Commissioner’s Decision #1423

Décision du commissaire n^{o} 1423

TOPIC: O00 (Obviousness); B00 (Ambiguity or indefiniteness)

SUJET: O00 (Évidence); B00 (Caractère ambigu ou indéfini)

Application No.: 2,477,870

Demande n°: 2 477 870

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,477,870, 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 if the necessary amendments are not made.

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INTRODUCTION

[1] This recommendation concerns the review of rejected patent application number 2,477,870, which is entitled "Electrode assembly for constant-current electroporation and use" and owned by Advisys, Inc. The outstanding defects to be addressed are whether the claimed invention is obvious and whether the subject matter of claims 7, 27, 33-35 and 43 is indefinite. A review of the rejected application has been conducted by the Patent Appeal Board pursuant to paragraph 30(6)(*c*) of the *Patent Rules*. As explained in more detail below, our recommendation is that the Applicant be notified that claims 1-61 as proposed in the letter of July 20, 2015 are "necessary" amendments under subsection 30(6.3) of the *Patent Rules* for compliance with the *Patent Act* and *Patent Rules*.

BACKGROUND

The application

[2] Patent application 2,477,870 was filed in Canada on March 6, 2003 and published on September 18, 2003.

[3] The application relates to an electroporation system, and its use, for facilitating the introduction of a macromolecule into cells of a selected tissue in a body or plant. Electroporation, also termed electropermeabilization, is a technique in which an electrical field is applied to cells or tissues to increase the cell membrane permeability. The application of controlled electric pulses to cells creates temporary pores in the cell membranes through which polynucleotides and other macromolecules of interest may pass into the interior of the cell. Over time, the pores close, trapping the molecules which in turn may exert a biological effect.

History

[4] On January 19, 2015, a Final Action ("FA") was written pursuant to subsection 30(4) of the *Patent Rules*. The FA states that the claims on file are obvious, contrary to section 28.3 of the *Patent Act* and that claims 7, 27, 33-35 and 43 are indefinite, contrary to subsection 27(4) of the *Patent Act*.

[5] In a response to the FA ("R-FA") dated July 20, 2015, the Applicant submitted an amended claim set (the "Proposed Claims") and argued that the claimed invention would not have been obvious to the person of ordinary skill in the art at the claim date and that the Proposed Claims overcome the indefiniteness defect.

[6] As the Examiner considered that the application did not comply with the *Patent Act* and was not convinced that the Proposed Claims submitted by the Applicant in the R-FA would render the application allowable, the application was forwarded to the Patent Appeal Board ("the Board") for review, along with a Summary of Reasons ("SOR") that maintains that the application was defective. With regard to the proposed amendments made in the R-FA, the SOR explains that the indefiniteness defect would have been withdrawn in light of the proposed amendments had the Proposed Claims been found non-obvious in view of the cited prior art and otherwise compliant with the *Patent Act* and *Patent Rules*. However, the SOR states that the Proposed Claims are obvious in view of the cited prior art.

[7] In a letter dated October 20, 2015 (the "Acknowledgement Letter"), the Board forwarded the Applicant a copy of the SOR and offered the Applicant an opportunity to make further written submissions and/or attend an oral hearing. In a letter dated January 19, 2016 ("R-SOR"), the Applicant provided written submissions in response to the SOR and expressed the wish to participate in an oral hearing in the event that the Examiner's rejection as set out in the SOR is maintained.

[8] 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.

[9] It is considered that an oral hearing is not required at this time because, based on the review of the application and record as it presently stands, our recommendation is to notify the Applicant that the Proposed Claims constitute amendments that are "necessary" for compliance with the *Patent Act* and *Patent Rules*.

ISSUE

[10] There are two issues to address in this review:

1. whether the subject matter defined by the claims on file is obvious, contrary to section 28.3 of the *Patent Act*; and

2. whether claims 7, 27, 33-35 and 43 on file are indefinite, contrary to subsection 27(4) of the *Patent Act*.

