Commissioner’s Decision #1378

Décision du Commissaire #1378

TOPIC: O00

SUJET: O00

Application No.: 2,549,931

Demande n°.: 2,549,931

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,549,931 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* by the Patent Appeal Board and the Commissioner of Patents. The recommendation of the Board and the decision of the Commissioner are as follows:

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INTRODUCTION

[1] This is a review of patent application number 2,549,931 (herein "the '931 application") entitled "Use of L-Butylphthalide in the Manufacture of Medicaments for Prevention and Treatment of Cerebral Infarct" which was filed in Canada on September 29, 2004, by the Applicant Shijiazhuang Pharma. Group Zhongqi Pharmaceutical Technology (Shijiazhuang) Co. Ltd., et al. The '931 application was rejected in a Final Action on February 7, 2012, because the claimed invention was considered obvious in view of two prior art publications. In response, the Applicant provided arguments and submitted amended claims 1-10, which are now the claims on file, on August 7, 2012. The Examiner did not consider the claims to have overcome the grounds for rejection.

[2] The application was therefore referred to the Patent Appeal Board for review, and this panel was established. The panel conducted an initial review and sent a letter on July 24, 2014 clarifying certain issues, inviting the Applicant to attend a hearing, and providing a Supplemental Analysis requisitioned by the panel. The Applicant declined the invitation to attend a hearing before the panel, opting instead to supplement the record with written submissions which included proposed claims 1-7 on September 22, 2014.

[3] This review is based on claims 1-10 on file, and also considers whether the obviousness defect is overcome by the potential amendments of proposed claims 1-7. For the reasons that follow, we recommend that the application be refused.

BACKGROUND

[4] "Ischemia" is a term which describes the interruption of blood flow to an organ or tissue which can result when a vessel or artery becomes blocked, by a blood clot for example. "*Cerebral* ischemia" is a term which indicates the interruption of blood flow was to the brain.

[5] When blood flow to an organ is interrupted for more than a few seconds, a localized area of dead tissue called an "infarct" can form. When the dead tissue is located

within the brain it is called a “cerebral infarct.” This application relates to a compound which can be used to treat cerebral infarct caused by cerebral ischemia.

[6] Compounds which decrease the amount of infarcted brain tissue or decrease neurological deficits in animals would be considered potential candidates for study in human stroke clinical trials. One such compound which has been shown to be effective in both human and animal studies is n-butylphthalide (“DL-NBP”). The Applicant holds a Chinese patent for this compound, which was published in 1995 and issued in 1999. This compound was approved for the treatment of acute ischemic cerebral stroke by China’s State Drug Administration in 2002.

[7] DL-NBP is a “racemate”, meaning it is a mixture of equal amounts of two structurally related yet different compounds called enantiomers or optical isomers. The two compounds, called the dextro-rotatory (“D”) and levo-rotatory (“L”) enantiomers, are related because they are mirror images of one another, causing them to rotate plane-polarized light in opposite directions. In the case of DL-NBP, its dextro- and levo-rotatory enantiomers are referred to as D-NBP and L-NBP, respectively.

[8] Enantiomers can behave differently from one another when interacting with other chiral compounds, such as with human or animal receptors and enzymes. If a receptor is thought of as a “lock”, the enantiomers may represent two different “keys”: an “active” enantiomer can have a complimentary structure and fit the lock, and an “inactive” enantiomer might not. This can give rise to different pharmacological activities and toxicities.

[9] The Applicant explains starting on page 4 of the description that the present invention follows the “international new drug discovery” requirement that drugs which are racemates be separated into their respective enantiomers so their individual properties, particularly those of therapeutic potency and toxicity, can be identified. When one enantiomer is found to have an increased therapeutic effect or lower toxicity compared to the racemate, it may be developed into a new drug (pages 4-5, 12 and 13).

[10] According to the background, the Applicant conducted a comparative study of the therapeutic effects of the racemate and each of the two enantiomers on cerebral infarct. Based on the results, the ‘931 application claiming the use of L-NBP for the treatment of cerebral infarct was filed.

[11] The sole question in this review is whether or not claims to the use of L-NBP in treating cerebral infarct are obvious in view of two prior art documents.

LEGISLATIVE AND LEGAL PROVISIONS

Purposive Construction

[12] 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.

