Commissioner’s Decision #1490

Décision de la Commissaire #1490

TOPIC: K11 (Treatment)

SUJET: K11 (Traitement)

Application No.: 2,597,700

Demande n°.: 2 597 700

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,597,700, having been rejected under subsection 30(3) of the *Patent Rules*, has subsequently been reviewed in accordance with paragraph 30(6)(*c*) of the *Patent Rules*. 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 2,597,700, which is entitled "Dosage regimes for trans-clomiphene" and is owned by Repros Therapeutics Inc. The outstanding defect to be considered is whether the subject-matter of the claims on file lies outside the definition of "invention" in section 2 of the *Patent Act*. A review of the rejected application has been conducted by the Patent Appeal Board ("the Board") pursuant to paragraph 30(6)(*c*) of the *Patent Rules*. As explained in more detail below, our recommendation is that the application be refused.

BACKGROUND

The application

[2] Patent application 2,597,700 (the instant application), based on a previously filed Patent Cooperation Treaty application, is considered to have been filed in Canada on March 17, 2006 and was laid open to the public on September 28, 2006.

[3] The claimed subject-matter of the application relates to the use of pharmaceutical compositions comprising trans-clomiphene for increasing testosterone levels, thereby treating hypogonadism or a disorder related thereto. More specifically, the application relates to a dosage regime for the treatment of hypogonadism or a disorder related thereto wherein the pharmaceutical compositions comprising trans-clomiphene are for administration according to a dosage regime that includes an initial period of daily dosing followed by a period of intermittent dosing.

Prosecution history

[4] On April 4, 2016, a Final Action (FA) was written pursuant to subsection 30(4) of the *Patent Rules*. The FA explained that the claims on file are directed to a method of medical treatment, subject-matter that lies outside the definition of "invention" in section 2 of the *Patent Act*.

[5] In a response to the FA (RFA) dated October 4, 2016, the Applicant submitted arguments as to why the subject-matter of the claims on file was patentable and not open to objection for the reasons outlined in the FA.

[6] As the Examiner was not persuaded by the Applicant's arguments, the application and an accompanying Summary of Reasons (SOR) were forwarded to the Board for review. The SOR maintained that the claims on file are directed to a method of medical treatment. In a letter dated January 25, 2017, the Board forwarded the Applicant a copy of the SOR.

[7] The present Panel was formed to review the application under paragraph 30(6)(*c*) of the *Patent Rules* and make a recommendation to the Commissioner as to its disposition. In a preliminary review letter dated April 8, 2019 (the PR Letter), we set out our preliminary analysis and rationale as to why the claims on file are directed to subject-matter that amounts to a method of medical treatment, subject-matter that is excluded from the definition of an invention as set out in section 2 of the *Patent Act*.

[8] The PR Letter also offered the Applicant the opportunity to make further written submissions and to attend an oral hearing in response to the Panel's preliminary review. The PR Letter indicated that in absence of a reply by May 10, 2019, the Panel would complete the review and provide its recommendation to the Commissioner.

[9] Since the Applicant did not reply to the PR Letter by the expected date, the Applicant's representative was contacted by phone. On May 21, 2019, the

representative confirmed that the PR Letter had been received and that no reply would be forthcoming.

ISSUES

[10] In view of the above, a single issue is considered in this review: whether claims 1 to 460 define subject-matter that lies outside the definition of "invention" in section 2 of the *Patent Act*.

LEGAL PRINCIPLES AND PATENT OFFICE PRACTICES

Purposive construction

[11] Essential elements are identified through a purposive construction of the claims. The exercise is conducted from the standpoint of a person skilled in the art by considering the whole of the disclosure, including the specification and drawings: *Free World Trust v Électro Santé Inc*, 2000 SCC 66; *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at paras 49(f) and (g) and 52. Similarly, according to the *Manual of Patent Office Practice* [*MOPOP*] §13.05, the first step in the construction of the claims of a patent application is to identify the person of ordinary skill in the art (POSITA) and the relevant common general knowledge (CGK). The next step is to identify the problem addressed by the inventors and the solution disclosed in the application. Essential elements can then be identified as those elements of the claims that are required to achieve the disclosed solution.

Statutory subject-matter and methods of medical treatment

[12] The definition of invention is set out in section 2 of the *Patent Act*:

> [I]nvention means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.

[13] Methods of medical treatment and surgery are not statutory subject-matter and are excluded from the definition of invention (see *Tennessee Eastman Co v Commissioner of Patents* (1970), 62 C.P.R. 117 (Ex. Ct.), aff'd [1974] S.C.R. 111).