LEGISLATION AND LEGAL PRINCIPLES

Purposive construction

[11] In accordance with *Free World Trust v Électro Santé Inc.*, 2000 SCC 66, essential elements are identified through a purposive construction of the claims done by considering the whole of the disclosure, including the specification and drawings (see also *Whirlpool Corp v Camco Inc.*, 2000 SCC 67 at paras. 49(f) and (g) and 52). In accordance with the *Manual of Patent Office Practice* §13.05 [revised June 2015; MOPOP], the first step of purposive claim construction is to identify the person of ordinary skill in the art ("POSITA") and their 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.

Obviousness

[12] Section 28.3 of the *Patent Act* sets out the statutory requirement that the claimed subject-matter must not be obvious to the POSITA:

> 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.

[13] 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?

Indefiniteness

[14] Subsection 27(4) of the Patent Act states:

> 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.

[15] In *Minerals Separation North American Corp v Noranda Mines Ltd*, [1947] Ex CR 306, 12 CPR 99 at 146, the Court emphasized the obligation of an applicant to make clear in his claims the ambit of the monopoly sought, and the requirement that the terms used in the claims be clear and precise:

> By his claims the inventor puts fences around the fields of his monopoly and warns the public against trespassing on his property. His fences must be clearly placed in order to give the necessary warning and he must not fence in any property that is not his own. The terms of a claim must be free from avoidable ambiguity or obscurity and must not be flexible; they must be clear and precise so that the public will be able to know not only where it must not trespass but also where it may safely go.

ANALYSIS

Purposive construction

[16] We note that the FA does not provide a detailed purposive construction analysis of the claims on file and that the construction of the claims does not appear to be at issue in the present case.

[17] In addition, we consider that the claim terminology would be clear to the POSITA (defined below in the obviousness analysis section) and that the scope of the claims could be readily ascertained.

Obviousness of the claims on file (section 28.3 of the *Patent Act*)

Identify the POSITA and the relevant CGK

[18] On the third page, the FA identified the POSITA as an "engineer familiar with electroporation systems and, in general, electrical processes involving control and feedback". As the Applicant did not dispute this characterization, this characterization as the POSITA was adopted.

[19] In regard to the relevant CGK possessed by the POSITA, the FA described the CGK as including "the design and use of electroporation systems (voltage and current control), general physiology and the effects that electric simulation have on a patient".

[20] The R-FA and the R-SOR did not indicate disagreement with this assessment. Although this assessment appears to be generally consistent with the background information provided on pages 1-5 of the instant description, we consider that the CGK relating to the use of electroporation systems for facilitating the introduction of a macromolecule into cells of a selected tissue should be clarified. Based on our review of the instant description and the scientific review article Somiari et al., *Theory and in vivo application of electroporative gene delivery*, Mol Ther., 2(3), pp. 178-187, 2000, we consider that the relevant CGK includes the following:

- The most common electroporation protocols for tissues used predetermined voltage pulses. A voltage pulse that is too high causes excessive flow of current producing heat and associated irreversible cell damage, potentially reducing overall electroporation efficiency. Excessive resistive heating of the

tissue and associated cell damages negatively impact electroporation efficiency.

- Theoretic and empiric experimentation indicate that the critical parameters governing electroporation efficacy relate to the electrical field strength across a given cell, which is a function of applied voltage, the conductivity or resistance of regional tissue elements and extracellular fluids, and the electrode design and configuration.

- The electrode configuration influences the local electric field lines, and ultimately the distribution of electropermeabilized cells. Although a homogenous field distribution is desirable and models to predict electric field distribution have been developed, this sought after characteristic is not associated with any particular type of electrode or configuration. Electrical fields are typically administered with either needle or flat plate (caliper) electrode arrangements wherein the electrodes are arranged and energized in opposing pairs.

- The efficiency of electroporation varies under different experimental conditions and within different tissues. Empiric parameter optimization is a commonly used approach to obtain efficient electroporation in different tissues. The electroporation parameters (e.g., the duration, frequency, magnitude and number of voltage pulses) must be optimized for each tissue in order to maximize gene delivery while minimizing irreversible cell damage.

