.e., non-compliance with section 28.3 of the *Patent Act*. Accordingly, a review of the application has been conducted by the Patent Appeal Board (the Board) pursuant to paragraph 199(3)(c) of the *Patent Rules* (SOR/2019-251). For the reasons provided below, we recommend that the application be refused.

BACKGROUND

The Application

[3] The rejected application was filed on February 19, 2004 and was laid open to the public on September 10, 2004. It concerns a type of gene therapy aimed at treating sensory perception problems in an animal, e.g., hearing loss or balance disorders. As presently claimed, the invention makes use of a particular type of viral vector to deliver a nucleic acid sequence encoding a therapeutic protein to the inner ear. The therapeutic protein is termed "human atonal homolog 1" ("Hath1") and is capable of promoting the development of functional inner ear hair cells. The inventor posits that introduction and expression of Hath1 in the inner ear will generate new hair cells and thereby offset sensory perception problems associated with damage to such cells.

Prosecution History

[4] After several examination reports, prosecution was terminated on July 11, 2016 with the issuance of a Final Action (FA). It explained why the subject-matter of the claims would have been considered obvious to the skilled person, contrary to section 28.3 of the *Patent Act*. A minor claim dependency defect under subsection 87(2) of the *Patent Rules* (as they read immediately before October 30, 2019; now subsection 63(2)) was also identified in the FA.

[5] In its reply to the FA (R-FA) dated January 11, 2017, the Applicant provided a set of claims (proposed claims) it argued ought to be considered allowable. The Examiner

disagreed and referred the application to the Board for review. The Applicant was provided with the Examiner's Summary of Reasons (SOR) for rejecting the application on June 22, 2017.

[6] The present Panel conducted a preliminary review of the application, the claims on file and the prosecution record. We also undertook an assessment of the proposed claims submitted with the R-FA. The results were conveyed to the Applicant in a Preliminary Review (PR) letter dated February 10, 2020. In it, we explained why we were inclined at the time to recommend to the Commissioner of Patents that the application be refused because the subject-matter of both the claims on file and the proposed claims would have been considered obvious to the skilled person. An invitation to provide further submissions and to attend an oral hearing on the matter was also offered.

[7] Further submissions from the Applicant were received in a reply to the PR letter (R-PR) dated April 14, 2020. An oral hearing was held May 1, 2020.

ISSUE

[8] There is one substantive issue in relation to the claims on file: obviousness of the claimed subject-matter, i.e., non-compliance with section 28.3 of the Act. Disposition of the application does not hinge on the claim dependency defect also identified in the FA. In our view, that defect would be remedied if the proposed claims were otherwise compliant with the Act and Rules.

[9] The issue of obviousness focusses on the use of a particular type of adenoviral vector to deliver the nucleic acid sequence of the claimed invention to the inner ear: a serotype 28 adenoviral vector, abbreviated as "Ad28".

LEGAL PRINCIPLES

Obviousness

[10] Section 28.3 of the *Patent Act* requires that the subject-matter of a claim not be obvious:

> The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to

> (a) information disclosed more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and
>
> (b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere.

[11] In *Apotex Inc v Sanofi-Synthelabo Inc*, 2008 SCC 61 [*Sanofi*] at para 67, the Supreme Court of Canada stated that it is useful in an obviousness inquiry to follow the following four-step approach:

> (1)(a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

Should the Claimed Invention be Considered a Selection Patent?

[12] In the PR letter, we explained on page 4 that it was the Applicant's assertion during the course of prosecution that led us to consider the claimed invention as a type of "selection patent". According to *Sanofi* (paras 9-10), a selection patent may be granted in principle for the selection of a specific chemical compound from amongst a larger class of similar compounds that have been disclosed and claimed in an earlier patent. If "a special property of an unexpected character" is associated with the selection, then an inventive step may be acknowledged. A proper selection patent was described by the Court as having three conditions derived from the "*locus classicus*" decision describing them: *In re IG Farbenindustrie AG's Patents* (1930), 47 RPC 289 (Ch. D.).