Obviousness

[13] 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
>
> *(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.

[14] In *Apotex Inc v Sanofi-Synthelabo Inc*, 2008 SCC 61 ["*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 ISSUE

[15] This review addresses the following question: Are the claims obvious?

[16] We will begin our review by considering claims 1-10 on file which the Applicant submitted in response to the Final Action. Since these claims are found to be obvious, we will also consider whether the proposed amendments which include

proposed claims 1-7 submitted by the Applicant on September 22, 2014, overcome this defect.

PURPOSIVE CONSTRUCTION

The person skilled in the art

[17] The Supplemental Analysis characterized the skilled person as "a medicinal chemist with a background in pharmacology and an understanding of the use of drugs for the treatment of cerebrovascular disorders (including cerebral infarct)" (page 2).

Common general knowledge of the skilled person

[18] The Supplemental Analysis characterized the common general knowledge of the skilled person as including, at page 2:

- familiarity with "optical isomerism, and the general understanding that optically active drugs typically have one enantiomer that exhibits significantly greater pharmacological activity than the other"; and
- familiarity with the "rat-based transient focal cerebral ischemic model (tMCAO) appearing in the examples and the various measures that can be used to evaluate the effects of drugs on the extent of ischemic damage arising in such a model system (see (Chang et al.)[1] and references cited therein in relation to the methodologies used)" (emphasis added).

[19] The "references cited therein" above include Bederson et al[2], which is a journal article that discloses the "Bederson neurological grading scale" Chang et al. used to assess rats subjected to tMCAO. Bederson et al. discloses measuring infarct size and neurological behaviors in the rat model, and establishes there was a known correlation between the severity of neurological deficits and the size of the infarct.

[1] Chang et al. is a publication discussed in the following section, see [39] for the full citation
[2] Bederson et al., "Rat middle cerebral artery occlusion: evaluation of the model and development of a neurological examination", Stroke, vol. 17, no. 3, 1986, pages 472-476.

Therefore, based on the inclusion of the "references" in the last bullet above, the Supplemental Analysis suggests the skilled person would also have:

- knowledge of the Bederson neurological grading scale and knowledge of the general correlation between the severity of neurological deficits and infarct size in the MCAO rat model.

[20] The Applicant did not take issue with this characterization of the skilled person or their relevant common general knowledge as provided in the Supplemental Analysis, and made no submissions to the contrary. Based on the teachings of the description, we adopt these characterizations for the purpose of our review.

[21] In light of statements on page 5 of the '931 application that the pharmaceutical compositions "may be prepared according to the method(s) well known in the art", which are said to include combining the active ingredient "with one or more solid or liquid pharmaceutical vehicles and/or adjuvant if desired, so as to be formulated into suitable administration forms or dosage forms for human use or veterinary use", we also consider the skilled person would have:

- knowledge of the methods of drug formulation and delivery in humans and animals.

The problem and solution that the invention addresses

[22] The Applicant explains on page 1 of the description that the DL-NBP racemate was known to be useful in the treatment of cerebral infarct well before the claim date. The Applicant further explains on page 2 that the racemate had previously been separated into its individual L- and D-NBP enantiomers, although their individual properties in treating cerebral infarct had not been compared, which at the time of filing was advised according to the requirements of international new drug discovery (description, page 12-13). Based on the specification as a whole, it is our view the skilled person would consider the problem the Applicant set out to address was:

> to provide an NBP enantiomer for use as a new treatment for cerebral infarct by comparing the therapeutic potencies of each of

> the enantiomers (L-NBP; D-NBP) with the DL-NBP racemate and using the more potent enantiomer as the new treatment.

[23] The Applicant explains in the Summary of Invention on page 3 that to solve this problem it used the tMCAO rat model to determine that the L-NBP enantiomer has a superior therapeutic effect in treating cerebral infarct compared to both the D-NBP enantiomer and the racemate. Moreover, the results indicated that the presence of the D-NBP enantiomer in the racemate has an antagonistic effect on the L-NBP enantiomer that lowers the overall therapeutic activity of the racemate (page 4). Therefore, to address the above problem, the Applicant provides the following solution:

> to use L-NBP to treat cerebral infarct since it is the more therapeutically potent enantiomer and since it avoids the antagonistic effect of D-NBP present in the DL-NBP racemate.