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

[21] We consider that independent claim 1 is representative of the claimed subject matter:

1. A modular electrode system for facilitating the introduction of a macromolecule

into a cell of a selected tissue in a body or plant, comprising:

(a) a plurality of needle electrodes for penetrating the selected tissue, the plurality of needle electrodes being mounted on a support structure and arranged in a spaced relationship in which the plurality of needle electrodes are symmetrically arranged without opposing pairs, the support structure includes a sterile injection channel adapted to receive a syringe needle, the syringe needle being located in an area between the plurality of needle electrodes;

(b) a constant-current pulse generator subsystem in electrical communication with the plurality of needle electrodes, wherein the constant-current pulse generator subsystem is capable of applying a constant-current pulse between any plurality of electrodes and of maintaining a constant current independent of any resistance change in the selected tissue during the constant-current pulse; and

(c) a programmable constant-current pulse controller in communication with the constant-current pulse generator subsystem for managing the system to expose the selected tissue to a substantially constant current independent of any resistance change in the selected tissue during the constant-current electric pulse, the controller being capable of sampling, monitoring and recording voltage and current waveforms, the controller having an impedance meter in electrical communication with the plurality of needle electrodes and the constant-current pulse generator subsystem and configured to relay impedance information between the plurality of needle electrodes and the controller for measuring impedance of the tissue.

[22] Independent claims 25 and 37 essentially share the same elements. Independent claim 25 further defines how the electrodes are in electrical communication with the rest of the system and adds elements relating to the transfer of a constant–current pulse to only a subset (two electrodes) of the plurality of the needle electrodes (i.e., a switching mechanism and an input device for programming a logical sequence of

coded instructions). Independent claim 37 further specifies that the contemplated system is portable.

[23] According to the FA the inventive concept is the following:

> The inventive concept appears to be utilizing a constant-current controller to maintain a constant current between the electrodes irrespective of the electrical impedance found between the electrodes wherein the electrical impedance may change during the operation of the electroporation system and further wherein the electrodes are arranged symmetrically without opposing pairs.
>
> Accordingly, the problem to be solved is how to accurately control the current passing through the target area while also ensuring uniform energy delivery (Instant Application [0016]).

[24] We have considered the instant description, notably paragraphs [0015] to [0017] that underline different problems and constraints that are associated with known electroporation systems and methods and which limit the overall efficacy of the technique; namely, that the use of predetermined voltages can produce excessive heat in certain tissues and needle electrode arrays with opposing pairs delivers current focused on the center of the electrode assembly:

> **[0015]** The aforementioned patent disclosures along with many others describe electroporators and methods for use by utilizing a predetermined voltage between the electrodes. Because the impedance between electrodes that are embedded in a tissue can vary from case-to-case, or tissue-to-tissue, a predetermined voltage does not produce a predetermined current. Thus, prior art does not provide a means to delineate the exact dosage of current to which the cells are exposed and limits the usefulness of the electroporation technique. For this very reason, conventional electroporators generate tremendous amounts of heat is [*sic*] tissues that can easily kill cells. For example, a typical electronic 50ms pulse with an average current of 5 Amperes across a typical load impedance of 25 ohms can theoretically raise the temperature in tissue 7.5°C, which [is] enough to kill cells. In contrast, the power dissipation decreases in a constant-current system and prevents heating of a tissue, which reduces tissue damage and contributes to the overall success of the procedure.

[0016] The difficulties present in prior-art electrodes stem from the fact that the pulse energy is concentrated in the center of the array, the point where the material to be transfected is deposited.

As a result, the spatial distribution of energy delivery assumes a very non-uniform character. Therefore, only a fraction of the cells in the volume encompassed by the electrode assembly is electroporated.

[0017] Thus, there is a need to overcome the problems of prior art by providing a means to effectively control the dosage of electricity delivered to the cells in the inter-electrode space by precisely controlling the ionic flux that impinges on the conduits in the cell membranes.

[25] We have also considered the following passage found at paras [0054] to [0057] of the instant description that generally explains how the described invention addresses the shortcomings of the prior art by keeping the exact dosage of current under a certain threshold and by delivering the predetermined electroporative current to a volume of tissue without causing excessive concentration of cumulative current in any one location:

[0054] Controlling the current flow between electrodes allows one to determine the relative heating of cells. Thus, it is the current that determines the subsequent effectiveness of any given pulsing protocol and not the voltage across the electrodes. Predetermined voltages do not produce predetermined currents, and prior art does not provide a means to determine the exact dosage of current, which limits the usefulness of the technique. Thus, controlling an maintaining the current in the tissue between two electrodes under a threshold will allow one to vary the pulse conditions, reduce cell heating, create less cell death, and incorporate macromolecules into cells more efficiently when compared to predetermined voltage pulses.

