Commissioner’s Decision #1389

Décision du Commissaire n^{o} 1389

TOPIC: B00, F00, O00

SUJET: B00, F00, O00

Application No.: 2,398,030

Demande n°.: 2 398 030

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,398,030 having been rejected under subsection 30(3) of the *Patent Rules*, has been reviewed in accordance with paragraph 30(6)(*c*) of the *Patent Rules.* The recommendation of the Board and the decision follow.

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INTRODUCTION

[1] This is a review of patent application number 2,398,030 entitled "Therapeutic Agents for Achondroplasia" ["the '030 application"]. This application was filed in Canada on August 14, 2002 in the name of Kazuwa Nakao as both the Applicant and the Inventor. The Applicant originally requested priority on the basis of two earlier Japanese patent applications; however the Applicant was able to produce only one of those applications, JP 310322/2001 filed on October 5, 2001.

[2] For the reasons that follow, we recommend that the Applicant be notified that the proposed amendments are necessary for compliance with the *Patent Act* and *Patent Rules*.

PROSECUTION HISTORY

[3] The application was rejected in a Final Action dated April 25, 2013 on the basis that the claimed invention was obvious in view of two prior publications. The Applicant provided arguments in response in a letter dated October 25, 2013. The Examiner was not persuaded by these arguments and prepared a Summary of Reasons on January 29, 2014 concluding that the claimed invention was obvious.

[4] The application was referred to the Patent Appeal Board for review on February 28, 2014 and this panel was established. Following an initial review of the application, we raised two additional issues in a letter dated February 3, 2015: anticipation and claim language that is not distinct and explicit. Our letter also clarified certain issues and invited the Applicant to attend a hearing. In response, the Applicant provided written submissions in a letter dated April 7, 2015, which included proposed claims 1-4 [the "proposed claims"]. The Applicant also attended a hearing before the panel, conducted by videoconference, on April 10, 2015.

[5] This review is based on claims 1-4 on file, and also considers the proposed claims provided in the Applicant's letter of April 7, 2015.

BACKGROUND

[6] "Skeletal dysplasia" is an umbrella term that encompasses several conditions that affect bone and cartilage growth, including different types of dwarfisms. Achondroplasia is the most common dwarfism of genetic origin, occurring in one out of about 15,000 live births. It is caused by specific mutations in the gene for fibroblast growth factor 3 ["FGFR3"] that abnormally activate FGFR3 function and impair endochondral ossification—a process which includes forming bone tissue from a cartilage matrix.

[7] The specific FGFR3 mutations associated with achondroplasia reduce the size/thickness of the layer of cartilage cells (chondrocytes) in the epiphyseal growth plates that elongate limb bones, by reducing chondrocyte proliferation and delaying chondrocyte maturation. This results in a reduced cartilage matrix for conversion to bone, and hence shorter limb bones and dwarfism. Other mutations in FGFR3 can result in other types of skeletal dysplasia which are different from achondroplasia.

[8] The Applicant's description demonstrates that treatment with C-type Natriuretic Peptide ["CNP"] overcomes achondroplasia – a specific type of dwarfism. CNP is one member of a family of natriuretic peptides ["NPs"] which also includes Atrial Natriuretic Peptide ("ANP") and Brain Natriuretic Peptide ("BNP"). According to the Applicant's description, NPs were known to have a role as bone growth factors (paragraph bridging pages 2-3). The description states that CNP had previously been shown to promote longitudinal bone growth and the thickening of the cartilage layer of the growth plate (page 3).

[9] The claims on file are directed to the use of CNP-22 or CNP-53—two specific CNP peptides having 22 and 53 amino acids, respectively—to treat achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations.

ISSUES

[10] This review addresses the following three questions:

(1) Are the claims obvious in view of the cited prior art?

(2) Are the claims anticipated by an earlier filed application?

(3) Is the subject matter of the claims defined distinctly and in explicit terms?