[13] Our understanding of the presently claimed invention as a selection patent was based on the Applicant's correspondence dated March 27, 2014 saying as much. The ensuing prosecution, including the FA, was consistent with that understanding. In brief, the Applicant's focus on an Ad28 adenoviral vector for use in the invention reasonably

appeared to represent its selection from amongst the known genus of such vectors. Accordingly, a purported special advantage associated with its particular use came under scrutiny in view of case law we took as requiring its disclosure in the specification as originally filed: see *Pfizer Canada Inc v Ranbaxy Laboratories Ltd*, 2008 FCA 108 at para 59; *Eli Lilly Canada Inc v Apotex Inc*, 2007 FC 455 at para 89.

[14] However, in its latest submissions of April 14, 2020, as similarly reiterated at the oral hearing, the Applicant now says that "The present application is not a selection patent" and is "*per se* a patent for the use of Ad28 in generating inner ear hair cells" (R-PR, page 2). We were therefore directed away from the case law on selection patents, including to the extent that it might require disclosure of the advantage in the specification, in favour of approaching the present case as any other type of patent. Because it is not a selection patent, the Applicant's current position is that "no special advantages need be disclosed as of the filing date" (R-PR, page 4).

[15] Accordingly, for the purposes of our final review we will accede to the Applicant's argument and not debate whether the claimed invention ought to be considered a selection patent. Even if it was, we agree that "Selection patents are subject generally to the same rules that apply to any other type of patent" (R-PR, page 5). As acknowledged in the PR letter, we remain aware that it would not differ in its nature from any other patent and "a determination that the conditions for a selection patent have not been met does not constitute an independent basis upon which to attack the validity of a patent": see *Eli Lilly Canada Inc v Novopharm Limited*, 2010 FCA 197 stated at paras 27-28.

Advantages Associated With an Invention and Post-Filing Activities

[16] The Supreme Court in *Sanofi* indicated at paras 77-78 that considering the claim alone may in some cases not be sufficient to determine its inventiveness. The inventive concept of the claim in that case (a bare chemical formula) was determined to include an advantage disclosed in the specification that was associated with it.

[17] As indicated in the PR letter, the weight given to an applicant's post-filing recognition of advantages associated with an invention is of consequence. The courts have indicated, even outside the context of a selection patent, that such a factor is of secondary importance and is of "limited usefulness in considering inventive ingenuity as of the date of the invention": see *Janssen-Ortho Inc v Novopharm Ltd*, 2006 FC 1234 at paras 113-114, aff'd 2007 FCA 217 [*Janssen-Ortho*].

[18] Finally, we are not aware of any binding authority that stands for the proposition that an inventor can secure a patent for an invention based on an inventive step taken post-filing. Although the Supreme Court indicated in *Sanofi* (para 70) that the actual course of conduct which culminated in the making of the invention is a valid consideration in the obviousness inquiry, we do not see how that can be taken to include activities undertaken post-filing because the inquiry is conducted as of the claim date.

ANALYSIS OF THE CLAIMS ON FILE

The Person of Skill in the Art and the Common General Knowledge

[19] In the PR letter, the person of skill in the art was described in the same manner as it was in the FA: "as a researcher with experience in molecular biology and gene therapy". Since the Applicant did not take issue with this assessment in the R-PR or at the hearing we will proceed on the understanding that it is not contested.

[20] In the PR letter, the common general knowledge was also described as it was in the FA; that is, as including knowledge of the existence of some 51 serotypes of adenoviruses:

> The person skilled in the art would possess CGK in the construction of gene expression vectors available in the art (see paragraphs [0018]-[0048] of the description of the instant application), promoters available in the art (see paragraphs [0051]-[0056] of the description of the instant application), atonal-associated factors available in the art (see paragraphs [0044]-[0047] of the description of the instant application) and information pertaining to sensory hair cells available in the art (see paragraphs [0011]-[0014] of the description of the instant application). In addition, the person skilled in the art would have CGK of adenoviral serotypes, such as the adenoviral serotypes 1-51 which are available from the ATCC (see paragraph [0024], second last line of the description of the instant application).

