Citation: Mallinckrodt Hospital Products IP Limited (Re), 2021 CACP 6
Commissioner's Decision #1559
Décision du Commissaire #1559
Date: 2021-03-17

TOPIC:	O00	Obviousness
	J40	Mental Steps
	B00	Ambiguity or Indefiniteness
SUJET:	O00	Évidence
	J40	Processus psychologique
	B00	Caractère ambigu ou indéfini

Application No. : 2,671,029

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,671,029 having been rejected under subsection 30(3) of the *Patent Rules* (SOR/96-423) as they read immediately before October 30, 2019 (the former *Patent Rules*), has consequently been reviewed in accordance with paragraph 199(3)(c) of the *Patent Rules* (SOR/2019-251). The recommendation of the Patent Appeal Board and the decision of the Commissioner are to refuse the application.

Agent for the Applicant:

Gowling WLG (Canada) LLP

550 Burrard Street, Suite 2300, Bentall 5
Vancouver, British Columbia
V6C 2B5

INTRODUCTION

[1] This recommendation concerns the review of rejected Canadian patent application number 2,671,029, which is entitled "Methods of Treating Term and Near-Term Neonates Having Hypoxic Respiratory Failure Associated With Clinical or Echocardiographic Evidence of Pulmonary Hypertension" and is owned by Mallinckrodt Hospital Products IP Limited (the Applicant). A review of the rejected application has been conducted by the Patent Appeal Board (the Board) pursuant to paragraph 199(3)(c) of the *Patent Rules*.

[2] As explained in more detail below, our recommendation is that the Commissioner of Patents refuse the application.

BACKGROUND

The Application

[3] The application was filed on July 2, 2009. It was laid open to public inspection on December 30, 2010.

[4] The rejected application relates to methods of reducing the risk or preventing the occurrence of an adverse event (AE) or a serious adverse event (SAE) associated with the inhalation of nitric oxide in the treatment of pulmonary hypertension and hypoxic respiratory failure. The application teaches that nitric oxide is a lung-specific vasodilator that significantly improves blood oxygenation and reduces the need for extracorporeal oxygenation. The description discloses that administration of inhaled nitric oxide (iNO), in patients aged 4 weeks to 18 years who had pre-existing left ventricular dysfunction (LVD), was correlated with an increased risk of experiencing an AE or SAE.

[5] The application has 16 claims on file, which were received at the Patent Office on May 5, 2014.

Prosecution History

[6] On April 5, 2016, a Final Action (FA) was written pursuant to subsection 30(4) of the former *Patent Rules*. The FA states that the instant application is defective on the grounds that:

- claims 1–16 (all claims on file) do not comply with section 2 of the *Patent Act*;

- claims 1, 2, 4–6, 8–12, 15 and 16 are anticipated and do not comply with paragraph 28.2(1)(b) of the *Patent Act*;
- claims 1–16 (all claims on file) are obvious and do not comply with section 28.3 of the *Patent Act*; and
- claims 1, 4 and 10 are indefinite and do not comply with subsection 27(4) of the *Patent Act*.

[7] In a response to the FA (RFA) dated October 5, 2016, the Applicant proposed an amended set of 112 claims (proposed claims set-1) and submitted arguments addressing the defects raised in the FA.

[8] As the Examiner still considered the application not to comply with the *Patent Act* and the former *Patent Rules*, pursuant to paragraph 30(6)(c) of the former *Patent Rules*, the application was forwarded to the Board on June 29, 2017 for review along with an explanation outlined in a Summary of Reasons (SOR). Specifically, the SOR indicates that, in view of the Applicant's arguments presented in the RFA, the defect of anticipation is withdrawn. Further, proposed claims set-1 is considered to overcome the indefiniteness defect, but is not considered to overcome the defects raised under section 2 and section 28.3 of the *Patent Act*.

[9] In a letter dated July 5, 2017, the Board forwarded to the Applicant a copy of the SOR and requested that the Applicant confirm its continued interest in having the application reviewed.

[10] In a letter dated October 4, 2017, the Applicant confirmed its interest in having the review proceed, as well as providing a response to the SOR (RSOR).

[11] The present panel (the Panel) was formed to review the instant application under paragraph 199(3)(c) of the *Patent Rules*. The Panel sent a preliminary review letter (PR letter) dated December 21, 2020, which set out our preliminary analysis and opinion that claims 1, 4 and 10 are not indefinite as indicated in the FA and SOR but that claims 1–3 and 6–9 are directed to non-patentable subject-matter and do not comply with section 2 of the *Patent Act* and that all the claims on file are obvious and do not comply with section 28.3 of the *Patent Act*. The PR letter further provided a preliminary analysis of proposed claims set-1, indicating that this proposed claim set would not overcome the defects raised under section

2 and section 28.3 of the *Patent Act* and thus could not constitute a necessary amendment in accordance with subsection 86(11) of the *Patent Rules*. Further, we identified a new defect in respect of several of the claims in proposed claims set-1. The PR letter also provided the Applicant with an opportunity to make oral and/or written submissions.

[12] The Applicant responded to the PR letter on January 19, 2021 (RPR) proposing an amended set of 86 claims (proposed claims set-2) along with written submissions in support of the patentability of these claims. A hearing was held via videoconference on February 18, 2021.

ISSUES

[13] In view of the above, the following issues are considered in this review:

- whether claims 1–16 on file define non-patentable subject-matter and are therefore non-compliant with section 2 of the *Patent Act*;
- whether claims 1–16 on file are obvious and are therefore non-compliant with section 28.3 of the *Patent Act;* and
- whether claims 1, 4 and 10 on file are indefinite and are therefore non-compliant with subsection 27(4) of the *Patent Act*.

[14] After considering the claims on file, we will consider proposed claims set-2.

LEGAL PRINCIPLES AND PATENT OFFICE PRACTICES

Purposive construction

[15] In accordance with *Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust]*, 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). Purposive construction is performed from the point of view of the person of ordinary skill in the art (POSITA) in light of the relevant common general knowledge (CGK).