LEGAL PRINCIPLES

Purposive Construction

[11] Purposive construction is an interpretive exercise in determining the meaning and scope of the claims. Claims construction is antecedent to consideration of validity: *Whirlpool Corp v Camco Inc, 2000 SCC 67* at para. 43 ["*Whirlpool*"]. Purposive construction requires that the claims be interpreted from the point of view of the person skilled in the art, who possesses the common general knowledge of the particular art: *Whirlpool* at para 53. Construction is based on the patent specification itself without resort to extrinsic evidence: *Free World Trust v Électro Santé Inc,* 2000 SCC 66, at para 66 ["*Free World Trust*"]. Further, recourse should be had to the description to gain insight into what was meant by a particular word or phrase. Otherwise the scope of the claim or claims as written can be neither restricted nor enlarged: *Purdue Pharma v Pharmascience Inc,* 2009 FC 726, at para. 13. During purposive construction, the elements of the claimed invention are identified as essential or non-essential: *Free World Trust* at para 31. An element is considered non-essential if, based on a purposive construction, the skilled addressee would appreciate an element of the claim could be omitted or substituted without having a material effect on the working of the invention: *Free World Trust* at para 55. According to the Examination Practice Respecting Purposive Construction - PN2013-02, the essential elements of a claim are those elements that contribute to the proposed solution to the problem identified in the application.

[12] Subsection 27(5) of the *Patent Act* clarifies how a claim that defines subject matter in the alternative is to be interpreted when considering issues relating to anticipation or obviousness:

> For greater certainty, where a claim defines the subject-matter of an invention in the alternative, each alternative is a separate claim for the purposes of sections 2, 28.1 to 28.3 and 78.3.

[13] In *Abbott Laboratories v Canada (Minister of Health)*, 2005 FC 1332 ["*Abbott*"], at para. 52, Phelan J stated the following with respect to subsection 27(5):

> S. 27(5) is part of the provisions under the heading "Application for Patents". The section requires that if there are alternative claims, each alternative meet the test for patentability – novelty, utility and inventiveness. Failure to establish that each alternative meets the test for patentability would result in the alternative being invalid as well as the whole of the claim.

Obviousness

[14] Section 28.3 of the *Patent Act* sets out the information that may be considered in determining whether the subject matter of a claim is obvious:

> 28.3 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
>
> *(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.

[15] In *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para. 67 ["*Sanofi*"] 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?

The Supreme Court also stated that other factors may be taken into consideration at the fourth step of the obviousness inquiry (*Sanofi*, para. 69).

Anticipation

[16] Paragraph 28.2(1)(*d*) of the *Patent Act* requires that a claim must not define subject matter disclosed in a co-pending Canadian application that is based on a previously filed application filed before the claim date of the pending application:

> 28.2 (1) The subject matter defined by a claim in an application for a patent in Canada (the "pending application") must not have been disclosed
>
> (d) in an application (the "co-pending application") for a patent that is filed in Canada by a person other than the applicant and has a filing date that is on or after the claim date if
>
> (i) the co-pending application is filed by
>
> (B) a person who is entitled to protection under the terms of any treaty or convention relating to patents to which Canada is a party and who has, or whose agent, legal representative or predecessor in title has, previously regularly filed in or for any other country that by treaty, convention or law affords similar protection to citizens of Canada an application for a patent disclosing the subject matter defined by the claim,
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> (ii) the filing date of the previously regularly filed application is before the claim date of the pending application,
>
> (iii) the filing date of the co-pending application is within twelve months after the filing date of the previously regularly filed application, and
>
> (iv) the applicant has, in respect of the co-pending application, made a request for priority on the basis of the previously regularly filed application.

[17] When a co-pending Canadian application is cited under paragraph 28.2(1)(*d*) of the *Patent Act*, the "claim date" is "the filing date of the earliest priority application which supports the subject matter of the claim": Section 15.03 of the Manual of Patent Office Practice. If the co-pending application "contains material relating to subject matter invented after the priority date, that subject matter cannot benefit from that date": *Apotex Inc v Merck & Co Inc*, 2006 FCA 323, para. 55. In the absence of an explicit disclosure "the subject matter of the Canadian patent may nevertheless be inferable from the language of the priority document": *Pfizer Canada Inc v*

Ratiopharm Inc, 2010 FC 612 at para. 87, referring to *AstraZeneca AB v Apotex Inc*, 2007 FC 688, paras. 62-65.