[0055] One embodiment of the present invention to overcome the above problem by providing a means to effectively control the dosage of electricity delivered to the cells in the inter-electrode space by precisely controlling the ionic

flux that impinges on the conduits in the cell membranes. Thus, the precise dosage of electricity to tissues can be calculated as the product of the current level, the pulse length and the number of pulses delivered. In order to implement such a constant-current system, an electrode apparatus (as shown in Figure 3 and 4) connected to a specially designed circuit (as shown in Figure 5) must be considered.

[0056] One goal of the present invention to provide a means to deliver the electroporative current to a volume of tissue along a plurality of paths without, causing excessive concentration of cumulative current in any one location, thereby avoiding cell death owing to overheating of the tissue. For example, the maximal energy delivery from a particular pulse would occur along a line that connects two electrodes. Prior art teaches that the electrodes are present in pairs and that the voltage pulses are delivered to the paired electrodes of opposed polarity. Accordingly, the maximal energy delivery from a particular pulse would occur along a line that connects two electrodes. An example of the energy delivery pathway in a prior art electrode, which utilizes three pairs of radial electrodes with a center electrode, is described above and as in Figure 1. A distribution of the energy crosses at the center point of the electrodes, which may lead to unnecessary heating and decreased survival of cells.

[0057] The electrodes of one embodiment of the present invention are arranged in a radial and symmetrical array, but unlike prior art, the electrodes are odd numbered, and not in opposing pairs (Figure 2). Delivering an electric pulse to any two of the electrodes from an electric pulse generator results in a pattern that is best described as a polygon. Tracing this pattern would result in a five-point star with a pentagon of electrical pulses surrounding the center of the array in tissue where the concentration of molecules to be transfected is greatest. Although not wanting to be bound by theory, it is not the odd number of electrodes, per se, that makes a difference, but in the direction of the current paths. With the configuration of prior art, all the pulses generate a current that passes through the center of the assembly. The cumulated dose, i.e. the heating effect is therefore concentrated in the center, with the peripheral dose falling off rapidly. With the "five-pointed star" arrangement, the dose is spread more evenly, over a larger volume. For example, if the electrodes are arranged in an array of five electrodes, the pulses might be

> sequentially applied to electrodes 1and 3, then 3 and 5, then 5 and 2, then 2 and 4, then 4 and 1. However, because the tissue between the electrodes is a volume conductor, a certain current intensity exists along parallel lines, weakening as the distance from the center line increases. The cumulative effect of a sequence of pulses results in a more uniform distribution of the energy delivered to the tissues, increasing the probability that the cells that have been electroporated actually survive the procedure.

[26] Based on the claimed subject matter, the above passages of the instant description, and the CGK identified above, we consider that the inventive concept common to the independent claims is a modular electrode system adapted to receive a syringe needle that more uniformly distributes the electroporative current to a larger volume of tissue without causing excessive concentration of cumulative current, particularly immediately around the injection point wherein the material to be transfected is deposited, by combining:

i) a plurality of needle electrodes that are symmetrically arranged without opposing pairs; and

ii) means for maintaining a constant current independent of any resistance change in the tissue.

[27] According to the instant application, this inventive concept represents an advantage over conventional predetermined voltage electroporation systems and typical electrode assemblies comprising opposing pairs because predetermined voltage pulses may cause excessive cumulative current when applied to tissues of different electrical resistance and because typical needle electrode arrays with opposing pairs may lead to excessive concentration of cumulative current in the center of the electrode array.

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

[28] Two principal reference documents are cited in the FA for obviousness with respect to independent claim 1:

- United States patent application US 2002/0010415 A1 ("D1") having a publication date of January 24, 2002 (24-01-2002); and
- United States patent 5,873,849 ("D2") having a publication date of February 23, 1999 (23-02-1999).