[16] The Office's current practice with regard to purposive construction is explained in the Patent Notice dated 2020-11-03, entitled "*Patentable Subject-Matter under the Patent Act*" (*PN 2020-11-03*). The Office's practice was revised after the sending of the SOR, in

response to the Federal Court decision in *Yves Choueifaty v Attorney General of Canada*, 2020 FC 837.

[17] According to *PN 2020-11-03*, the purposive construction of a claim is carried out in light of the whole of the specification and takes into account what the POSITA would understand from the whole of the specification to be the nature of the invention. During purposive construction of a claim, the elements of the claimed invention are identified as either essential elements or non-essential elements. In carrying out this identification, all elements set out in a claim are presumed essential, unless it is established otherwise or is contrary to the language used in the claim.

Patentable subject-matter

[18] Once the subject-matter defined by a claim has been determined through the purposive construction, it is necessary to determine whether the subject-matter defined by a claim is patentable subject-matter having regard to both the definition of "invention" in section 2 of the *Patent Act*:

> "invention" 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.

and in accordance with subsection 27(8) of the *Patent Act*:

> No patent shall be granted for any mere scientific principle or abstract theorem.

[19] The Office's approach to determining if the subject-matter defined by a claim is patentable and not prohibited under subsection 27(8) of the *Patent Act* was also revised in *PN 2020-11-03*. According to *PN 2020-11-03*, the assessment of patentable subject-matter requires the identification of the actual invention defined by the subject-matter of the claim be grounded in a purposive construction of the claim: *Free World Trust* para 46. Further, *PN 2020-11-03* also considers the guidance in *Canada (Attorney General) v Amazon.com, Inc*, 2011 FCA 328 at paras 66-69 stating:

> To be both patentable subject-matter and not be prohibited under subsection 27(8) of the *Patent Act*, the subject-matter defined by a claim must be limited to or narrower than an actual invention that either has physical existence or manifests a discernible physical effect or change and that relates to the manual or productive arts

> […]
>
> Where an actual invention consists of a combination of elements cooperating together, all of the elements of the combination must be considered as a whole when considering whether there is patentable subject-matter and whether the prohibition under subsection 27(8) of the *Patent Act* is applicable.

Diagnostic methods

[20] The Office's approach with respect to diagnostic methods is also articulated in *PN 2020-11-03* as follows:

> A claim to a medical diagnostic method often includes an element correlating a specific analyte or the result of a medical test to a disease. A correlation, on its own, would generally be considered an abstract or disembodied idea. In many cases, a claim to a medical diagnostic method further includes one or more physical steps that comprise carrying out a medical test or determining the presence or quantity of the analyte in a sample. Such steps may include, for example, means for identifying, detecting, measuring, etc. the presence or quantity of an analyte.
>
> An abstract idea that is an element of a claim that cooperates with other elements of the claim becomes part of a combination of elements making up a single actual invention. In such cases, all of the elements of the combination are considered as a whole and may constitute patentable subject-matter if the actual invention either has physical existence or manifests a discernible physical effect or change.
>
> Thus, a diagnostic method claim that defines a combination of elements that cooperate together so as to form a single actual invention that includes physical means for testing or for identifying, detecting, measuring, etc. the presence or quantity of an analyte in a sample would be considered to be patentable subject-matter and not to be prohibited under subsection 27(8) of the *Patent Act.*

Obviousness

[21] Section 28.3 of the *Patent Act* sets out the statutory requirement that the claimed subject-matter must not have been 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 before the one-year period immediately preceding 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.

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

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

Indefiniteness

[23] Subsection 27(4) of the *Patent Act* requires claims to distinctly and explicitly define subject-matter:

> 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.

[24] In *Minerals Separation North American Corp v Noranda Mines Ltd*, [1947] Ex CR 306 at 352, 12 CPR 99, the Court emphasized both the obligation of an Applicant to make clear in the 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 OF THE CLAIMS ON FILE

Purposive construction

The claims on file

[25] There are 16 claims on file. On page 6 of the PR letter, we expressed our preliminary view that independent claims 1, 2, 4, 5, 10 and 12 are representative of the claims on file for the purposes of our analysis. Claims 1, 4 and 10 are as follows:

> 1. A diagnostic method to identify a patient between 4 weeks and 18 years of age suited to receiving nitric oxide by inhalation, for reducing the risk or preventing occurrence of an adverse event or serious adverse event associated with inhaled nitric oxide treatment, the method comprising:
>
> (a) identifying if the patient is diagnosed with pulmonary hypertension and eligible for treatment with nitric oxide by inhalation;
>
> (b) determining if the patient is diagnosed with pre-existing left ventricular dysfunction (LVD), the LVD comprising systolic dysfunction due to viral cardiomyopathy, idiopathic cardiomyopathy, autoimmune disease related cardiomyopathy, side effects due to drug-related cardiomyopathy, side effects due to toxin-related cardiomyopathy, structural heart disease, valvular heart disease, congenital heart disease, idiopathic pulmonary arterial hypertension, pulmonary hypertension and cardiomyopathy, or associations thereof, wherein the presence of pre-existing LVD comprises an increased risk of an adverse event or serious adverse event when treated with inhaled nitric oxide;
>
> (c) determining the risk of the patient experiencing an adverse event or serious adverse event based on step (b), thereby identifying if the patient is suited to receive nitric oxide by inhalation, and
>
> (d) preparing treatment protocol for the patient based on step (c) that includes inhaled nitric oxide treatment if the patient does not have pre-existing LVD.
>
> 4. A diagnostic method to identify a patient between 4 weeks and 18 years of age suited to receiving nitric oxide by inhalation, for reducing the risk or preventing occurrence of an adverse event or serious adverse event associated with inhaled nitric oxide treatment, the method comprising:
>
> (a) performing echocardiography to identify if the patient has pulmonary hypertension and is eligible for treatment with nitric oxide by inhalation;
>
> (b) determining if the patient is diagnosed with pre-existing left ventricular dysfunction (LVD), the LVD comprising systolic dysfunction due to viral cardiomyopathy, idiopathic