[18] If a single prior art publication discloses all of the essential elements of a claimed invention in an enabling manner, there is anticipation: *Free World Trust* at para. 25. Moreover, the Supreme Court of Canada endorsed using a two-step approach in an anticipation inquiry in which "prior disclosure" and "enablement" are considered separately: *Sanofi* at para. 28.

[19] The first consideration, whether there was "prior disclosure", is "assessed from the perspective of the skilled person, who must be in a position to understand the invention from the disclosure, with no room for trial or experimentation": *Bell Helicopter v Eurocopter*, 2013 FCA 219 at para. 107 ["*Bell Helicopter*"], citing *Sanofi* at paras. 24-25. In this regard, the Federal Court of Canada stated "that the disclosure does not have to be an exact description of the claimed invention": *Eli Lilly v Mylan*, 2015 FC 125, para. 145.

[20] For the second consideration, whether there was "enablement", "the question is no longer what the skilled person understands from the disclosure, but whether that person would be able to work the invention without undue burden": *Bell Helicopter*, para. 108, citing *Sanofi*, paras. 26 and 37.

Subject matter must be defined distinctly and in explicit terms

[21] Subsection 27(4) of the *Patent Act* requires that in setting the boundaries of the claim, the subject matter must be defined "distinctly and in explicit terms":

> The specification must end with a claim or claims defining distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed.

PURPOSIVE CONSTRUCTION

The person skilled in the art and common general knowledge

[22] In our letter of February 3, 2015, we proposed characterizing the skilled person as someone with research interests in the field of skeletal dysplasia, having significant

and extensive knowledge of experimental medicine and treatment options for the various types of dwarfisms, including achondroplasia. In the letter of April 7, 2015, the Applicant substantially agreed with our proposed characterization, adding that the skilled person would also be knowledgeable in the field of skeletal dysplasia diagnostics, including genetic testing of skeletal dysplasia. Based on the teachings of the description, we are in agreement with this characterization.

[23] Thus, the person skilled in the art would have research interests in the field of skeletal dysplasia, including achondroplasia, knowledge of the diagnosis of skeletal dysplasia, including by genetic testing, and knowledge of the treatment options, including experimental treatment options.

[24] To aid in our understanding of the state of the common general knowledge of the skilled person, the panel considered two review articles that were published in 1995, Hagiwara[1] and McDowell[2]. In our letter of February 3, 2015, we proposed several teachings from these review articles as being part of the common general knowledge. The Applicant agreed, in the letter of April 7, 2015, that the common general knowledge would at least include these points from Hagiwara and McDowell (page 2). Accordingly, the points considered as common general knowledge of the skilled person are the following:

- achondroplasia is caused by gain-of-function mutations in the FGFR3 gene;
- natriuretic peptides including CNP play a role in bone development, and CNP and its receptor GC-B (NPR-B) were known to be expressed in chondrocytes;
- the CNP gene produces a CNP precursor polypeptide of 126-amino acid residues (termed “pre-pro-CNP”), which is processed to give a CNP precursor of 103 residues (termed “pro-CNP”), which is further processed to provide two peptide forms: CNP-53 and CNP-22;

[1] Hagiwara et al., “Natriuretic Peptides and Their Receptors”, Zool. Sci., 1995, vol. 12, no. 2, pages 141-149.
[2] McDowell et al., “The natriuretic peptide family”, Eur. J. Clin. Invest., 1995, vol. 25, no. 5, pages 291-298.

- CNP-53 and CNP-22 are identical except for an extension of 31 amino acids at the amino-terminal end of CNP-53; and
- the abbreviation "CNP" was generally understood by the skilled person as referring to CNP-22.

The problem and solution in the '030 application

[25] In our letter of February 3, 2015, we proposed that the problem to be solved was "to find a therapeutic agent for the treatment of achondroplasia" (page 2).

[26] In response, the Applicant submitted in the letter of April 7, 2015 that "in the art, especially in scientific publications, the term 'achondroplasia' is sometimes used loosely and does not necessarily refer to a skeletal dysplasia caused by cartilage growth inhibition resulting from mutations in (FGFR3)" (page 3). Thus, the Applicant submitted that for maximal clarity the problem to be solved should reflect that a treatment was sought for achondroplasia *caused by a cartilage growth inhibition resulting from mutations in the FGFR3 gene* specifically. In support of this argument, the Applicant cited Horton et al.[3], a publication which states that chondrodysplasias, including achondroplasia, "are a diverse and genetically heterogeneous group of disorders associated with skeletal development" (page 3).