<u>The claims, purposively construed</u>

[24] Claims 1-10 on file contain three independent claims: claims 1, 4 and 7. Claim 4, which is representative of these three independent claims under review, is presented below:

> 4. Use of (L-NBP) for reducing the volume of a cerebral infarct and/or improving the neurological behaviors of a subject, thereby treating cerebral infarct in the subject, wherein the (L-NBP) is substantively free of (D-NBP) to eliminate the antagonistic effects of (D-NBP) on the treatment of cerebral infarct.

[25] Based on a plain reading of claim 4, it includes the following elements:

- use of L-NBP;
- for reducing infarct volume; and/or
- for improving the neurological behaviors;
- thereby treating cerebral infarct in a subject;
- wherein the L-NBP is substantively free of D-NBP to eliminate the antagonistic effects of D-NBP on the treatment of cerebral infarct.

[26] Before determining the essential elements of the claim, there are two terms used in the claim that require interpretation: “subject”; “and/or”.

“Subject”

[27] The description explains the pharmaceutical compositions are formulated “for human use or veterinary use” (page 5), and the appropriate dosage depends on “the individual response of the patient or animal” in question (page 7). Based on these teachings, the skilled person would understand the “subject” in the claim to be either human or animal.

“And/Or”

[28] The expression “and/or” would generally be regarded as indicating three alternative embodiments, such that the use of L-NBP treats cerebral infarct by;

i) reducing infarct volume,
ii) improving neurological behaviors, or
iii) both reducing infarct volume and improving neurological behaviors.

[29] However, the skilled person would know that when the tMCAO rat model is used, “treating cerebral infarct” involves both a reduction in infarct volume and an improvement in neurological behaviors. Bederson et al. (see [19]) explains that when the rat’s middle cerebral artery is surgically occluded, a cerebral infarct of a uniform size will predictably form, and that when neurological behaviors are assessed 24 hours after occlusion, there will be a correlation between the size of the infarct and the severity of the resulting neurological deficits. Thus, in our view, since the tMCAO rat model is used in the present case, the skilled person would consider a reduction in infarct volume and an improvement in neurological behaviors as being jointly associated with the treatment of cerebral infarct in a subject, and not as alternative embodiments.

Essential Elements

[30] There was no dispute that the skilled person would construe "use of L-NBP", "treating cerebral infarct in a subject" and the absence of the "antagonistic effects of D-NBP" as essential elements of the claim. The skilled person would understand that these features are essential elements based on the teachings of the description. The only point in dispute between the Supplemental Analysis (page 3, letter of July 16, 2014) and the written submissions filed by the Applicant in response (page 2, letter of September 22, 2014) was whether "reducing the volume of a cerebral infarct" and "improving the neurological behaviors" should be construed as essential elements of the claim.

[31] Based on the common general knowledge set out above, the skilled person would understand that these are terms associated with treating cerebral infarct, which is the therapeutic utility of L-NBP and an undisputed essential element of the claim. The skilled person would not consider these as being elements distinct from the therapeutic treatment, they would be considered together: cerebral infarct is treated by reducing infarct volume and improving neurological behaviors.

[32] With this understanding in mind, we adopt for the purposes of our review the following features as essential elements:

- use of L-NBP;
- substantively free of D-NBP to eliminate the antagonistic effects of D-NBP on treating cerebral infarct;
- to treat cerebral infarct in a subject, by reducing infarct volume and improving neurological behaviors.

[33] The additional features of the dependent claims will be addressed within the body of our obviousness analysis in the following section.

[34] With the above understanding of the claims in mind, we turn to the issue of obviousness.

ARE THE CLAIMS OBVIOUS?

Analysis of the claims on file using the *Sanofi* Four-Step Approach

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

[35] The person skilled in the art and their common general knowledge have already been identified at paras [17]-[21].

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

[36] According to the Supplemental Analysis "when the claims are read in light of the description, the inventive concept that emerges is that (L-NBP) is more effective in treating cerebral infarct than (D-NBP) or racemic (DL-NBP)" (page 3). In support of this inventive concept, the Examiner referred to para 77 of the *Sanofi* decision, where the Supreme Court of Canada indicated that in the case of chemical subject matter, it may be acceptable to read the specification in the patent to determine the inventive concept. The panel notes that as in the *Sanofi* case, the present application involves a claim to the use of a compound selected from a previously known group of compounds. In the present case, the group of compounds is the racemate. As in *Sanofi*, consideration is given to a comparison between the selected compound and the broader group and its members.