> cardiomyopathy, autoimmune disease related cardiomyopathy, side effects due to drug-related cardiomyopathy, side effects due to toxin-related cardiomyopathy, structural heart disease, valvular heart disease, congenital heart disease, idiopathic pulmonary arterial hypertension, pulmonary hypertension and cardiomyopathy, or associations thereof, wherein the presence of pre-existing LVD comprises an increased risk of an adverse event or serious adverse event when treated with inhaled nitric oxide; and
>
> (c) determining the risk of the patient experiencing an adverse event or serious adverse event based on step (b), thereby identifying if the patient is suited to receive nitric oxide by inhalation.
>
> 10. Use of nitric oxide formulated for administration by inhalation for the treatment of pulmonary hypertension in a patient in need thereof, the patient between 4 weeks and 18 years of age and having been diagnosed as suited for treatment with nitric oxide by inhalation by a diagnostic method comprising:
>
> (a) determining if the patient has pulmonary hypertension and is eligible for treatment with nitric oxide by inhalation;
>
> (b) determining if the patient has pre-existing left ventricular dysfunction (LVD), the LVD comprising systolic dysfunction due to viral cardiomyopathy, idiopathic cardiomyopathy, autoimmune disease related cardiomyopathy, side effects due to drug-related cardiomyopathy, side effects due to toxin-related cardiomyopathy, structural heart disease, valvular heart disease, congenital heart disease, idiopathic pulmonary arterial hypertension, pulmonary hypertension and cardiomyopathy, or associations thereof, wherein the presence of pre-existing LVD comprises an increased risk of an adverse event or serious adverse event when treated with inhaled nitric oxide; and
>
> (c) determining the risk of the patient experiencing an adverse event or serious adverse event based on step (b), thereby identifying if the patient is suited for treatment with nitric oxide by inhalation.

[26] Claims 2, 5 and 12 differ from claims 1, 4 and 10, respectively, in that the patient is a term or near neonate of greater than 34 weeks gestation (rather than 4 weeks to 18 years of age) that has been diagnosed with hypoxic respiratory failure (rather than pulmonary hypertension).

[27] The Applicant did not contest or comment on the Panel's consideration of claims 1, 2, 4, 5, 10 and 12 as being representative of the claims on file in the RPR, or at the oral hearing. Likewise, the Applicant did not contest our characterization of dependent claims 3, 6–9, 11 and 13–16 as providing further limitations with regard to: symptoms associated with hypoxic respiratory failure (claims 3 and 13), the age of the patient (claims 6 and 11), symptoms associated with pre-existing LVD (claims 7 and 14) and the type of adverse

event or serious adverse event (claims 8, 9, 15 and 16).

The POSITA and the relevant CGK

[28] In the PR letter, on pages 8-9, we said the following in regard to the POSITA and the CGK:

> On pages 2–3, the FA identifies the POSITA and their relevant CGK:
>
> > The skilled person, who may be a team of people, is a skilled physician/surgeon/pediatrician specializing in the field of pulmonary circulation.
> >
> > The use of inhaled nitric oxide is well known in treating patients with pulmonary hypertension. The use of nit[r]ic oxide is also well known for the treatment of term and near-term neonates having hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension (see present application, paragraphs [003] and [004]).
>
> The RFA did not express disagreement with these characterizations. After reviewing the specification and the references cited therein, we agree with these characterizations and would elaborate that the well known use of iNO includes: knowledge of the product monograph for INOmax® which details the full prescribing information for its safe and effective use. Notably, the well-known exclusion of iNO in the treatment of neonates known to be dependent on right-to-left shunting of blood is highlighted in the prescribing information of the INOmax® package insert prior to the filing of the present application (document submitted by the Applicant with the response dated July 25, 2013, see also page 6 of that response and page 12 of the response dated January 16, 2012, wherein the Applicant explains that the contraindication had always appeared in the prescribing information). Likewise, we consider that the assessment of clinical signs and symptoms of heart failure and echocardiographic diagnostic screening are well known techniques used for identifying patients with pre-existing LVD (see para 0029).

[29] The Applicant did not contest or comment on the Panel's characterization of the POSITA and their relevant CGK in the RPR, or at the oral hearing. Accordingly, we adopt the above characterizations for this review.

Essential elements

[30] On pages 9-10 of the PR letter, we expressed our preliminary view on the essential elements of the claims:

The construction put forth in the FA is based on previous guidance that no longer applies. The following preliminary construction is carried out in accordance with the guidance provided in *PN 2020-11-03*.

There is no use of language in the independent claims indicating that any of the steps in these claims are optional, a preferred but non-essential embodiment or a substitutable alternative with the exception of the list of alternative causes of systolic dysfunction.

In our preliminary view, for independent claims 1 and 2, the POSITA would identify the essential elements of these diagnostic methods are:

- identifying if a patient between 4 weeks and 18 years of age is diagnosed with pulmonary hypertension (claim 1)/ identifying if a term or near term neonate patient being of greater than 34 weeks gestation is diagnosed with hypoxic respiratory failure (claim 2) and eligible for treatment with nitric oxide by inhalation;

- determining if the patient is diagnosed with pre-existing LVD, the LVD comprising systolic dysfunction, wherein the presence of pre-existing LVD comprises an increased risk of an adverse event or serious adverse event when treated with inhaled nitric oxide;

- determining the risk of the patient experiencing an adverse event or serious event, thereby identifying if the patient is suited to receive nitric oxide by inhalation; and

- preparing a treatment protocol for the patient that includes inhaled nitric oxide treatment if the patient does not have pre-existing LVD are identified as suited to receiving nitric oxide by inhalation.