[27] In our view, the skilled person would understand from the teachings of the Applicant's description that a treatment was sought for achondroplasia caused by cartilage growth inhibition resulting from mutations in the FGFR3 gene. Thus, the skilled person would consider the following as the problem to be solved:

> To find a treatment for achondroplasia caused by cartilage growth inhibition resulting from mutations in the FGFR3 gene.

[28] Likewise, from the teachings of the Applicant's description, the skilled person would consider the following as the solution to that problem:

[3] Horton, "Progress in Human Chondrodysplasias: Molecular Genetics", Ann. NY Acad. Sci., June 8, 1996, 785, pages 150-159.

> Use of CNP-22 or CNP-53 to treat achrondroplasia caused by cartilage growth inhibition resulting from mutations in the FGFR3 gene.

The claims, purposively construed

[29] Claims 1-4 on file contain two independent claims, claims 1 and 3. Claim 1 reads:

> A therapeutic agent for achondroplasia caused by a cartilage growth inhibition resulting from mutations in (FGFR3), comprising C-type natriuretic peptide (CNP)-22 or CNP-53.

[30] Claim 3 reads:

> Use of a C-type natriuretic peptide (CNP)-22 or CNP-53 for treating achondroplasia caused by a cartilage growth inhibition resulting from mutations in (FGFR3).

[31] In our letter of February 3, 2015, we informed the Applicant that in our view the skilled person would construe "CNP-22" and "CNP-53" as alternative embodiments (page 3). The Applicant did not take issue with this statement and made no submissions to the contrary. Hence, pursuant to subsection 27(5) of the *Patent Act*, CNP-22 and CNP-53 will be construed as alternative embodiments for analysis under paragraph 28.2(1)(*d*) and section 28.3 of the *Patent Act* in this review.

[32] Both of the independent claims on file are 'use' claims. Claim 1 defines a 'peptide for use', and claim 3 defines the 'use of a peptide'. In our view, the skilled person would not consider the scope of these claims to be different. We will, therefore, consider these claims jointly in our analysis.

"Therapeutic agent"

[33] In our letter of February 3, 2015, we notified the Applicant that we considered the meaning of "therapeutic agent" in claim 1 on file to be ambiguous since it is not clear if the "therapeutic agent" is a composition comprising a CNP peptide, or if this expression is directed to the CNP peptide itself. Claim 2, which depends on claim 1, also refers to the therapeutic agent.

[34] Without contesting the above, the Applicant submitted, in the letter dated April 7, 2015, proposed claims 1 and 2 to remove the references to "therapeutic agent" in order to clarify that the proposed claims relate to the CNP peptide, and not a composition. As will be seen, we conclude that these proposed deletions are necessary for compliance with subsection 27(4) of the *Patent Act*, which requires subject matter be defined distinctly and in explicit terms. In any event, in this case, whether the therapeutic agent is construed as a CNP peptide, or as a composition comprising a CNP peptide, would not change the outcome of the anticipation or obvious analyses. For the purposes of the review of the claims on file, we will adopt the construction that the "therapeutic agent" in claims 1 and 2 on file is a direct reference to a CNP peptide, CNP-22 or CNP-53.

Essential Elements

[35] In view of the discussion above, the skilled person would read independent claims 1 and 3 as including the following elements:

- the use of C-type natriuretic peptide CNP-22 or CNP-53;
- for treating achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3.

[36] In our view, the skilled person would consider these elements as being essential to the solution of the problem identified above at para. [28].

[37] The additional feature in each corresponding dependent claim will be addressed within the body of our analysis in the sections that follow.

ARE THE CLAIMS OBVIOUS IN VIEW OF THE CITED PRIOR ART?

Analysis of the claims on file

Step 1: Identify the notional "person skilled in the art" and the common general knowledge of that person

[38] The person skilled in the art and their common general knowledge have been identified at paras. [23] and [24].