[21] This proposed characterization of the common general knowledge was not disputed in the R-PR. Any disagreement concerning knowledge of an Ad28 serotype vector appears to stem from denial of its disclosure in the cited prior art reference (discussed below), not as a denial of its existence as a matter of common general knowledge. To this knowledge we would add, as suggested in the R-PR (page 3), that the "adenoviral vectors most commonly used are Ad2 and Ad5".

[22] Accordingly, we take it that the skilled person would have knowledge of the various types of adenoviral vectors, including the Ad28 serotype, but would regard the Ad5 and Ad2 serotypes types as the ones more commonly known to deliver a nucleic acid sequence

encoding a therapeutic protein into cells.

Identify the Inventive Concept of the Claim in Question

[23] Having reviewed the R-PR, and acceding to the Applicant's argument that we not treat the present invention as a selection patent, we do not see how the Applicant's arguments could change the inventive concept as stated both in the FA and in the PR letter.

[24] The FA rejected all 36 claims on file for obviousness. In the R-FA the dependent claims on file were not argued to represent non-obvious subject-matter for reasons that differ from the independent claims. In relation to the claims on file, we therefore proceed with our analysis on the understanding that all claims either stand or fall together.

[25] The analysis provided in the FA focussed on the two independent claims. Both are medical "use" claims that differ only in their format. Claim 1 is illustrative:

> Use of a serotype 28 adenoviral vector (Ad28) for changing the sensory perception of an animal, wherein the Ad28 adenoviral vector comprises a nucleic acid sequence encoding human atonal homolog 1 (Hath1) operably linked to a promoter that functions in supporting cells of the inner ear, wherein the nucleic acid sequence is expressed to produce Hath1, resulting in generation of sensory hair cells that allow perception of stimuli in the inner ear.

[26] In the PR letter, we agreed with the FA's understanding of the inventive concept, which was stated more or less as a paraphrase of the claim:

> Based on a reading of the specification, the person skilled in the art, in light of their CGK, would consider the inventive concept of these claims to be a serotype 28 adenoviral vector (Ad28) encoding human atonal homolog 1 (Hath1) gene operatively linked to a promoter that functions in supporting cells of the inner ear for changing the sensory perception of an animal by generating sensory hair cells that allow perception of stimuli in the inner ear.

[27] It was notable to us that it does not include a purportedly unexpected advantage associated with the use of an Ad28 serotype vector. A purported advantage described in a declaration by the inventor (Dr. Douglas E. Brough) dated February 24, 2009 was based on the results of experiments he conducted after filing: "the Ad28 and Ad35 vectors exhibited enhanced delivery to the utricle cultures, as compared to the Ad5 vector" and "the Ad28 vector exhibits enhanced delivery to utricle tissue as compared to the Ad5 vector". Since the Applicant seemed to rely heavily on the purported advantage to establish non-obviousness during prosecution, the PR letter dealt to a considerable extent with the question of whether it ought to be included as part of the inventive concept. We preliminarily concluded that it

should not.

[28] Based on our understanding of the Applicant's position at the time that the claimed invention is a type of selection patent, we explained in the PR letter that the purported advantage should not be included in the inventive concept because (1) it was discovered only after filing; and as a separate consideration, (2) it was not properly disclosed in the specification as filed. We do not see how this conclusion could change by not describing the claimed invention as a selection patent.

[29] In the R-PR, the Applicant has argued that the purported advantage need not be disclosed in the specification as filed because the invention is not a selection patent. However, it has not fully explained why the inventive concept must nonetheless include it. Rather, the Applicant suggested "the advantage from use of Ad28 over the rest of the genus was indeed possessed by the serotype as of the filing date" (R-PR, page 5). That does not explain why the discovery of an advantage after filing would merit consideration as part of the inventive concept, or more generally, as part of an obviousness inquiry conducted as of the claim date.

[30] The Applicant has shifted tact and now suggests that "[t]he inventive step of the present application is the finding that different serotypes of the adenovirus (i.e. different from Ad5) have utility/efficacy in aiding the generation of inner ear hair cells" (R-PR, page 3). In limiting the claim to the Ad28 serotype, the Applicant goes on to suggest that it is "claiming less than one [it] is entitled to claim" (R-PR, page 4).