[14] However, medical "use" claims have been considered to be directed to patentable subject-matter (see *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 (*AZT*)). In the *AZT* case, the Supreme Court suggested that a complication may arise in a case where a claim, although drafted as a medical use, nonetheless attempts to "fence in" an area of medical treatment by indicating "how and when" (e.g., by indicating a dosage range or treatment regime) a pharmaceutical composition is to be used. In that decision, the Supreme Court considered a claim directed to a pharmaceutical composition comprising an old compound (AZT) for a new use in treating AIDS and found at para 50 that the patentee had not attempted to fence in a method of medical treatment:

> The AZT patent does not seek to "fence in" an area of medical treatment. It seeks the exclusive right to provide AZT as a commercial offering. How and when, if at all, AZT is employed is left to the professional skill and judgment of the medical profession.

[15] A number of lower court decisions have considered the validity of medical use claims that concern a dosage range or regime (*Axcan Pharma Inc v Pharmascience Inc*, 2006 FC 527; *Merck & Co, Inc v Pharmascience Inc*, 2010 FC 510; *Janssen Inc v Mylan Pharmaceuticals ULC*, 2010 FC 1123; *AbbVie Biotechnology Ltd v Canada (Attorney General)*, 2014 FC 1251 [*AbbVie*].

[16] Upon reviewing prior decisions, the Federal Court in *AbbVie* concluded the following at paras 112 to 114:

> [112] The respondent cautioned against relying on catch phrases rather than principles. In my view, the jurisprudence reflects that approach – the principle has been applied regardless of the Courts' references to "fencing in" or to "fixed dosages". The issue in every case has been whether the patent claims a method of medical treatment. In applying the same principles, claims to fixed dosages and

> schedules which do not involve any professional decision-making have been accepted as patentable.
>
> [113] However, just because the claims involve a fixed dosage and schedule does not mean that they are automatically patentable, nor does it mean that they constitute unpatentable subject matter. The fixed dosage and schedule may be a good signal or starting point, but the evidence about that claimed dosage regime and schedule may indicate that it is not exactly as it is claimed and that adjustments are needed which requires skill and judgment.
>
> [114] The review of the relevant case law supports the appellants' understanding of the principles from the jurisprudence and demonstrates that the Courts have consistently found that a claim directed to the exercise of professional skill or judgment is not patentable. However, a claim which does not restrict, or interfere with, or otherwise engage professional skill or judgment – including a claim for a fixed dosage and or a fixed dosage schedule or interval- is not impermissible subject matter where there is no evidence to contradict that claimed dosage. Contrary to the Commissioner's decision and the respondent's position, Janssen has not changed the law. [emphasis added]

[17] The Office's current practice with regard to the patentability of medical use claims is explained in Practice Notice 2015-01, entitled *Revised Examination Practice Respecting Medical Uses* [*PN 2015-01*]. The Office's practice was revised during the course of prosecution of the instant application between the sending of the Examiner's report dated July 28, 2014 and the FA, in response to the decision in *AbbVie*.

[18] According to *PN 2015-01*, the determination of whether the subject-matter of a claim is statutory is based on the essential elements of the claim as determined by a purposive construction, as outlined in *MOPOP* §13.05. If it is determined after a purposive construction that a dosage range, or dosage regimen that includes a range, is an essential element of a claim encompassing the use of a known compound in an established treatment, then the claim may cover a method of medical treatment. Where an essential element only serves to instruct a medical professional "how" to treat a patient, rather than "what" to use to treat the patient, it must be determined whether the essential element prevents, interferes with or requires the professional skill of a physician. If the answer is "yes", this will lead to the conclusion that the

claimed use encompasses a method of medical treatment that does not comply with section 2 of the *Patent Act*.

[19] Notably, *PN 2015-01* recognizes that there may be instances where essential elements serve to instruct a medical professional "how" to treat a patient but are not considered to prevent, interfere with or require the professional skill of a physician. For example, essential elements that narrow treatment to a fixed dosage or a fixed dosage regimen are not considered to point to a limitation of a physician's professional skill or judgment.

ANALYSIS

Purposive construction

[20] In our view, independent claim 1 is representative of all the independent claims on file, as they all recite generally similar subject-matter. Claim 1 reads as follows.