Step 2: Identify the inventive concept of the claim in question or if that cannot readily be done, construe it

[39] According to the Final Action, the inventive concept is the use of CNP-22 or CNP-53 to treat achondroplasia caused by cartilage growth inhibition resulting from mutations in the gene for FGFR3. The Applicant did not dispute this characterization of the inventive concept or make submissions to the contrary. Notably, this inventive concept consists of the essential elements identified for the independent claims above. We adopt this as the inventive concept of claims 1 and 3.

Step 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

[40] The following journal articles were cited as prior art in the Final Action and Summary of Reasons:

FEBS, 276, No.1, 2, pp. 209-213	Published 1990	Kojima et al.
PNAS, 98, No.7, pp. 4016-4021	Published March 2001	Chusho et al.

<u>*Kojima et al.*</u>

[41] Kojima et al. is a journal article that was published in 1990. Kojima et al. discloses that cDNA encoding CNP produces a pre-pro-CNP—a precursor peptide—that is processed to a pro-CNP, and that is further processed to generate a CNP peptide in two forms, CNP-22 and CNP-53. CNP-53 is an N-terminally elongated form of the shorter CNP-22 peptide.

[42] We note that these teachings have been identified as common general knowledge of the skilled person at para. [24].

<u>*Chusho et al.*</u>

[43] Chusho et al. is a journal article that was published on March 27, 2001 by the Applicant. Chusho et al. discloses that mice lacking CNP, as a result of the engineered disruption of their natural CNP gene, have severe dwarfism as a result of impaired endochondral ossification. The observable skeletal defects in these mice

resemble those in patients with achondroplasia. In order to determine if a treatment involving targeted expression of CNP could remedy the dwarfism observed, the mice were cross-bred with transgenic mice engineered to express CNP in growth plate cartilage. The resulting generation of mice having both the targeted disruption of the CNP gene and targeted expression of CNP in the growth plate were of normal appearance, their skeletons being indistinguishable from normal (wild type) mice. Chusho et al. suggested "that CNP may be one of the causative genes for such skeletal dysplasias of unknown origin and may be useful for treatment of achondroplasia" (page 4020).

Summary of differences

[44] The difference between the state of the art and the inventive concept is that neither the Kojima nor the Chusho reference teaches the treatment of achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations. Chusho et al. concerns the treatment of a different form of dwarfism, one that is caused by the absence of CNP.

[45] Chusho et al. treats the dwarfism using a CNP transgene, instead of using one of the peptides CNP-22 and CNP-53. However, the skilled person would not consider this to be a difference. The skilled person would understand that the CNP transgene used in Chusho et al. will produce CNP-22 and CNP-53 (by way of pre-pro-CNP), based on the teachings of Kojima et al.

Step 4: 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?

[46] We agree with the Examiner that Chusho et al. suggests to the skilled person that CNP may have potential for treating achondroplasia. However, this was based solely on visible similarities (i.e., similar phenotypes) between the skeletal defects of the dwarfed mice lacking CNP in Chusho et al. and patients with achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations. An invention is not obvious merely because the prior art suggests to the skilled person that something

may be worth trying. It would have to be more or less self-evident to the skilled person that using CNP to treat achondroplasia ought to work. In our view, the skilled person would not expect that a therapeutic agent known to treat one type of dwarfism (caused by a defective CNP gene) would necessarily treat a different type of dwarfism (caused by mutations in the FGFR3 gene), solely on the basis that the physical manifestations of the two diseases appear similar.

[47] The skilled person in the field of skeletal dysplasia having knowledge of the genetic testing associated therewith would know that for complementation or rescue of a gene defect, the supplemented gene product must either be downstream of the defective gene product in the same pathway, or in a parallel functional pathway. However, there was no known connection between CNP and FGFR3 to suggest their role in a common pathway, a parallel pathway, or that the pathway of one affected the other. Moreover, no definitive link between achondroplasia and CNP, or FGFR3 and CNP, was taught in either of the cited documents, nor was there such a link within the common general knowledge of the skilled person. In our view, it would not have been obvious to the skilled person that CNP-22 or CNP-53 could be used to treat achondroplasia resulting from FGFR3 mutations based on the teachings of Kojima et al. and Chusho et al., in view of their common general knowledge.