[31] However, neither the description nor the claims suggest the invention broadly concerns, for example, "the use of serotypes of adenovirus different from Ad5". The inventive concept is not changed by limiting the claims to Ad28. Further, neither the description nor the claims explicitly mention an advantage that might be associated with its use. Even if the skilled person were to refer to the description, they would not understand the claimed subject-matter to include a benefit or advantage associated with the use of an Ad28 serotype vector.

[32] We therefore proceed with the same inventive concept set out in the PR letter.

<u>The Differences Between the Matter Cited as Forming Part of the "State of the Art" and the Inventive Concept of the Claim</u>

[33] One prior art reference, document "D1", was cited in the FA: WO 00/73764 A2, published

December 7, 2000. According to the FA (pages 3-4), document D1 discloses:

> [c]ompositions for generating hair cells, for promoting mechanoreceptive cell growth and for treating hearing impairment or imbalance comprising a vector (e.g. a replication deficient adenoviral vector) encoding an atonal association factor, such as Math1 or Hath1 (see pages 9, 27-28, 32-34, 71-72 and examples 14-15). A number of promoters are disclosed in D1 for expressing the atonal association factor, including those specific for cells of the inner ear (see page 7, line 8, or page 30, line 20). D1 discloses specific examples of their invention using Ad5 vectors (see examples 14-15), and throughout the description of D1, adenoviral vectors in general (which encompass Ad28 vectors) are referred to (see page 33, line 5 or page 96, lines 11-13 for example). D1 does not disclose the Ad28 serotype vector by name.

[34] In the PR letter we concluded that the singular difference between the inventive concept and D1 is the following: the inventive concept specifically relies on the use of a certain serotype of adenoviral vector, serotype 28 (i.e., "Ad28"), to deliver a nucleic acid sequence encoding human atonal homolog 1 (Hath1) to the inner ear, *whereas D1 is generic in its description of adenoviral vectors* (with the exception of the Ad5 serotype) and does not specifically discuss the Ad28 serotype.

[35] In the R-PR (page 3), the Applicant argued that D1 does not disclose that adenoviral vectors other than Ad5 can be used to deliver a nucleic acid to the inner ear. It argues that only the more commonly known Ad5 serotype is disclosed, and that lesser known types are not taught or suggested:

> There is no support in the description of D1 for the use of any adenoviral vector serotypes other than Ad5, let alone Ad28.
>
> Only one serotype is mentioned in D1, that of Ad5, in Example 14 (of 22 examples) on page 97 of the description. Indeed, it was only referenced once in passing as "Ad5-transformed human embryonic kidney cell lines have been developed to provide the essential viral proteins in trans."
>
> . . .
>
> [l]esser known serotypes for use in the generation of hair cells that allow perception of stimuli in the inner ear were <u>not</u> contemplated, taught or suggested in D1 as of the filing date.

[36] We disagree. The FA refers to page 96 lines 11-13 of Example 14 of D1 which, in our view, the skilled person would regard as generic in its discussion of adenoviral vectors despite the fact that the example goes on to discuss the use of the Ad5 serotype in particular:

> Human adenoviruses are double-stranded DNA tumor viruses with genome sizes of approximate 36 kb. As a model system for eukaryotic gene expression, adenoviruses have been widely studied and well characterized, which makes them an attractive system for development of adenovirus as a gene transfer system. This group of viruses is easy to grow and manipulate and they exhibit a broad host range *in vitro* and *in vivo*. [emphasis added]

[37] More generally, D1 also discloses at page 33, lines 5-7 (and in claims 28-29) the use of any suitable viral vector, including adenoviruses writ large: "In a specific embodiment said viral vector is an adenovirus vector, a retrovirus vector, or an adeno-associated vector, including a lentivirus vector, Herpes virus vector, alpha virus vector, *etc*."

[38] In our view, the skilled person would therefore regard D1 as acknowledging the use of adenoviral vectors in general, and as suggesting that members other than Ad5 are suitable for delivering a Hath1 nucleic acid to the inner ear. Although the skilled person might see the Ad5 serotype as preferred, D1 does not direct the skilled person away from using alternate adenoviral vectors.