Independent claims 4 and 5 define diagnostic methods in the same manner as claims 1 and 2 except that the step of identifying if the patient has pulmonary hypertension (claim 4) or hypoxic respiratory failure (claim 5) is more narrowly defined as being carried out by performing echocardiography. In addition to the essential elements identified above for claims 1 and 2, our preliminary view is that the POSITA would identify this step of performing echocardiography as an essential element in claims 4 and 5.

Claims 10 and 12 are medical use claims and are directed to the use of nitric oxide in patients that have been diagnosed according to diagnostic method steps similar to those defined in claims 1 and 2. It is our preliminary view that the POSITA would consider that in addition to the essential elements identified above, these claims also include the following essential elements:

- use of nitric oxide formulated for administration by inhalation;

- for the treatment of pulmonary hypertension (claim 10) or hypoxic respiratory failure (claim 12) in a patient between 4 weeks and 18 years of age (claim 10) or a term or near term neonate (claim 12) in need thereof;

- the patient having been diagnosed as suited for treatment with nitric oxide by inhalation.

Dependent claims 3, 6–9, 11 and 13–16 define narrower embodiments or further limitations from the essential elements of the independent claims.

[31] The Applicant did not contest or comment on our preliminary identification of the essential elements in the RPR, or at the oral hearing. Accordingly, our analysis will proceed on the above identification of the claim elements that are essential.

Patentable subject-matter

Diagnostic methods

[32] Our preliminary analysis was put forth on pages 10-11 of the PR letter as follows:

> According to the FA and the SOR, the diagnostic methods of claims 1–9 relate to a mere scheme, plan, rule or mental process. However, this assessment is based on guidance that has since been rescinded. As explained above, the Office's revised position *vis-à-vis* diagnostic methods considers whether the actual invention is a combination of elements that has physical existence or manifests a discernible physical effect or change.
>
> With respect to claims 1 and 2, these claims define a method of diagnosing if a patient is suited to receiving nitric oxide by inhalation along with a number of steps that together provide that diagnosis. Specifically, the steps of a) identifying patients with pulmonary hypertension (claim 1) or hypoxic respiratory failure (claim 2), b) determining their LVD status and c) correlating the LVD status with an increased risk of adverse events cooperate and together identify whether or not the patient is suited to receive iNO. By contrast, the step of preparing a treatment protocol is not an element that cooperates to provide the diagnosis. Our preliminary view is that the combination of steps a)-c) together form the actual invention.
>
> In regard to whether or not the actual invention has physicality, the RFA said the following on page 6:
>
> > Step a) of old claims 1 and 2 is directed to identifying whether, respectively, the child patient has been diagnosed with pulmonary hypertension and so is eligible for treatment with inhaled nitric oxide gas (claim 1), or the term or near term neonate patient has been diagnosed with hypoxic respiratory failure and so is eligible for treatment with inhaled nitric oxide (claim 2). Similarly, step b) of old claims 1 and 2 is directed to identifying whether the patient has been diagnosed with pre-existing left ventricular dysfunction (LVD).

> Applicant submits that steps a) and b) of old claims 1 and 2 comprise active steps of data acquisition from patient records [Emphasis in original].

The RSOR, at page 4, further argues:

> The diagnostic method claims at issue here are not directed to a mere scientific principle or abstract method, nor to a "disembodied idea" as that term is used in the definition of patentable art prescribed in Shell Oil Co. v. Commissioner of Patents [1982] 2 S.C.R. 536. Rather, the claims […] are directed to methods having practical application. Steps a) and b) of claims 1 and 2 dated May 5, 2014 [the claims on file] comprise active steps of identifying if a child/neonate patient is diagnosed with pulmonary hypertension and determining if the patient is diagnosed with pre-existing left ventricular dysfunction. […] Such steps are not akin to the performance of calculations or manipulations of data for intellectual or aesthetic significance as outlined in MOPOP 12.06.02 [now *MOPOP* §17.03.08].

The Applicant's submissions are that the steps of identifying patients with pulmonary hypertension or hypoxic respiratory failure and determining if the patient has pre-existing LVD involve retrieving information from a record. Our preliminary view is that this is not a physical step. Since the correlation step is also disembodied, our preliminary view is that the actual invention of claims 1 and 2 is not something with physical existence or something that manifests a discernible effect or change. Moreover, this result would not change even if the element of preparing a treatment protocol, which is also disembodied, was considered to form part of the actual invention.

Dependent claims 3 and 6–9 do not define any narrower embodiments or further limitations from the essential elements of claims 1 and 2 that provide physicality to the actual invention of these claims. It follows that claims 3 and 6–9 are also considered to define non-patentable subject-matter.

By contrast, the step of identifying if a patient has pulmonary hypertension or hypoxic respiratory failure in claims 4 and 5, respectively, involves a physical step of performing echocardiography. For the same reasons explained above for claims 1 and 2, our preliminary view is this step is part the actual invention. As such, our preliminary view is that the actual invention in claims 4 and 5 satisfies the physicality requirement.

In light of the above, it is our preliminary view that claims 1–3 and 6–9 are directed to non-patentable subject-matter and do not comply with section 2 of the *Patent Act*. It is also our preliminary view that claims 4 and 5 are directed to patentable subject-matter that falls within the definition of an invention as set out in section 2 of the *Patent Act*.