[48] Based on the foregoing analysis, we conclude that the subject matter of independent claims 1 and 3 on file would not have been obvious on the claim date.

[49] It follows that dependent claims 2 and 4, which depend directly from claims 1 and 3, respectively, are also not obvious.

ARE THE CLAIMS ANTICIPATED BY AN EARLIER FILED APPLICATION?

Analysis of the claims on file

[50] As mentioned above, paragraph 28.2(1)(*d*) of the *Patent Act* requires that a claim must not define subject matter disclosed in a co-pending Canadian application that is based on a previously filed application filed before the claim date of the pending application.

[51] As a preliminary matter, the claim date of the claims on file in the ’030 application must be ascertained. As mentioned in para. [1], the present application originally claimed priority on the basis of two Japanese patent applications, however the Applicant was only able to produce one of those applications, JP 310322/2001 filed on October 5, 2001.

[52] Independent claims 1 and 3 on file are directed to the use of CNP-22 or CNP-53 for treating achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3. Since this subject matter is explicitly disclosed in the Japanese priority document, the claim date of these claims is October 5, 2001.

[53] Next, we must determine if this subject matter is disclosed in the co-pending application. In so doing, we must also determine if the subject matter in the co-pending application is entitled to priority based on the filing date of its previously filed application.

[54] In accordance with the two-step approach endorsed in *Sanofi* (and outlined above at paras. [18]-[20]), if we determine there is “prior disclosure” of the subject matter in the co-pending application, we will then consider enablement.

Disclosure: Independent claims 1 and 3

[55] In our letter of February 3, 2015, we cited the following co-pending Canadian application:

Co-pending Canadian patent application (Golembo)

CA 2,441,815 A1 Priority date: March 20, 2001 Golembo[4]

Golembo is a Canadian Patent Application that was filed on March 20, 2002 and was published on September 26, 2002[5]. The application was granted and a Canadian patent issued on September 23, 2014. Golembo claims priority from two previously

[4] This document was first cited in the Examiner’s action of December 21, 2009, but was later withdrawn.
[5] This document was not considered in the obviousness analysis because it was published after the claim date of the ’030 application. To be considered under section 28.3 of the *Patent Act*, subject matter must have been disclosed before the claim date.

regularly filed applications for patents in Israel and the United States, both filed on March 20, 2001. These two documents contain the same information. For the sake of convenience, we will refer only to passages from the Israeli application ["the priority document"] in our analysis, even though the statements and subject matter accord equally to both priority documents.

[56] Golembo discloses the use of CNP for treating achondroplasia caused by cartilage growth inhibition resulting from mutations in the gene for FGFR3. In Example 1, bone elongation is induced when leg bones taken from achondroplasia model mice are cultured in the presence of CNP. Importantly, the model mice have achondroplasia caused by FGFR3 mutations which, according to page 2, "affect the process of endochondral ossification by inhibiting proliferation and delaying maturation of chondrocytes in the growth plate cartilage of long bones, resulting in decreased elongation" (lines 22-25). Example 2 discloses that an analysis of the cellular composition of the growth plate in samples treated with natriuretic peptides revealed an increase in the size of the proliferative region and in the size of the hypertrophic zone (page 17, lines 25-27). Golembo suggests that it is "an increase in proliferation which leads to a larger growth plate" (paragraph bridging pages 17-18). In Example 4, encapsulated cells engineered to secrete CNP were implanted in achondroplasia model mice to treat achondroplasia; the encapsulated cells were also implanted in normal (wild type) mice. The encapsulated cells were prepared by first infecting fibroblast cells with a retrovirus expressing mouse CNP, confirming CNP secretion from the infected cells, and finally encapsulating these infected cells.

[57] All of the matter referred to above is disclosed in the priority document. Thus, at least this subject matter benefits from the earlier filing date of the priority document, which is March 20, 2001.

Does Golembo disclose the use of CNP-22 in the treatment of achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3?

[58] One notable discrepancy between Golembo and its priority document is that only Golembo explicitly identifies CNP as "CNP-22", referring to it as the active form of

CNP (Example 6). Golembo also claims CNP-22 (as SEQ ID NO:1) for use in treating achondroplasia. In contrast, the priority document refers generally to "CNP" without any mention of "CNP-22" or "CNP-53". However, we have established at para. [24] that the skilled person would have understood a general reference to CNP as implicitly referring to CNP-22.