[39] Any doubt that known specific alternatives to the Ad5 serotype were available to the skilled person is dispelled through the disclosures of a document cited earlier in prosecution but apparently not pursued in view of a response from the Applicant that characterized the invention as a selection patent. Since the Applicant no longer asserts that the claimed invention is a type of selection patent, the document may again be considered pertinent to the obviousness analysis.

[40] Document D9 (United States patent 6,492,169, published December 10, 2002) was cited in a report dated September 27, 2013 to bolster the case for obviousness when combined with D1. D9 was said to disclose Ad28 as an attractive adenoviral vector because "the percentage of the population that has neutralizing antibodies to Ad28 is very low (at 13%) relative to other human adenovirus (see example 1 and figure 1)". The Applicant replied March 27, 2014 by saying D9 was irrelevant because it "only discloses serotype 28 adenovirus in the context of comparing its seroprevalence in humans to the adenovirus serotype that was actually selected for the complementing cell line, i.e., serotype 35". Further, it "suggests that Ad28 would not be an ideal serotype to use for therapeutic purposes because it has a higher percentage of neutralization in a given geographic area" (page 3; underlining added).

[41] In our view, the skilled person would understand from D9 that using an adenoviral serotype with low seroprevalence in the population would be an attractive alternative to using an

Ad5 serotype vector because, *relative to Ad5*, their efficacy would be less impaired by pre-existing host antibodies:

> [r]ecombinant El-deleted adenoviruses based on Ad35 or one of the other above mentioned serotypes have an important advantage compared to recombinant vectors based on Ad5 with respect to clearance of the viruses by neutralizing antibodies. [D9, col. 7, lines 16-20; emphasis added]

[42] As the Applicant suggests, the Ad28 serotype admittedly might not be regarded by the skilled person as the single best alternative to Ad5. Ad35 would seem to claim that privilege. Nonetheless, the skilled person would see it as attractive alternative because it would still have less seroprevalence relative to Ad5, regardless of its geographic use.

[43] Therefore, with respect to D1, the difference between the matter cited as forming part of the "state of the art" and the inventive concept of the claim remains unchanged from the PR letter: D1 is generic in its description of adenoviral vectors (with the exception of the Ad5 serotype) and does not specifically discuss the Ad28 serotype.

[44] If there is a need to more firmly establish that alternatives (including the Ad28 serotype) to the Ad5 serotype vector exemplified in D1 were known to the skilled person, that, in our view, has clearly been done through D9.

Viewed Without any Knowledge of the Alleged Invention as Claimed, Does This Difference Constitute a Step Which Would Have Been Obvious to the Person Skilled in the Art or Does it Require any Degree of Invention?

[45] In the PR letter, we preliminarily concluded that no inventive step had been taken as of the relevant date and the invention now claimed represents an arbitrary selection of subject-matter that would have been obvious to the skilled person in view of document D1. Having heard from the Applicant and considered its latest submissions, we remain of that view, even if the invention is not described as a selection patent.

[46] It warrants first clarifying that the actual course of conduct that culminated in the making of the invention now claimed includes key activities and a realization that occurred only after filing. They are therefore not relevant to the analysis. The Applicant has not disputed that the claiming of the Ad28 serotype is based on the inventor's experiments conducted post-filing, as described in his declaration.

[47] Moreover, nothing in the description supports the conclusion that the inventive step taken

as of the relevant date included these activities. As mentioned in the FA, the description does not mention the use of an Ad28 serotype vector in particular. No specific information concerning the use of an Ad28 serotype vector for changing the sensory perception of an animal is disclosed, making it difficult to see how the skilled person would regard its use in the claimed invention as remarkable. If anything, the description is equivalent to the teachings of D1. Like D1, it too exemplifies only the use of an Ad5 serotype vector and suffers from the same shortcomings noted by the Applicant: there is no "knowledge or expectation that the use of any modified serotype would be 'more beneficial…less beneficial, or toxic, or otherwise useless'" (R-PR, page 3).