[33] In the RPR, the Applicant did not address any of the above and instead proposed to cancel claims 1–3 and amend claims 6–9 to only depend on those claims that we had preliminarily identified as being directed to patentable subject-matter. Our conclusion is therefore that

claims 1–3 and 6–9 are directed to non-patentable subject-matter and do not comply with section 2 of the *Patent Act*. By contrast, claims 4 and 5 define physical steps and are directed to patentable subject-matter that falls within the definition of an invention as set out in section 2 of the *Patent Act.*

New patient population/Restricting use

[34] Our preliminary analysis was put forth on page 12 of the PR letter as follows:

> According to the FA and the SOR, medical use claims 10–16 do not comply with section 2 of the *Patent Ac*t as they do not satisfy the definition of an invention. As explained on page 2 of the SOR:
>
> > [U]se claims 10-16 identify a non-adult patient that will not experience an adverse event or serious adverse event and that is suited to receive inhaled nitric oxide gas; however, what results is a sub-population that is being treated the exact same way. The new patient group being identified by the use claims and which benefits from the claim will continue to use nitric oxide in the same manner as previously known. Essentially, what is left is a "new patient group" using a known product for the same intended and known use. The use claims do not comply with section 2 of the *Patent Act* as they do not satisfy the definition of an invention which must be to 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 [Emphasis in original].
>
> Page 9 of the RSOR disagrees with this assessment, arguing this approach to the question of whether the claims comply with section 2 is flawed in that it imports concepts of novelty and utility into the subject-matter analysis.
>
> As indicated above, the determination of whether the subject-matter of a claim is patentable is based on the elements of the claim that form the actual invention and whether those elements have a physical existence or manifest a discernible physical effect or change. Our preliminary view is that the actual invention in these medical use claims lies in the combination of all three of the essential elements working together so that the use of iNO to treat patients is restricted to the sub-population of patients diagnosed as being suited for it. It is evident that this use has a method of practical application that would manifest a discernible effect or change in the physical state of the sub-population of patients being treated.
>
> Further, there is no evidence that any of the essential elements of the actual invention restrict, prevent, interfere with or require the exercise of the professional skill and judgment of a medical professional. This is consistent with the position in the SOR which

> acknowledges the persuasiveness of the arguments presented on page 10 of the RFA with respect to the medical use claims not requiring the exercise of professional skill.
>
> Our preliminary view is therefore that claims 10–16 on file define an actual invention that satisfies the physicality requirement and are therefore directed to subject-matter that is patentable under section 2 of the *Patent Act*.

[35] In the RPR, the Applicant acknowledged the preliminary conclusions reached in the PR. Our conclusion is therefore that claims 10–16 on file define an actual invention that satisfies the physicality requirement and are therefore directed to subject-matter that is patentable under section 2 of the *Patent Act.*

Obviousness

[36] All 16 claims on file were rejected in the FA for obviousness.

The POSITA and the relevant CGK

[37] The POSITA and the relevant CGK have been set out above as part of the purposive construction of the claims. The above identification of the relevant CGK as of the publication date is also considered to be valid as of the claim date and thus applicable for the purpose of assessing obviousness.

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

[38] As indicated in the PR letter, we have considered the essential elements of the claims on file in our assessment of obviousness. The Applicant did not dispute this approach in the RPR, or at the oral hearing. Accordingly, our analysis will consider the essential elements of the claims as construed above.

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 PR letter, the following two documents cited in the FA were applied against the claims on file:

> D7: Hess, "Heliox and Inhaled Nitric Oxide", Mechanical Ventilation, Chapter 28, pages 454–480, 2001.

D11: Bernasconi et al., “Inhaled nitric oxide applications in paediatric practice”, Images Paediatr. Cardiol., Vol 4(1), pages 4–29, Jan–Mar 2002.

[40] D7 is a book chapter that reviews clinical applications of iNO, including its use in the treatment of diseases characterized by pulmonary hypertension and hypoxemia (page 457). D7 discloses that although the toxicity of iNO appears to be low when the drug is used by clinicians familiar with its use, there are a number of potential toxicities and complications. In particular, on page 465, D7 states that:

> Several studies have examined the effects of inhaled NO in patients with left ventricular dysfunction. At high doses (40-80 ppm), inhaled NO has been reported to decrease pulmonary vascular resistance and increase pulmonary capillary wedge pressure in some patients with severe left ventricular dysfunction. Presumably, the acute reduction of right ventricular afterload may produce an increase in pulmonary venous return to the left heart. This would increase left ventricular filling pressure and might worsen pulmonary edema. Although this effect may be dose related, inhaled NO should be avoided in patients with severe left ventricular dysfunction (pulmonary capillary wedge pressure ≥25 mm Hg).

[41] D11 is a review article which “details the delivery and monitoring aspects of inhaled NO, its potential toxic and side effects and its applications in several cardiopulmonary disorders in **paediatrics**” (see Abstract) [Emphasis added]. D11 discloses that “[i]n pediatrics, the use of iNO in term neonates with hypoxaemic respiratory failure, in the assessment of pulmonary vascular reactivity and in the treatment of postoperative pulmonary hypertension in congenital heart disease is well recognised and accepted” (see page 17). However, D11 also advises “caution must be the rule with a drug that shows potential adverse and toxic effects” (see page 17). In particular, D11 reports that in patients with LVD, “a decrease in pulmonary vascular resistance (induced by iNO) will lead to an increase in pulmonary venous return and hence to an increase in left atrial and left ventricular filling pressures; this may not be tolerated by a failing left ventricle” and “[t]his effect may lead to rapid left heart failure and pulmonary oedema” (see page 11). D11, on page 11, also emphasizes that these adverse effects “highlight the need for careful observation and intensive monitoring during NO inhalation in patients with left ventricular failure, if left ventricular afterload is not lowered concomitantly.”