[29] D1 discloses the importance of limiting the current and associated charge density in the tissue, by use of partially conducting electrodes or by delivering the electrostimulation in constant current mode, to allow the effective electroporation of a selected tissue while minimizing the otherwise expected deleterious side effects of applied electrical energy, such as involuntary muscle movements and joule heating (see paras [0012], [0031], [0033], and [0040]).

[30] D1 discloses that voltage and current delivered to the portion of the body are measured using a data acquisition system, teaches that electrical resistance of the tissue being treated may vary during the electroporation treatment and discloses the use of a feedback arrangement that is configured to control for constant current so that the signal generator adjust the voltage output level if the average current increases above or decreases below a predetermined value (see para [0063]).

[31] With respect to the nature of the electrodes and their possible configurations, D1 teaches the use of any configuration of electrodes in which at least two or more opposed electrodes are provided, including an array of separate or coupled anode and cathode electrodes in opposed pairs. The electrodes can be subdivided to provide discrete or distributed levels of conductive contact with the tissue, so as to provide current paths that subtend the volume of tissue into which the pharmaceutical agent

to be delivered has been infused (see para [0038]). D1 further teaches that one must consider not only the spatial extent or area of current distribution, but also factor in the nature and orientation of the treatment electrodes to both the macroscopic anatomy as well as the microscopic structure of the host tissue under treatment (see para [0115]).

[32] In addition, D1 discloses that the electroporation system could comprise an injecting needle/electrode holder for guiding the needle and electrodes into the proper orientation with respect to the portion of the body and with respect to the electrodes so that a mounted injecting needle can discharge a pharmaceutical agent into a space between the electrodes or electrode array (see para [0035]).

[33] D2 teaches that in order to achieve electroporation, the electric fields propagated in tissue by the delivery of specific electrical waveforms must apply sufficient transmembrane voltage and pulse duration to induce cell membrane permeability, yet not exceed inherent upper limits leading to cell death, and that a two opposing pair electrode system is poorly suited to establish uniform electric field coverage (see column 1, lines 59-64 and column 2, lines 25-29).

[34] D2 discloses the use of an electrode array ("tricell") comprising at least three individually addressable electrodes disposed so as to form a triangle in a plane intersecting the electrodes to achieve uniform electroporation, allowing a therapeutic agent to permeate the cells of the tissue being treated while mitigating electric field-induced cell lysis.

[35] In the tricell needle electrode array of D2, the plurality of needle electrodes are symmetrically arranged in a circular configuration without opposing pairs wherein no congruent electroporation overlap points develop and wherein a decentralized pattern shaped as a triangle is produced during electroporation (Figures 4-6). Further, D2 teaches that alternative electrode array geometries have disadvantages

when compared to the tricell needle electrode array (see Figures 7-9 and column 9, lines 26-43).

[36] With regard to the electroporation parameters, D2 teaches that the voltage should be adjusted so that the generated electric field has sufficient intensity to make the membranes of cells in the tissue transiently permeable (see column 7, lines 5-22). In order to mitigate the cell death associated with the more intense electric fields in certain areas around the electrodes, D2 teaches that optimal pulse parameters could be achieved by using a cascaded pulse sequence where applied voltages are cascaded from lower values initially, being progressively increased in each subsequent round and reaching optimal therapeutic pulse parameters in a final round of pulsing (see column 10, lines 33-51).

[37] In sum, the differences between the cited references, considered individually, and the inventive concept of the independent claims identified above are the following:

- The electroporation system disclosed in D1 does not comprise a plurality of needle electrodes that are symmetrically arranged without opposing pairs; and

- The electroporation system disclosed in D2 does not comprise means for maintaining a constant current independent of any resistance change of the tissue undergoing electroporation.

[38] When the references are combined, we consider that there are no longer any differences between the inventive concept and the state of the art.

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?

[39] Although there is no difference between the state of the art and the inventive concept when the two references are combined, it is still necessary to determine whether the

POSITA would have been led to take the step of substituting a needle electrode array without opposing pairs, as disclosed in D2, in place of needle electrode arrays with opposing pairs in an electroporation method that delivers the electrostimulation in constant-current mode as disclosed by D1.