[37] At para 10 of *Sanofi*, the Supreme Court set out the conditions that must be satisfied for a selection to be valid, one being "(t)here must be a substantial advantage to be secured or disadvantage to be avoided by the use of the selected member." In the Supreme Court's obviousness analysis, the advantage to be secured and disadvantage to be avoided in using the selected member featured prominently in the inventive concept, and in our view it is appropriate to adopt a similar approach here.

[38] In the Supplemental Analysis a single inventive concept was formulated for the three independent medical use claims on file (of which claim 4 is representative). This approach was taken because all three use claims were considered to be directed to the same subject matter, differing only in their respective use claim formats. Since

the Applicant did not take issue with this approach or make submissions to the contrary, we too will approach our review of independent claims 1, 4 and 7 on the basis of one common inventive concept:

> The use of L-NBP to treat cerebral infarct since it exhibits greater therapeutic potency compared to D- and DL-NBP in reducing infarct volume and improving neurological behaviors, and since it avoids the antagonistic effect of D-NBP.

The analysis of the additional features of the dependent claims will follow our analysis of this inventive concept.

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

[39] In the Final Action and Summary of Reasons, the following references were cited as prior art:

Patent Application:

CN 1100097A[3]	Published March 15, 1995	Feng et al.

Journal Article:

Acta Pharma Sin, 24, 8, 796-804	Published August 2003	Chang et al.

Feng et al.

[40] Feng et al. is Chinese patent application published on March 15, 1995 with the same inventors of the present application. Feng et al. discloses that in treating cerebral infarct in both rats and humans, the DL-NBP racemate was consistently found to reduce infarct volumes and improve neurological behaviors. Infarct volumes were expressed as a percentage of the total hemispheric volume, and the Bederson scale was used to assess neurological deficits in rats subjected to MCAO. In the rat studies

[3] In the absence of an English translation, a machine translation was obtained and the contents were confirmed at CIPO by a Chinese-speaking Patent Examiner from the Chemical Division of the Patent Office.

DL-NBP was administered orally or by intraperitoneal (IP) injection, and in the human studies it was administered orally.

Chang et al.

[41] Chang et al. is a journal article that discloses treating cerebral ischemia in rats using DL-NBP, D-NBP and L-NBP. According to Chang et al., focal cerebral ischemia was induced in the tMCAO rat-model, and the therapeutic effects of D-, L- and DL-NBP on neurological behaviors and apoptosis (i.e., cell death) were studied and compared. Notably, the optical purity of the L- and D-NBP enantiomers used in the experiments was greater than 99%. The first experiment involved inducing focal cerebral ischemia by completely blocking the rat's middle cerebral artery, administering the racemate, the D- or L-enantiomer or a control 10 minutes later, restoring blood flow after two hours, and assessing their neurological behaviors using the Bederson scale after the rats had recovered for 24 hours.

[42] Administration of L-NBP after cerebral ischemia was induced was shown to markedly inhibit neurological deficits compared to the control group (i.e., neurological behaviors were significantly improved), and the D-NBP enantiomer showed no such effect. Also, the L-NBP compound reduced neurological deficits to a greater extent than a sample of the DL-NBP racemate that contained the same amount of the L-NBP compound. The authors concluded that the superior therapeutic effect of the L-NBP compound compared to the DL-NBP racemate, which was also observed in the apoptosis studies, "strongly suggested a possible antagonistic mechanism between the (L-NBP) and (D-NBP)" enantiomers (page 803).

Summary of Differences

[43] There are two differences with Feng et al. and the inventive concept. First, L-NBP and its superior therapeutic potency are not disclosed. Second, the antagonistic effect of D-NBP on L-NBP in the DL-NBP racemate is not disclosed. These differences are provided for in Chang et al.

[44] There is one difference with Chang et al. and the inventive concept. The embodiment of "reducing infarct volume" is not disclosed. This difference is provided in Feng et al.

[45] While there are differences between the inventive concept and the individual prior art documents, when the documents are considered together there are no differences overall.