[42] The Applicant, in the RPR and at the oral hearing, expressed their disagreement with how the POSITA would interpret the warnings in the prior art regarding the risks associated with the use of iNO. Specifically, the Applicant’s arguments focussed on the “real differences” between adult LVD and childhood LVD and why the POSITA “would be

aware that [*sic*] one cannot extrapolate from the observed effects of iNO in **adult** LVD patients to an expectation that iNO will have a similar effect in the context of **childhood** LVD" [Emphasis in original]. Although these submissions were made in respect of proposed claims set-2, the Applicant indicated in the oral hearing that they are also applicable to the claims on file. As explained on pages 6-12 of the RPR:

> In order to understand the teachings of the prior art regarding inhaled nitric oxide (iNO) in the context of left ventricular dysfunction (LVD), it is important to understand that there is a fundamental difference between the type of LVD commonly seen in adults (i.e., "diastolic" LVD) and the type that is typical in babies and children (i.e., "systolic" LVD). Diastolic LVD is usually the result of damage to the heart done by years of high blood pressure, type 2 diabetes, obesity, prior heart attacks, and/or coronary artery disease, i.e., conditions that occur in adults. It is characterized by a "non-compliant" left ventricle, i.e., a left ventricle that is stiff and relatively unable to expand to accept the blood flowing in from the left atrium. In marked contrast, childhood (systolic) LVD is characterized by the opposite: an "overly-compliant" left ventricle that is soft and flabby so that it expands rapidly to accept the inflow of blood, but is relatively unable to contract and push the blood out into the systemic circulation. These stark physiological differences between adult-type and pediatric type LVD have medically significant implications that are well known in the art. See, e.g., the following statement from a 2000 review article on the topic:
>
> > There appears to be **real differences** in incidence, implications, expectations, causes, treatment styles, and prevention **between children and adults with ventricular dysfunction suggesting that for ventricular dysfunction, children should not be considered 'small adults'**. [Emphasis in original]
>
> […]
>
> Given the broad understanding in the art that pediatric LVD is very different from adult LVD, and that one cannot predict outcomes in pediatric LVD patients based on observations of adult LVD, the Preliminary Review's reliance on Hess (D7) seems misplaced.
>
> […]
>
> Furthermore, the Panel refers to D11 to support that "it is not presently clear that the findings of the adult studies cannot be relevant to non-adult patients" (Preliminary Review, Page 16). The Panel's attention is drawn again to the evidence provided above, clearly establishing that, in the context of LVD, finding in adult studies are *not* considered by those of skill in the art to be predictive of results in non-adults. Moreover, it is important to note that D11 is a review article, which means that it attempts to summarize results previously reported in the literature, and not to report new results. Accordingly, a POSITA would know to interpret any statement in a review article in light of the more detailed findings reported in the source articles cited in support of the statement. This point is pertinent because the source articles cited in D11 do not support the Preliminary Review's interpretation of that reference.

> This means that a POSITA would be aware one cannot extrapolate from the observed effects of iNO in adult LVD patients to an expectation that iNO will have a similar effect in the context of childhood LVD, regardless of whether the LVD is classified as systolic or diastolic dysfunction or a mix of both.

[43] These statements suggest that D7 and the teachings in D11 that relate to adults are not relevant to child and neonate patients with LVD. The recognition that adult patients with LVD are a different patient population than child and neonate patients with LVD has been acknowledged in the FA, in the PR letter, and again as part of this final review. However, we do not agree that these differences would suggest to the POSITA that the identification of left ventricular dysfunction as a risk factor for treatment with iNO in adults cannot be extrapolated to child and neonate patients.

[44] Firstly, the hemodynamic effects of iNO in adults and children have been shown to be similar. As indicated at para [0034] of the description:

> Due to the selective, non-systemic nature of iNO to reduce pulmonary hypertension, physicians skilled in the art further employ INOmax® to treat or prevent pulmonary hypertension and improve O2 levels in a variety of other clinical settings, including both pediatric and adult patients suffering from acute respiratory distress syndrome (ARDS), pediatric and adult patients undergoing cardiac or transplant surgeries, pediatric and adult patients for testing to diagnose reversible pulmonary hypertension, and in pediatric patients with congenital diaphragmatic hernia. In most, if not all, of these applications, INOmax® acts by preventing or treating reversible pulmonary vasoconstriction, reducing pulmonary arterial pressure and improving pulmonary gas exchange.

[45] Further, we note that the review articles cited in the RPR pertain to the differences in the pathophysiology of heart failure, and in particular ventricular dysfunction, in adults compared with children in the context of preventative and treatment strategies for ventricular dysfunction. However, in the context of pulmonary hypertension, it is our view that the POSITA would consider that any hemodynamic abnormalities in patients with ventricular dysfunction would be similar, regardless of etiology.

[46] In that regard, the description at para [0029] explains that, notwithstanding etiology, left ventricular dysfunction is characterized by an elevated pulmonary wedge pressure:

> Left Ventricular Dysfunction. **Patients having pre-existing LVD may be described in general as those with elevated pulmonary capillary wedge pressure, including those with diastolic dysfunction** (including hypertensive cardiomyopathy), **those with systolic dysfunction**, including those with cardiomyopathies (including ischemic or viral cardiomyopathy, or idiopathic cardiomyopathy, or autoimmune disease related

> cardiomyopathy, and side effects due to drug related or toxic-related cardiomyopathy), or structural heart disease, valvular disease, congenital heart disease, idiopathic pulmonary arterial hypertension, pulmonary hypertension and cardiomyopathy, or association thereof. [Emphasis added]

[47] Therefore, in our view, the POSITA would consider adult studies disclosing the hemodynamic effects of iNO in patients with pulmonary hypertension and LVD can be extrapolated to pediatric patients. As explained above, patients with LVD have an elevated pulmonary capillary wedge pressure, including those with diastolic dysfunction and those with systolic dysfunction. The skilled person reading D11 would know that the vasodilation in the lungs caused by iNO leads to a surge of blood travelling to the left ventricle causing the wedge pressure—which is already elevated for all LVD patients, regardless of age or etiology—to increase further, and that this may not be tolerated by a failing left ventricle. Indeed, no extrapolation is necessary given the clear warnings in D11 regarding the risks associated with inhaled nitric oxide in patients with LVD.