[40] In that respect, the FA asserts that the POSITA would have been led directly and without difficulty to combining D1 with D2, but we note that neither the FA nor the SOR explains how the POSITA having one of the references would have been led directly and without difficulty to combine it with the other to arrive at the claimed invention (FA at page 5):

> As such, it is clear that D1 envisions the invention being implemented in embodiments where multiple electrodes are arranged in an array where two or more electrodes may be energized at any given time whereas D2 clearly discloses that it may be used in conjunction with any type of electrodes. Accordingly, a person skilled in the art would be led directly and without difficultly to combining D1 to D2. Furthermore, utilizing the electrode arrays of D2 in conjunction with the electroporation system of D1 would not have required any inventive ingenuity as the use of electrode arrays was clearly contemplated by D1. [Emphasis added]

[41] We also note that the above passage suggests that the instant application discloses a combination invention. A given combination is not necessarily obvious because each part of the combination is known. In that regard, the Federal Court of Appeal in *Bridgeview Manufacturing Inc. v. 931409 Alberta Ltd. (Central Alberta Hay Centre)*, 2010 FCA 188, stated the following at para 51:

> I agree with Bridgeview that the 334 patent discloses a combination invention. It is not fair to a person claiming to have invented a combination invention to break the combination down into its parts and find that, because each part is well known, the combination is necessarily obvious: see, for example, *Stiga Aktiebolag v. S.L.M. Canada Inc.* (1990), 34 C.P.R. (3d) 216 at page 245 (F.C.T.D.), which quotes this passage from *Wood & Amcolite Ltd. v. Gowshall Ltd.* (1936), 54 R.P.C. 37 at page 40 (per Greene L.J.):
>
> > The dissection of a combination into its constituent elements and the examination of each element in order to see whether its use is obvious or not is, in our view, a method which ought to be applied with great caution since it tends to obscure the fact that the invention claimed is the combination. Moreover, this method also tends to obscure the facts that the

> conception of the combination is what normally governs and precedes the selection of the elements of which it is composed and that the obviousness or otherwise of each act of selection must in general be examined in the light of this consideration. The real and ultimate question is "Is the combination obvious or not?"
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> See also *Omark Industries (1960) Ltd. v. Gouger Saw Chain Co. et al* (1964), 45 C.P.R. 169 (Ex. Ct.) and *Canamould Extrusions Ltd. v. Driangle Inc.*, 2003 FCT 244 (affirmed 2004 FCA 63). [Emphasis added]

[42] The climate in the relevant field at the time the invention was made and the motivation at the claim date to solve a recognized problem are also relevant considerations as to whether one might reasonably expect the POSITA to combine elements of the prior art to come up with the claimed combination (see *Novopharm Limited v. Janssen-Ortho Inc.*, 2007 FCA 217 at para 25).

[43] Based on the instant description, notably paras [0015]-[0017] and [0054]-[0057] cited above, it is our view that the inventors' idea of combining the claimed elements is derived from their observations that:

i) electrical resistance varies from tissue-to-tissue, leading to excessive heating in certain tissues if a predetermined voltage is applied; and

ii) the pulse energy is concentrated in the center of the electrode array when typical needle electrode arrays with opposing pairs are used, which is an important consideration in the context of an electrode system adapted to receive a syringe needle that delivers the macromolecules in the center of the electrode array.

[44] With regard to the CGK and the climate in the field of the design and use of electroporation systems, we are of the view that the observations that lead to the conception of the claimed combination invention were not generally known. As mentioned above, a homogenous field distribution was a commonly known desirable characteristic at the claim date and models to predict the field strength across tissues for different electrode configurations were known. Some common electrode

configurations were known to develop a more homogenous electrical field than others but the few tested electrode arrangements had opposing pairs. Hence, we are of the view that an observed problem of lack of electrical field distribution uniformity in a given tissue was typically addressed by using different electrode configurations, all having opposing pairs, that would show satisfactory electrical field uniformity. Accordingly, we also consider that the concentration of the pulse energy at the center of typical electrode arrangements with opposing pairs was not generally perceived as a critical factor with regard to the uniformity of the electrical field. Further, we are of the view that potential excessive delivery of current associated with a predetermined voltage pulse and the tissue electrical resistance variation were not perceived as problems needing a solution because any observed excessive heating in a target tissue resulting from a too high voltage pulse or from changing target tissue was typically resolved by adjusting the electrical pulse parameters through empiric experimentations.