> 1. A composition comprising 0% w/w cis-clomiphene and 100% w/w trans-clomiphene or a salt or solvate thereof as active agent for administration to a hypogonadal human male at a dose of about 12.5 mg trans-clomiphene according to a dosage regime, wherein the composition is for daily administration to achieve a pharmacologically effective blood concentration of testosterone and thereafter for administration at a 3 day interval between two consecutive doses for raising testosterone levels in the male to treat the hypogonadism or a disorder related thereto.

[21] The other independent claims 2 to 224 and 231 to 454 recite different amounts of trans-clomiphene (5, 25, 37.5, 50, 62.5, 75 or 100 mg) and/or different time intervals (3, 4, 5,…, 30 day interval).

[22] Accordingly, we consider that the following claim template constitutes a fair representation of the subject-matter of the independent claims wherein "**X**" and "**Y**" will vary depending on the particular independent claim:

> A composition comprising 0% w/w cis-clomiphene and 100% w/w trans-clomiphene or a salt or solvate thereof as active agent for administration to a hypogonadal human male at a dose of about **X** mg trans-clomiphene according to a

> dosage regime, wherein the composition is for daily administration to achieve a pharmacologically effective blood concentration of testosterone and thereafter for administration at a **Y** day interval between two consecutive doses for raising testosterone levels in the male to treat the hypogonadism or a disorder related thereto.

[23] Dependent claims 225 to 230, and 455 to 460 further specify that the male suffers from secondary hypogonadism (claims 225 and 455) or a disorder related thereto (claims 226 to 228 and 456 to 458), specify that the male is fertile and that the fertility is maintained (claims 229 and 459) and specify that the salt of trans-clomiphene is the citrate salt (claims 230 and 460).

[24] The above views were presented to the Applicant in the PR Letter.

The POSITA and the relevant CGK

[25] In the PR Letter, we adopted from the FA the following identifications of the POSITA and some elements of the CGK:

> [A] physician or clinician in the field of male infertility with significant experience treating hypogonadism and extensive knowledge of the various treatment options. They would have knowledge of clomephene [*sic*] (both cis- and trans-isomers) and its use for therapeutic intervention in men with low testosterone levels. They would have knowledge of clomiphene (both cis- and trans-isomers) and its use for therapeutic intervention in men with low testosterone levels (page 5, lines 3-18 of the present description).

[26] Further, we agreed with the Applicant that a pharmacologically effective blood concentration of testosterone should also be considered CGK and expressed the view that the POSITA would consider 300 ng/dl to be the commonly known lower limit of a pharmacologically effective blood concentration of testosterone.

The problem to be solved and the proposed solution

[27] In the PR Letter, we stated the following with regard to the problem to be solved and the corresponding solution:

> [W]e are of the preliminary view that he problem to be solved by the subject-matter of the claims on file is a need for an improved treatment schedule for the therapeutic use of trans-clomiphene to treat hypogonadism or a disorder related thereto and that the corresponding solution encompassed by the subject-matter of the claims is to switch from a daily administration schedule to an intermittent administration schedule once a pharmacologically effective blood concentration of testosterone is achieved and still achieve therapeutic effect.

The essential elements that solve the identified problem

[28] In the PR Letter, we identified the following elements in the independent claims wherein "**X**" and "**Y**" will vary depending on the particular independent claim:

A. a composition comprising 0% w/w cis-clomiphene and 100% w/w trans-clomiphene or a salt or solvate thereof as active agent for raising testosterone levels in the male to treat the hypogonadism or a disorder related thereto;

B. a dose of about **X** mg trans-clomiphene;

C. a first daily administration schedule to achieve a pharmacologically effective blood concentration of testosterone; and

D. a following administration schedule at a **Y** day interval between two consecutive doses.

[29] Having in mind the solution identified above, we expressed the view that step C dictates when step D is to begin and therefore considered that a first daily administration schedule to achieve a pharmacologically effective blood concentration of testosterone is an essential element of independent claim 1 and of all the other claims on file.

[30] As there has been no reply to the PR Letter by the Applicant, we therefore adopt for the purposes of this review the above identifications of the POSITA and the relevant CGK, as well as the characterization of the problem to be solved, the solution and the essential element identified above.

Subject-matter and methods of medical treatments

[31] The FA offered the following analysis of the essential element of a first daily administration schedule to achieve a pharmacologically effective blood concentration of testosterone:

> The physician would be required to monitor the patient's progress and make adjustments to the amount, and to know whether a pharmacologically effective blood concentration of testosterone is achieved in order to determine when to start the follow-up period. In other words, the claims require the physician to exercise his/her skill and judgement. The exercise of skill or judgement is not, in this case, limited to choosing whether or not to use the dosage regimen claimed. A claim directed to the exercise of professional skill or judgement is not patentable. [emphasis in the original]

[32] The RFA recited the following arguments as to why the claims are directed to statutory subject-matter:

- The claims on file are directed to specific dosages and specific time intervals between consecutive dosages, effectively removing the need for skill or judgment by the medical practitioner.