[48] Secondly, as explained above, the Applicant's latest submissions as they may relate to the inventive concept do not change its nature. The inventive concept of the claims on file does not relate to the use of serotypes of adenovirus different from Ad5. It focusses on the use of the Ad28 serotype. The purported advantage associated with its use does not form part of the inventive concept. Although "the advantage from use of Ad28 over the rest of the genus was indeed possessed by the serotype as of the filing date" (R-PR, page 5), it was discovered only after filing (see again the Brough declaration). We therefore also decline to give that consideration any weight, per *Janssen-Ortho, supra*.

[49] Setting those considerations aside and turning to the state of the art, we note that the Applicant has most recently again argued that D1 fails to disclose or suggest the use of an Ad28 serotype vector. For that reason the claimed subject-matter is said to be both novel and non-obvious:

> Since adenoviruses other than Ad5, such as Ad28, for use in the generation of hair cells that allow perception of stimuli in the inner ear was not disclosed or even contemplated in D1, the present subject matter is both novel and non-obvious in view of D1.[R-PR, page 4]

[50] However, the shortcomings of D1 have been acknowledged in the FA, in the PR letter, and again as part of this final review. The issue here is obviousness, not novelty. It is therefore understood that there must exist a gap in the teachings of any one piece of prior art. That gap is admittedly D1's failure to specifically disclose the use of an Ad28 serotype vector. Yet, as explained above, we are of the opinion that the skilled person would consider D1 to be generic in its disclosure of adenoviral vectors. As a starting point, this suggests that the skilled person reading D1 would have understood that a vector other than the one specifically exemplified in D1 (the Ad5 serotype) could be used to deliver a Hath1 nucleic acid to the inner ear.

[51] The Applicant's arguments also appear to overlook the fact that an Ad28 serotype vector was known as a matter of common general knowledge. It would be one of the 51 possible alternatives suggested and claimed in D1. Considering D1 in light of the common general knowledge would therefore appear to account for all aspects of the inventive concept. In our view, it would have been obvious to the skilled person that available and commonly known adenoviral vector alternatives to Ad5 would be suitable to deliver a nucleic acid sequence encoding human atonal homolog 1 (Hath1) to the inner ear, including Ad28.

[52] The skilled person's knowledge that the Ad5 and Ad2 serotypes types are the ones more commonly known does not mean that the use of alternative vectors, such as the Ad28 serotype, would be considered non-obvious. As explained in *Eli Lilly Canada Inc v Apotex Inc*, 2018 FC 736 at para 120:

> As Justice Hughes stated in *Shire Biochem Inc v Canada (Health)*, 2008 FC 538 at paragraph 80, "the existence of a number of possible routes to solve a problem does not mean that the route taken was not obvious." This statement was endorsed by Justice Barnes in *Janssen Inc v Teva Canada Limited*, 2015 FC 184 [*Janssen*] at paragraph 113. Justice Barnes also endorsed the notion that "a route may be an obvious one to try even if it is not possible to be sure that taking it will produce success, or sufficient success to make it commercially worthwhile" (*Janssen* at para 113, citing *Brugger v Medic-Aid Ltd*, [1996] RPC 635 at p 661).

[53] In other words, electing to use any one of the known serotypes of adenoviral vectors, including Ad28, would therefore be open to the skilled person and would not require any degree of invention.

[54] To go further, D9 also specifically discloses a variety of known adenoviral vectors, including Ad28, and teaches motivation to adopt less common ones, such as Ad28, as an alternative that overcomes known sero-reactivity problems associated with more commonly known serotypes, such as Ad5. In our view, any potential gap remaining in the teachings of D1 and the common general knowledge would have been bridged by the skilled person's knowledge of D9.

Conclusion on the Claims on File

[55] In view of the above, we conclude that the subject-matter of the claims on file would have been obvious to the skilled person as of the relevant date, contrary to section 28.3 of the *Patent Act*.

ANALYSIS OF THE PROPOSED CLAIMS

[56] In the R-FA, the Applicant submitted 32 proposed claims in an effort to obviate the rejection of the application. In the PR letter, it was our preliminary opinion that they would not remedy the obviousness defect dealt with above in relation to the claims on file. The R-PR provided no submissions in relation to the proposed claims. Our final opinion therefore relies on our earlier analysis, as reiterated below. In brief, the proposed claims incorporate features that would have been obvious to the skilled person, even when combined with the features of the claims on file, in view of additional state of the art references.