[45] With respect to cited prior art document D1 and a possible motivation to use needle electrode arrays other than the typical ones with opposing pairs, the closest teaching appears to be found at para [0115]. In the context of the whole disclosure of D1, this passage teaches that although the overall current density incurred by a given tissue is an important parameter, the nature and orientation of the treatment electrodes must be taken into consideration because the tissue in which the current is propagating is neither spatially isotropic nor homogeneous. Hence, the concerns are directed to the problematic complex character of certain tissues rather than to the type of electrodes to be used. Further, nothing in this passage suggests that a needle electrode array without opposing pairs would address the tissue-related anatomical challenges. Moreover, it is our understanding that D1 is mainly concerned with keeping the overall current density applied to the target tissue to a minimum to prevent or minimize the involuntary muscle movements and joule heating (see paras [0012], [0031], [0033], and [0040]). D1 addresses such concerns by using partially insulating electrodes and a constant voltage or by maintaining the overall current density under a predetermined value sufficient to obtain the biological enhancement

effects sought (see para [0122]). We are of the view that D1 does not recognize excessive joule heating in the center of electrode arrays with opposing pairs or the general lack of uniformity in the energy distribution within electrode arrays with opposing pairs as a problem that needed to be addressed. D1 is arguably pointing to many obvious choices of CGK electrode pairs and electrodes arrays, but we consider that an electrode array without opposing pairs was not one of them.

[46] D2 teaches that a tricell needle electrode array advantageously achieves uniform electroporation in the area between the electrodes, but D2 does not recognize the potential excessive current problem associated with the use of a predetermined voltage. D2 teaches that the voltage should be adjusted so that the generated electric field has sufficient intensity to make the membranes of cells in the tissue transiently permeable (see column 7, lines 5-22), but, unlike the instant application, D2 does not disclose or suggest the advantages of using constant current instead of a predetermined voltage to do so.

[47] In view of the above and taking into account the CGK at the claim date, the nature of the problems and shortcomings of the known electroporation systems and methods that lead to the conception of the combination, and the absence of clear motivation in the cited prior art to address the same problems faced by the Applicant, we consider that there was no clear motivation in neither the cited references nor the CGK at the claim date to combine the cited references. Further, we are not persuaded that the POSITA at the claim date would have been led directly and without difficulty to combining D1 with D2 without hindsight of the inventors' idea of combining the claimed elements to concurrently address the tissue electrical resistance variation and the risk of excessive accumulation of current, particularly in the center of electrode arrays with opposing pairs.

[48] Accordingly, we are of the view that the subject matter claimed in independent claims 1, 25 and 37 is not a combination that would have been obvious to the POSITA at the claim date in view of D1, D2 and the CGK.

Conclusion on obviousness

[49] In our view and for the reasons above, the subject matter defined by the independent claims on file would not have been obvious to the POSITA in view of D1, D2 and the CGK, and accordingly, the claims on file comply with section 28.3 of the *Patent Act*.

Indefiniteness

[50] The FA states that claims 7, 27, 33-35 and 43 on file do not comply with subsection 27(4) of the *Patent Act*:

> Claims 7, 27 and 43 are indefinite and do not comply with subsection 27(4) of the *Patent Act.* The limitation "*the plurality of needle electrodes are non-symmetrically arranged around a center point*" is in direct contradiction of the claims from which they depend. Each independent claim contains the limitation "*the plurality of needle electrodes are symmetrically arranged*". It is impossible for "*the plurality of needle electrodes*" to by [sic] simultaneously "*non-symmetrically*" and "*symmetrically*" arranged. Claims 7, 27 and 43 should be removed.
>
> Claim 33 is indefinite and does not comply with subsection 27(4) of the *Patent Act.* It is unclear how the "*input device*" may "*comprise*" the listed elements. This is especially ambiguous given the contents of claim 32. It appears that claim 33 was intended to state "*wherein the coded instructions comprise*".
>
> Claims 34-35 are indefinite and do not comply with subsection 27(4) of the *Patent Act.* The term "programmable current pulse controller" has no antecedent. Only the element "*current pulse controller circuit*" is present in claim 25.