[59] We are satisfied that in spite of the absence of an explicit reference to CNP-22, the skilled person would infer the use of CNP-22 to treat achondroplasia from the priority document of Golembo, and that this subject matter benefits from the earlier priority date of March 20, 2001.

[60] Moreover, we are satisfied that the skilled person would understand that the disease being treated in Golembo is achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3 (Golembo at page 2, outlined above at para. [56]).

Does Golembo disclose the use of CNP-53 in the treatment of achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3?

[61] There is no explicit disclosure of CNP-53 in Golembo or its priority document. As noted previously, the skilled person would implicitly understand the general references to CNP throughout Golembo and its priority document to mean CNP-22. The priority document refers exclusively to CNP, and to functional variants or derivatives of CNP. While no definition is provided for the variants or derivatives in the priority document, Golembo defines the terms as modified versions of the native sequence (page 11). Specifically, the natural amino acid sequence is altered either by shortening its length, or by deleting or substituting amino acids (page 11). Since CNP-53 is an unmodified natural form of CNP, and is longer than CNP-22, the skilled person would not have considered it to be among the variants or derivatives.

[62] Based on the above, when Golembo is read as a whole, we are satisfied that the skilled person would not understand CNP, or a CNP functional variant or derivative, to encompass CNP-53.

[63] The only other consideration is whether the skilled person reading Example 4 in Golembo, wherein "mouse CNP" is secreted from encapsulated cells *in vivo*, would consider this as a disclosure of using CNP-53 to treat achondroplasia. This would depend on how the skilled person interprets "mouse CNP": as CNP-22 or pre-pro-CNP (which will be processed to CNP-53 and CNP-22, and would thus inherently include CNP-53).

[64] The above question was put to the Applicant at the hearing. In response, the Applicant submitted that the skilled person would have no reason to think that the mouse CNP being secreted was anything other than CNP-22. The Applicant argued that there was no indication that a different form, such as the pre-pro-CNP, was used to prepare the cells. The Applicant submitted that in view of the limited information provided, and in the absence of any detail pertaining to the construct used to engineer the cells, the skilled person would conclude, based on the teachings of Golembo as a whole, that "mouse CNP" in Example 4 referred to CNP-22.

[65] We concur that this interpretation is consistent with the teachings of Golembo as a whole and with the common general knowledge that general references to CNP would have been implicitly understood by the skilled person to mean CNP-22. It is also our view that this would be the understanding of a skilled person reading or replicating Example 4 in Golembo. It is our conclusion that the skilled person would not consider the use of CNP-53 to treat achondroplasia to be disclosed in Example 4 of Golembo.

[66] Based on the foregoing, we conclude that CNP-53 is neither explicitly nor implicitly disclosed in Golembo.

Disclosure: Dependent claims 2 and 4

[67] Dependent claims 2 and 4, which depend on claims 1 and 3 respectively, both include the feature that treatment of achondroplasia is effected by rescuing cartilage growth inhibition by enlarging hypertrophic chondrocytes and increasing the extracellular matrix of the proliferative chondrocyte layer. Golembo also discloses this feature in Example 2 in the treatment of achondroplasia using natriuretic

peptides, which includes CNP (above at para. [56]). Moreover, this mode of action is an inherent feature of using CNP-22 to treat achondroplasia that will necessarily result when Examples 1 and 4 in Golembo are performed. We are satisfied that the subject matter of the dependent claims pertaining to CNP-22 is disclosed in Golembo. However, as stated above, insofar as dependent claims 2 and 4 refer to CNP-53, the subject matter is not disclosed by Golembo.

Summary regarding disclosure

[68] The use of CNP-22 for treating achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations is disclosed in Golembo. Moreover, the enlarging of hypertrophic chondrocytes and increasing extracellular matrix of the proliferative chondrocyte layer are also disclosed. The use of CNP-53 is not disclosed.