[57] Of the proposed claims, only claims 1, 3, 4, 17, 19 and 20 were specifically argued in the R-FA to define non-obvious subject-matter on the basis of their newly incorporated features. The proposed claims argued to be non-obvious fall into two groups: independent claims 1 and 17, and dependent claims 3, 4, 19 and 20. Because the remaining claims neither were argued nor appear to recite additional features that could lend patentability to the claims, they are considered to either stand or fall together with the claims of each grouping, as the case may be.

The Person of Skill in the Art and Their Relevant Common General Knowledge

[58] The person of skill in the art and their relevant common general knowledge remains as stated in respect of the analysis provided above for the claims on file.

The Inventive Concept of the Claims in Question

Independent Claims 1 and 17

[59] Claims 1 and 17 are independent claims drafted in medical "use" format. Apart from their differing formats, they are otherwise identical. Proposed claim 1 is representative; it reads:

> Use of a serotype 28 adenoviral vector (Ad28) for changing the sensory perception of an animal, wherein the Ad28 adenoviral vector comprises a nucleic acid sequence encoding human atonal homolog 1 (Hathl) operably linked to a promoter that functions in supporting cells of the inner ear, wherein the nucleic acid sequence is expressed to produce Hathl, resulting in generation of sensory hair cells that allow perception of stimuli in the inner ear, wherein the adenoviral vector is replication deficient and comprises an adenoviral genome having a deficiency in at least one replication-essential gene function of the El region and comprises a deficiency in at least one replication-essential gene function of the E4 region and comprises a spacer in the E4 region.

[60] In relation to claim 1 on file, the R-FA explains that the proposed claim places four additional limitations on the adenoviral vector of the invention:

1. the adenoviral vector is replication deficient;
2. the adenoviral genome has a deficiency in at least one replication-essential gene function of the El region;
3. the adenoviral genome comprises a deficiency in at least one replication-essential to gene function of the E4 region; and
4. the adenoviral vector comprises a spacer in the E4 region.

[61] A revised inventive concept for proposed claims 1 and 17 therefore takes into account these four additional features.

Dependent Claims 3, 4, 19 and 20

[62] The R-FA specifically points out that dependent claims 3, 4, 19 and 20 recite features not considered in the FA. Claims 3 and 19 depend from claims 1 and 17, respectively, and specify that the promoter of the independent claim is a "CMV" promoter—meaning a promoter derived the "**C**yto**m**egalo**v**irus". Claims 4 and 20 themselves depend from claims 3 and 19, respectively, and further specify that the CMV promoter is the "immediate-early" CMV promoter.

[63] In addition to the four features mentioned above in relation to proposed claims 1 and 17, the inventive concepts of dependent claims 3, 4, 19 and 20 further include their features.

The Differences Between the Matter Cited as Forming Part of the "State of the Art" and the Inventive Concepts of the Claims

[64] In addition to document D1, discussed above, the SOR indicates that two other prior art references (referred to hereinafter as documents D2 and D3) form part of the state of the art for the purpose of assessing the proposed claims. The first is document D2: D.E. Brough et al, *A gene transfer vector-cell line system for complete functional complementation of adenovirus early regions El and E4,* J. Virol., 70: 6497-6501, 1996. The second is document D3: United States patent 5,851,806, issued December 22, 1998.

[65] The SOR (page 2) explains that document D1 is relevant to the analysis of the proposed

claims since, in addition to the features recited in relation to the claim 1 on file, it further discloses the new features the Applicant has incorporated into the proposed claims:

> In Example 14 of D1, the use of replication-deficient adenoviruses is disclosed. In addition, the specific genes which can be disrupted to produce said vectors, including the El and E4 regions, are disclosed. Dl does not specifically disclose a replication-deficient adenovirus vector comprising the specific combination of an adenoviral genome having a deficiency in at least one replication-essential gene function of the El region and comprising a deficiency in at least one replication essential gene function of the E4 region and comprising a spacer in the E4 region; however, these features are derived from dependent claims and, as stated in the Final Action, are readily apparent to the person skilled in the art.