[48] In light of the foregoing, it is our view that the POSITA would consider the teachings in both D11and D7 regarding the risks associated with using iNO in patients with LVD to be relevant to pediatric patients. Accordingly, we maintain the differences between the claims on file and the cited prior art as identified in the PR letter on page 14:

> We consider that D11 is the closest prior art. The difference between D11 and the essential elements of the independent claims is that while D11 does make a clear distinction between patient groups with and without LVD in terms of risk of iNO treatment, it does not explicitly disclose that child and neonate patients without LVD are particularly suited to treatment with iNO. However, D7 discloses, albeit in a different patient population, that adults with severe LVD are at risk of worsening pulmonary edema and that iNO should be avoided in these patients.

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?

[49] In the PR, we expressed our view on page 15 that avoiding iNO treatment altogether in this patient population would have been self-evident to the POSITA as an alternative option based on the teachings of D11:

> Although the Applicant points to a lack of explicit disclosure in D11 of the identification of child and neonate patients with pre-existing LVD as unsuitable for treatment with iNO, D11 does emphasize that these adverse effects “highlight the need for careful observation and

> intensive monitoring during NO inhalation in patients with left ventricular failure, if left ventricular afterload is not lowered concomitantly." In our view, the POSITA using their CGK would understand that the risk of an adverse or serious adverse event, such as pulmonary edema, would also be reduced by avoiding treatment of this sub-population altogether.
>
> […]
>
> The fact that D11 specifies treating patients with pre-existing LVD and monitoring or treating with concomitant afterload reduction as an alternative does not teach away from the other lower risk option of avoiding treatment altogether. Our preliminary view is that POSITA would have considered both as viable options at the claim date. [Emphasis added]

[50] In response, the Applicant argued on page 12 of the RPR that the use claims define treating a new patient sub-population that avoids a previously unknown disadvantage (risk of an adverse event) fulfilling the criteria for a selection patent. However, as indicated above, D11 already identifies the sub-population of pediatric patients with pulmonary hypertension and LVD as being at risk of an adverse event. The corollary to that being the sub-population of patients with pulmonary hypertension and without LVD are not at risk of experiencing an adverse event. Therefore, it is our view that the claims do not define a new sub-population of patients and are not considered a selection.

[51] The Applicant, in the RPR on pages 9-10 and at the oral hearing, further argued that the approval of the INOT22 study to include LVD subjects is evidence that the claims are not obvious:

> Once the study sponsor became aware (mid-study) of the serious adverse events experienced by LVD subjects who received iNO, the protocol was revised to ensure no more LVD subjects would be enrolled in the study. One can presume from this fact that, if the risk had indeed been "obvious" before the start of the study, the original protocol would have excluded LVD subjects.
>
> Finally, if it had been "obvious" to a POSITA prior to completion of the INOT22 study that iNO posed a particular risk when used as a treatment for pulmonary hypertension or hypoxic respiratory heart failure in pediatric LVD patients, as the above-quoted language from the Preliminary Review supposes, FDA and the equivalent in other countries would have required the warning about LVD to be added to the INOMAX label long before the 2009 date when INOT requested the label change. The fact that the warning was not required to be added until after the results of the INOT22 study were available and reviewed by FDA is conclusive proof that the risk to pediatric LVD patients was not obvious to the experts at FDA and equivalent administrative agencies in other countries prior to 2009, nor to the company that manufactured and sold INOMAX.

[52] We disagree that the enrolment of patients with LVD in the INOT22 study is conclusive proof that the risk to pediatric patients was not obvious. As indicated above, D11 explicitly warns of the risks associated with iNO in patients with pulmonary hypertension and LVD and suggests treating with monitoring or concomitant lowering of wedge pressure.

[53] It is not clear from the record before us if the INOT22 team was unaware of D11, or if they were aware of this document and proceeded with careful observation and monitoring, thereby mitigating the risk to LVD patients, as suggested by D11. Nevertheless, whether the INOT22 team was aware of D11 or not, the question to be answered is whether the POSITA reading D11 would have considered the option of avoiding treatment in LVD patients altogether as an obvious alternative, based on the explicit warnings for this patient group. In this regard, we note that the description and RPR explain that, in view of the experiences in the INOT22 study, the same risk warning originally disclosed from D11 was added to the iNO label, however the use in these patients was not contraindicated. This is consistent with the teachings of D11.

[54] In view of the above, we consider that the POSITA reading D11 at the claim date would have seen avoiding treatment in this patient group altogether as an obvious alternative to the options of intensive monitoring or concomitantly lowering wedge pressure during iNO administration. The fact that there was more than one obvious option, or that the POSITA would not necessarily have chosen one over the other at the claim date, would not have made the option of avoiding treatment altogether any less obvious: *Eli Lilly Canada Inc v Apotex Inc*, 2018 FC 736 at para 120.

[55] Accordingly, we conclude that the difference between the essential elements of independent claims 1, 2, 4, 5, 10 and 12 and D11 are not steps which would have required any degree of invention. The POSITA would consider that reducing the risk or preventing occurrence of an adverse event or serious adverse event associated with iNO treatment in a child or neonate patient with pre-existing LVD by avoiding treatment would be an obvious alternative to the treatment options disclosed in D11.

[56] In the PR letter, we expressed our preliminary view that none of the additional features recited in claims 3, 6-9, 11 or 13-16 would have required any degree of invention from the POSITA in a manner separate from the subject-matter defined in the independent claims. The RPR did not contest or comment on these preliminary conclusions.

[57] Our conclusion is therefore that the subject-matter of claims 1–16 on file would have been obvious to the POSITA as of the relevant date, contrary to section 28.3 of the *Patent Act*.