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] The question is whether the skilled person, in view of Feng et al. and Chang et al., would have required any degree of invention to arrive at the inventive concept. The skilled person would have found it obvious to substitute the DL-NBP racemate used to treat cerebral infarct according to Feng et al. with the L-NBP enantiomer having superior therapeutic potency taught by Chang et al. Since the skilled person had a "general understanding that optically active drugs typically have one enantiomer that exhibits significantly greater pharmacological activity than the other" (para [18]), the skilled person would understand from Chang et al. that L-NBP was the active enantiomer with superior therapeutic potency in treating cerebral infarct. Thus, it would not have required any degree of invention to arrive at the inventive concept.

[47] It has been established that the skilled person had an understanding of the use of drugs to treat cerebral infarct, familiarity with the tMCAO rat-model of cerebral ischemia, knowledge of the Bederson neurological grading scale used in that model, and knowledge of the general correlation between the severity of neurological deficits and infarct size (paras [17]-[19]). Notably, the infarct size in Bederson et al. was measured as "infarct area", which is a two-dimensional measurement that considers the size of the infarct in relation to the entire cross-section of a given brain slice or scan. The skilled person would know that infarct size could also be expressed as "infarct volume" within the whole hemisphere by integrating the infarct areas from successive brain slices or scans.

[48] Based on the common general knowledge, the skilled person would expect that where neurological behaviors are improved, there will also be reduced infarct volume. Thus, in substituting the racemate in Feng et al. with the active L-NBP enantiomer, the skilled person would have expected to see a superior reduction in infarct volume in the same manner Chang et al. demonstrated a superior improvement in neurological behaviors compared to the racemate and D-NBP.

[49] Therefore, in considering the inventive concept, which is the same for claims 1, 4 and 7, the skilled person would have found claims 1, 4 and 7 obvious.

[50] The additional feature of dependent claims 2, 5 and 8 is that the cerebral infarct is induced by focal cerebral ischemia (i.e., by a blockage located within the brain itself). Since this feature was also disclosed in both Feng et al. and Chang et al., adding it to the inventive concept stated at [38] and considering the claims as a whole would not render them inventive. The skilled person would have found claims 2, 5 and 8 obvious.

[51] The additional feature of dependent claims 3, 6 and 9 is that L-NBP has an optical purity of at least about 99%. Since Chang et al. teaches the use of L-NBP with the same degree of optical purity, adding this feature to the inventive concept stated at para [38] and considering the claims as a whole would not render them inventive. The skilled person would have found claims 3, 6 and 9 obvious.

[52] Dependent claim 10 adds that “the pharmaceutical composition is in the form of tablets, capsules, pills, injections, sustained release formulations, controlled release formulations, and various micro-particle delivery system” [*sic*]. Since the skilled person had knowledge of the methods of drug formulation and delivery in humans and animals (see para [21]), these various types of dosage forms were within their common general knowledge. Adding them to the inventive concept stated at para [38] and considering the claims as a whole would not render them inventive. Moreover, Feng et al. discloses pharmaceutical compositions in the form of capsules, and both Feng et al. and Chang et al. disclose injection formulations. The skilled person would have found claim 10 obvious.

[53] It is our conclusion that claims 1-10 on file would have been obvious to the skilled person, and are therefore non-compliant with subsection 28.3 of the *Patent Act*.

[54] Since we have found the claims on file would have been obvious, we will consider the proposed claims submitted on September 22, 2014.

Proposed Amendments

[55] In response to our letter of July 24, 2014—which asked the Applicant to comment on the relevance of the neurological behavior results presented in Chang et al. when addressing differences with the prior art documents—the Applicant submitted proposed claims 1-7 in the letter of September 22, 2014. This claim set contains three general amendments over the claims on file. First, the expression "improvement of neurological behaviors" was deleted from the proposed claims. Second, the proposed claims specified "oral" administration, and removed "injections" from the scope of one of the dependent claims. Finally, independent claim 4 on file, and those claims which depended on claim 4, were cancelled.