Enablement

[69] Examples 1 and 4 in Golembo enable the skilled person to use CNP-22 to treat achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations. The enlarging of hypertrophic chondrocytes and increasing of the extracellular matrix of the proliferative chondrocyte layer will inevitably follow when these examples are carried out. Golembo is an enabling disclosure of the subject matter of claims 1 to 4 insofar as the claims refer to CNP-22.

[70] We have determined that CNP-53 is not disclosed, and so there is no need to consider if it is enabled.

Conclusion: Anticipation of the claims on file

[71] The subject matter of the claims on file, with respect to the use of CNP-22 in the treatment of achondroplasia caused by cartilage growth inhibition resulting from FGFR3 mutations, is disclosed and enabled in Golembo. According to subsection 27(5) of the *Patent Act*, and in view of the judicial interpretation of that statute in *Abbott* (above at para. [13]), if a claim defines subject matter in the alternative, and one of the alternatives is anticipated, the claim is anticipated. The claims on file are therefore non-compliant with paragraph 28.2(1)(*d*) of the *Patent Act*.

[72] Since we have found that the claims on file are anticipated, we will consider the proposed claims submitted on April 7, 2015.

Analysis of the proposed claims

[73] Proposed claims 1-4 are identical to the claims on file except for the deletion of CNP-22 alternative and the deletion of an ambiguous expression (which is addressed in the section that follows). The proposed claims are only directed to the use of CNP-53 to treat achondroplasia caused by cartilage growth inhibition resulting from mutations in FGFR3. We have already determined at para. [68] that this subject matter is not disclosed in Golembo.

[74] Further, proposed claims 1-4 are narrower in scope than the claims that we have found unobvious, and thus they also comply with section 28.3 of the *Patent Act*.

[75] In our view, based on our conclusions on anticipation above, the proposed deletion of CNP-22 from the claims on file overcomes the anticipation defect, does not introduce any new defects, and is therefore a specific amendment which is "necessary" according to subsection 30(6.3) of the *Patent Rules*.

IS THE SUBJECT MATTER OF THE CLAIMS DEFINED DISTINCTLY AND IN EXPLICT TERMS?

[76] As mentioned at para. [33], we notified the Applicant in our letter of February 3, 2015 that we considered the meaning of "therapeutic agent" in claim 1 on file to be ambiguous since it is not clear whether the "therapeutic agent" used to treat achondroplasia in the claims is a composition comprising a CNP peptide, or if this expression refers to the CNP peptide itself. Claim 2, which depends on claim 1, also refers to the therapeutic agent. This ambiguity contravenes subsection 27(4) of the *Patent Act* which requires subject matter be defined distinctly and in explicit terms.

[77] In response, the Applicant proposed deleting the references to "therapeutic agent" from claims 1 and 2 in order to clarify that the claims are for the use of the CNP peptide to treat achondroplasia. In our view, the proposed deletions would clarify the language. These are specific amendments which are necessary for compliance with

subsection 27(4) of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[78] We have concluded that claims 1 to 4 on file do not comply with paragraph 28.2(1)(*d*) of the *Patent Act*, and that claims 1 and 2 on file do not comply with subsection 27(4) of the *Patent Act*. We have also concluded that proposed claims 1-4 overcome these defects and do not introduce any new defects. We therefore recommend that the Applicant be notified, in accordance with subsection 30(6.3) of the *Patent Rules*, that the amendments proposed in the correspondence of April 7, 2015, namely the deletion of claims 1 to 4 on file and the insertion of proposed claims 1 to 4, are necessary for compliance with the *Patent Act* and *Patent Rules*.

Cara Weir Member	Paul Fitzner Member	Jacinth Abraham Member

DECISION

[79] I concur with the findings and recommendation of the Patent Appeal Board. In accordance with subsection 30(6.3) of the *Patent Rules*, I hereby notify the Applicant that the above amendments must be made within three (**3**) months of the date of this decision, failing which I intend to refuse the application. In accordance with paragraph 31(*b*) of the *Patent Rules*, the following amendments, and only these amendments, may be made to the application:

i) delete claims 1-4 on file; and

ii) insert proposed claims 1-4 submitted in the correspondence of April 7, 2015.

Agnès Lajoie
Assistant Commissioner of Patents

Dated at Gatineau, Quebec,
this 24 day of August, 2015