[66] According to the SOR (page 2), documents D2 and D3 are also relevant:

> Replication-deficient adenovirus vectors with disruptions in the El and E4 regions and a spacer in the E4 region are well known in the art. For example, [document D2] discloses vectors with these feature and their advantages. Also refer to [document D3] as highlighted in paragraph 28 of the instant description.

[67] In relation to the CMV promoter features recited in dependent claims 3, 4, 19 and 20, the SOR (page 2) points out that they too are disclosed as preferred embodiments in Dl: see the Summary of the Invention (page 9, lines 20-22) and Example 15.

[68] Having reviewed the cited documents, we are satisfied that they have been accurately summarized in the SOR. We would add that D3 specifically discloses all of the newly recited features of proposed claims 1 and 17 in combination, at least in Examples 2 and 3, as well as in claims 32 and 36. Figures 2 and 3 of D3 also disclose the use of a CMV promoter in combination with the features recited in proposed claims 1 and 17.

[69] Therefore, apart from the select use of an Ad28 vector, dealt with above in relation to the claims on file, there are no difference between the combined disclosures of D1, D2 and D3 and the inventive concepts of independent claims 1 and 17 and dependent claims 3, 4, 19 and 20.

<u>Viewed Without any Knowledge of the Alleged Invention as Claimed, do These Differences Constitute Steps Which Would Have Been Obvious to the Person Skilled in the Art or do They Require any Degree of Invention?</u>

[70] In the R-FA, the Applicant simply submitted that the "presently claimed combination of features [of the proposed claims] is not taught or suggested by the prior art." No specific

discussion of the prior art, including D1, was provided.

[71] As discussed immediately above, the SOR demonstrates a considered analysis of the prior art, including D1, as well as two other pertinent references, documents D2 and D3. It also explains how the skilled person would apply their teachings in an obvious manner in order to arrive at the invention defined by the proposed claims:

> At the time of the filing date of the instant application, a person skilled in the art would routinely apply these features to adenovirus vectors and be acutely aware of their advantages. Furthermore, as detailed in the Final Action, no surprising advantage has been disclosed regarding said claimed combination of elements. Indeed such a vector has not been made or exemplified in the description.

[72] It therefore appears that apart from the singular difference concerning the use of an Ad28 vector, there are no differences between the combined teachings of the cited references and the inventive concepts of the proposed claims. Secondly, our analysis provided above in relation to the claims on file (even not considering D9) has led us to the conclusion that the use of an Ad28 vector would have been obvious to the skilled person. The SOR also provides an entirely reasonable assessment of the proposed claims. Finally, no arguments have been presented in relation to the proposed claims as to why the skilled person would have considered their subject-matter non-obvious in view of D1, D2 and D3.

[73] As such, we agree with the analysis provided in the SOR and find that the skilled person would have also regarded the proposed claims as defining obvious subject-matter.

Conclusion on the Proposed Claims

[74] The proposed claims would not remedy the obviousness defect dealt with in relation to the claims on file because they do not add anything to the claims that would not have been considered obvious by the skilled person.

[75] We therefore do not consider the proposed claims necessary amendments and decline to recommend to the Commissioner that they be incorporated into the application, as subsection 86(11) of the *Patent Rules* would otherwise permit.

RECOMMENDATION OF THE BOARD

[76] In our view, both the claims on file and those proposed by the Applicant in the R-FA define subject-matter that would have been obvious to the skilled person as of the relevant date.

[77] We therefore recommend that the application be refused for non-compliance with section 28.3 of the *Patent Act*.

Ed MacLaurin	Marcel Brisebois	Cara Weir
Member	Member	Member

DECISION OF THE COMMISSIONER

[78] I concur with the findings of the Board and its recommendation to refuse the application because the claims on file do not comply with section 28.3 of the *Patent Act*.

[79] Accordingly, I refuse to grant a patent for this application. Under section 41 of the *Patent Act*, the Applicant has six months to appeal my decision to the Federal Court of Canada.

Johanne Bélisle
Commissioner of Patents

Dated at Gatineau, Quebec

this 28th day of May, 2020