[56] In support of the patentability of the proposed claims, the Applicant submitted in the letter of September 22, 2014 that "the significant improvement in the symptoms of a cerebral infarct patient (infarct volume and neurological behavior score) obtained by administration of oral compositions/medicaments could not be expected based on (Chang et al.)", and since Chang et al. administered the drug *10 minutes* after ischemia by the *IP route* (which the skilled person would know delivers the drug to the target faster than the oral route), it was not more or less self-evident that oral medicaments would be suitable even when used up to *15 minutes* after ischemia, as in the '931 application (page 3). Moreover, the Applicant submitted that administration of drugs by IP injection is much more common in veterinary medicine and animal models, but is rarely used in humans. For human patients oral dosage forms are much more practical since IP injections must be administered by a medical professional at a hospital or clinic (page 3).

[57] All of the above submissions address differences between the proposed claims and Chang et al. only, the teachings of Feng et al. were not addressed. As noted at [40],

Feng et al. teaches that oral administration of the DL-NBP racemate reduces infarct volume and improves neurological behaviors in both rats and humans. In the first example, Feng et al. demonstrated the effects when the racemate was administered to rats—by either oral administration or intraperitoneal (IP) injection—15 minutes after focal cerebral ischemia was induced. There was a resulting reduction in both infarct volumes and neurological deficits by both routes of administration. In another example a significant reduction in infarct volume (based on comparative CT scans) and neurological deficits was observed after a two week course of soft capsules, formulated for oral administration, was administered to human stroke patients.

[58] While the proposed amendments would have the effect of introducing an additional difference over Chang et al., when the documents are considered together there are once again no differences overall.

[59] The question is whether any degree of invention was required, or if the skilled person would have found it obvious, in light of the common general knowledge and the state of the art, to use L-NBP, substantively free of D-NBP, by the oral route to reduce infarct volume, treat cerebral infarct and avoid the antagonistic effect of D-NBP.

[60] As we have already established at para [48], the skilled person would have expected that using L-NBP would reduce infarct volume based on the teachings of Chang et al. and Feng et al. The deletion of "improvement of neurological behaviors" from the claims does not change that conclusion.

[61] In view of their background in pharmacology (see para [17]), the skilled person would know that the bioavailability of a drug—i.e., the fraction of a drug introduced to the body that reaches circulation and is able to have an active effect—changes depending on the route of administration. The skilled person would understand from Feng et al. that when the racemate—which contains equal amounts of D-NBP and L-NBP—is orally administered to humans and rats, sufficient levels of the active component reach circulation to have a therapeutic effect on reducing infarct volume and improving neurological behaviors. The skilled person would have no reason to

think the bioavailability would change if L-NBP alone were used instead of the DL-NBP racemate. The skilled person would therefore expect L-NBP to be sufficiently bioavailable to have a therapeutic effect by the oral route in both rats and humans.

[62] Regarding the Applicant's argument that oral dosage forms are much more practical than IP injection in humans, the skilled person would share this view but would not consider the claims as being limited to humans (para [27]). Even if the "subject" were limited to humans and this effectively eliminated IP injection, as suggested, we have already determined the skilled person would have expected that administering L-NBP by the oral route in humans would successfully treat cerebral infarct, based on their common general knowledge and the prior art.

[63] The person skilled in the art would have found proposed claims 1-7 obvious, and therefore non-compliant with subsection 28.3 of the *Patent Act*, in light of the common general knowledge and the teachings of Chang et al. and Feng et al.

Conclusions

[64] Claims 1-10 on file, and proposed claims 1-7, would have been obvious to the skilled person and are therefore non-compliant with section 28.3 of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[65] The panel recommends that the application be refused because the claims on file, namely claims 1-10, would have been obvious to the person skilled in the art on the claim date and thus contravene section 28.3 of the *Patent Act*. No proposed amendments have been identified that would overcome this defect and render the claims patentable.

Cara Weir	Ed MacLaurin	Michael O'Hare
Member	Member	Member

DECISION OF THE COMMISSIONER

[66] I concur with the Patent Appeal Board's findings and its recommendation that the application be refused because the claims on file, namely claims 1-10, would have been obvious to the person skilled in the art on the claim date and thus contravene section 28.3 of the *Patent Act*. No proposed amendments were identified that would overcome this defect and render the claims patentable.

[67] In accordance with section 40 of the *Patent Act*, I refuse to grant a patent for this application. Under section 41 of the *Patent Act*, the Applicant has six months within which to appeal my decision to the Federal Court of Canada.

Sylvain Laporte
Commissioner of Patents

Dated at Gatineau, Quebec,
this 2nd day of March, 2015