- It is clear from *AbbVie* that a fixed dosage and schedule, while not necessarily automatically patentable, equally cannot be dismissed out of hand as constituting non-statutory subject-matter. Rather, a purposive construction based on the specification will reveal whether the claims require the professional skill and judgment of a physician.

- The initial period of achieving a pharmacologically effective blood concentration of testosterone does not require the physician to exercise his/her skill and judgment because the relevant CGK includes a specific and art-accepted definition of what constitutes a pharmacologically effective blood concentration of testosterone in the context of the present claims.

> Further, it is incorrect to assert that the physician would be required to "make adjustments" to the amount and to know whether a pharmacologically effective blood concentration of testosterone is achieved.

[33] We also noted that the Applicant's submissions in the RFA acknowledge on page 3 that "the patient's testosterone level must be routinely monitored during the initial phase".

[34] In the PR Letter, although we agreed with the Applicant that the pharmacologically effective concentration of testosterone in the blood is a matter of CGK, this does not mean that it can be disregarded simply on that basis or that the professional skill and judgement of a physician are not involved in determining whether the appropriate level has been reached in an individual patient. While a physician's decision-making may be informed by commonly known blood concentrations of metabolites or hormones, it does not follow that such knowledge is therefore sufficient to conclude that their judgment is removed from the process.

[35] In the PR Letter, we also agreed with the Applicant that the physician would not be required to make adjustments to the amount of trans-clomiphene during the initial period of achieving a pharmacologically effective blood concentration of testosterone as the amount of trans-clomiphene recited in the claims is fixed. However, we disagreed with the Applicant's submission that the physician would not be required to know whether a pharmacologically effective blood concentration of testosterone is achieved to perform the claimed subject-matter because we considered that such knowledge of the patient's blood concentration of testosterone serves to define in the claims when the initial daily administration schedule ends and when the intermittent administration schedule begins.

[36] Also relevant to the analysis is our view that *Abbvie* indicates that if the physician would be required to monitor the patient's treatment evolution to make a decision in order to perform the subject-matter of a claim, it is suggestive of the exercise of skill and judgment:

> In *Janssen*, the claims involved a range with several variables; the titration regimen is itself a type of range and the physician must start slowly and adjust the dosage amount, over time, based on the progress of the patient. In addition, the expert evidence indicated that the physician would be required to monitor the patient's progress and make adjustments to the amount and to know when to increase the amount (that is, exercise his skill and judgment). Justice Barnes also noted that the patent claimed a known drug for an established purpose using the well-known titration treatment or approach. The patenting of that dosage regime, which was found to require the same exercise of skill and judgment as always, could not be patented and was a method of medical treatment. [para 117]

[37] In the instant case, the duration of the initial period of achieving a pharmacologically effective blood concentration of testosterone is not fixed and we consider that the physician must monitor the patient's testosterone levels during the initial period in order to make a professional judgment on the basis of the relevant CGK regarding pharmacologically effective blood concentrations of testosterone and to know/decide when to switch from a daily administration schedule to an intermittent administration schedule. We are therefore of the view that performing the subject-matter of the claims would require the physician to exercise his/her professional skill and judgment.

[38] In light of the above, and in the absence of submissions in response to the PR Letter from the Applicant, we are of the opinion that the claims on file are directed to a method of medical treatment, subject-matter that lies outside of the definition of an "invention" as set out in section 2 of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[39] For the reasons set out above, we recommend that the application be refused on the basis that the claims on file are directed to a method of medical treatment, subject-matter that lies outside of the definition of an "invention" as set out in section 2 of the *Patent Act*.

Marcel Brisebois Member	Ed MacLaurin Member	Stephen MacNeil Member

DECISION OF THE COMMISSIONER

[40] I concur with the findings of the Patent Appeal Board and its recommendation that the application should be refused because the claims on file are directed to a method of medical treatment, subject-matter that lies outside of the definition of an "invention" as set out in section 2 of the *Patent Act*.

[41] Accordingly, I refuse to grant a patent on 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.

Johanne Bélisle
Commissioner of Patents
Dated at Gatineau, Quebec,
this 5th day of August, 2019