[51] In the R-FA, the Applicant did not provide arguments with regard to the indefiniteness issue. Instead, the Applicant proposed a new claim set and submitted that the Proposed Claims overcome the indefiniteness defect.

[52] We agree with the FA and are of the view that claims 7, 27, 33-35 and 43 on file are not free from avoidable ambiguity or obscurity because:

- the phrase “the plurality of needle electrodes are non-symmetrically arranged around a center point” cause ambiguity in claims 7, 27 and 43 when they respectively depend on independent claims 1, 25 and 37 that recite “the plurality of needle electrodes are symmetrically arranged”;

- it is not clear how the input device recited in claim 33 could comprise “a current level”, “a pulse length” and “a pulse count”; and

- the element “programmable current pulse controller” recited in claims 34 and 35 has no antecedent in claim 25.

[53] Therefore, we are of the view that the claims 7, 27, 33-35 and 43 on file do not comply with subsection 27(4) of the *Patent Act*.

ANALYSIS OF THE PROPOSED CLAIMS

[54] Since we consider that claims 7, 27, 33-35 and 43 on file do not comply with subsection 27(4) of the *Patent Act*, we will consider the Proposed Claims 1-61 as submitted on July 20, 2015 with the R-FA.

[55] Aside from the deletion of the subject matter of claims 7, 27 and 43 of the claims on file, the only significant differences between the Proposed Claims and corresponding claims of the claims on file are the minor amendments made to claims 33-35 in order to address the ambiguities identified in the FA. Specifically, claim 33 has been amended to replace “wherein the input device for programming comprise” with “wherein the input device is a user-settable input device comprising” and claims 34 and 35 have been amended to replace “programmable current pulse controller” with “pulse controller”.

Obviousness

[56] As the Proposed Claims and the corresponding claims on file are essentially identical in scope, we consider that the Proposed Claims comply with section 28.3 of the *Patent Act* for the reasons provided previously with respect to the claims on file.

Indefiniteness

[57] With regard to the Proposed Claims and the indefiniteness issue, the SOR states that "[t]he indefiniteness defects identified in claims 7, 27, 33-35 and 43 are corrected by the applicant in the proposed claims 1-61 dated 2015-07-20". We agree that the deletion of claims 7, 27 and 43 overcome the indefiniteness defect noted in the FA. We also agree that the input device recited in proposed claim 31 (corresponding to claim 33 on file) can comprise "a current level", "a pulse length" and "a pulse count" without causing a lack of clarity. Finally, we agree that "the pulse controller" recited in proposed claims 32 and 33 (corresponding to claims 34 and 35 on file) has an antecedent in proposed claim 24 (corresponding to claim 25 on file). For these reasons, we have reasonable grounds to believe that the Proposed Claims overcome the indefiniteness defect noted in the FA with regard to the claims on file.

CONCLUSIONS

[58] We have determined that the claims on file comply with section 28.3 of the *Patent Act*. We have also determined that claims 7, 27, 33-35 and 43 on file do not comply with subsection 27(4) of the *Patent Act*.

[59] Finally, we have determined that claims 1-61 as proposed in the letter of July 20, 2015 overcome the above remaining defect and do not introduce any new defects. Thus, these proposed claims are considered to be "necessary" under subsection 30(6.3) of the *Patent Rules* for compliance with the *Patent Act* and *Patent Rules*.

RECOMMENDATION OF THE BOARD

[60] We therefore recommend that the Applicant be notified, in accordance with subsection 30(6.3) of the *Patent Rules*, that the deletion of the claims on file and the insertion of claims 1-61 as proposed in the letter of July 20, 2015 are "necessary" for compliance with the *Patent Act* and *Patent Rules*.

Marcel Brisebois Member	Ed MacLaurin Member	Lewis Robart Member

COMMISSIONER'S DECISION

[61] I concur with the findings and the recommendation of the Panel. 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.

[62] 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 1-64 on file; and
ii) insert claims 1-61 as proposed in the letter of July 20, 2015.

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Johanne Bélisle
Commissioner of Patents
Dated at Gatineau, Quebec,
this 22nd day of June, 2017