Indefiniteness of claims 1, 4 and 10 on file

[58] Our preliminary analysis was put forth on pages 17-18 of the PR letter as follows:

> On page 15, the FA considers that the subject-matter of claims 1, 4 and 10 is indefinite because:
>
> > The inclusion of ambiguous expressions such as "between 4 weeks and 18 years of age" does not clearly and explicitly define the claimed subject-matter. It is not clear from the expression, "between 4 weeks and 18 years of age" whether the claim is related to identifying a non-adult patient (pediatric group) or whether it can also include adult patients.
>
> In that regard, the FA explains that in some regions adolescents aged 16-18 are considered adults and so it is not clear that the underlying clinical systolic dysfunction associated with pre-existing LVD, which is more commonly seen in children, would be guaranteed to be present in adolescents.
>
> In the RFA the Applicant argues that the standard for indefiniteness applied in the FA: "whether or not an element of the invention can or cannot be guaranteed" is too stringent. As explained on page 18 of the RFA:
>
> > The correct standard for indefiniteness is whether a person who is possessed of all the technical knowledge required would be able to fully understand the terms used and the principles involved. (Kramer v Lawn Furniture Inc. (1974), 13 CPR (2d) 231 at 237 (FCTD)). Therefore, a person of skill in the art would understand that the pre-existing LVD recited in claims 1, 4 and 10 is a systolic-type clinical presentation that is more commonly found in child patients aged 4 weeks to 18 years old and term or near term neonate patients being of greater than 34 weeks gestation, as opposed to adult patients.
>
> We agree with the Applicant that a guarantee is not the correct standard for indefiniteness. As stated above, subsection 27(4) of the *Patent Act* requires that applications clearly set out the ambit of the monopoly sought and to ensure that the terms used in the claims are distinct and explicit.
>
> Having reviewed claims 1, 4 and 10 on file, we consider that the POSITA would readily understand what the expression "between 4 weeks and 18 years of age" means. We also note that there is no lack of clarity as to what this expression is intended to mean in view the teachings of the description: "the term "children" includes those being around 4 weeks to 18 years of age" (para 0023) and that "the term "adult" includes those being over 18 years of age" (para 0024).

> Therefore, our preliminary view is that claims 1, 4 and 10 on file are definite and comply with subsection 27(4) of the *Patent Act*.

[59] In the RPR, the Applicant acknowledged the preliminary conclusions reached in the PR. Our conclusion is therefore that claims 1, 4 and 10 on file are definite and comply with subsection 27(4) of the *Patent Act*.

ANALYSIS OF THE PROPOSED CLAIMS

[60] As indicated above, with the RPR the Applicant submitted proposed claims set-2. According to the RPR, the claims of proposed claims set-2 are directed to subject-matter identified as being patentable in the Preliminary Review. Notably, the claims we considered defective for non-compliance with section 2 of the *Patent Act* were excluded. Likewise, the RPR indicates that the claims of proposed claims set-2 do not correspond to any of the indefinite claims that were identified in respect of proposed claims set-1 in the PR letter. We agree with these statements. Therefore, it is our view that proposed claims set-2 is directed to patentable subject-matter that falls within the definition of an invention as set out in section 2 of the *Patent Act* and proposed claims set-2 is directed to definite subject-matter and is compliant with subsection 27(4) of the *Patent Act.*

[61] With respect to the obviousness defect, the proposed amendments would introduce the following claim elements:

- specifying that the origin of pulmonary hypertension is idiopathic;
- identifying if the patient has pre-existing LVD is expressly limited to retrieving that data from a patient record;
- identifying from a patient record if the patient is dependent on right-to-left shunting of blood;
- notifying a medical practitioner of a candidate’s suitability to receive iNO gas treatment; and
- providing the medical practitioner with pharmaceutically acceptable nitric oxide gas.

[62] With respect to limiting the scope of pulmonary hypertension to idiopathic pulmonary hypertension, as indicated above, inhaled nitric oxide reduces pulmonary hypertension by acting as a selective pulmonary vasodilator. Accordingly, in our view, the POSITA would consider that inhaled nitric oxide would have the same effect on the pulmonary vasculature, regardless of the cause of pulmonary hypertension.

[63] The remaining limitations were also present in proposed claims set-1, for which we provided the following analysis in the PR letter on pages 21-22:

> With respect to determining if a candidate patient is not dependent on right-to-left shunting of blood, we note that we have already considered that the CGK of the POSITA would include knowledge of the prescribing information contained in the INOmax® product monograph, available at the claim date, which specifically discloses that iNO is contraindicated in the treatment of neonates known to be dependent on right-to-left shunting of blood. Accordingly, our preliminary view is that this step would not have involved any degree of invention. Therefore, it is our preliminary view that the additional limitations, when considered in combination with the other essential elements of the claims, would have been obvious to the POSITA.
>
> With respect to the additional steps of notifying a medical practitioner of a candidate's suitability to receive iNO gas and providing the iNO to the medical professional, in our preliminary view these are also not steps that would have required any degree of invention.
>
> The remaining proposed dependent claims do not add any features beyond those found in the dependent claims on file. As we stated above, in our preliminary view, we do not recognize any additional features from the dependent claims as requiring any degree of invention. Therefore, our preliminary view is that the proposed claims would not comply with section 28.3 of the *Patent Act*.

[64] Therefore, considering the above elements together with the subject-matter of the claims on file, our reasoning and conclusions concerning the obviousness of the claims on file also apply to proposed claims set-2. It follows that proposed claims set-2 are not considered a necessary specific amendment under subsection 86(11) of the *Patent Rules*.

RECOMMENDATION OF THE BOARD

[65] In view of the above, the Panel recommends that the application be refused on the basis that:

- claims 1–3 and 6–9 are directed to non-patentable subject-matter and do not comply with section 2 of the *Patent Act*; and
- claims 1–16 are obvious and do not comply with section 28.3 of the *Patent Act*.

Christine Teixeira	Marcel Brisebois	Cara Weir
Member	Member	Member

DECISION OF THE COMMISSIONER

[66] I concur with the findings of the Board and its recommendation to refuse the application because the claims on file do not comply with section 28.3 of the *Patent Act* and further claims 1–3 and 6–9 are directed to non-patentable subject-matter and do not comply with section 2 of the *Patent Act*.

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

Virginie Ethier
Assistant Commissioner of Patents

Dated at Gatineau, Quebec

this 17th day of March, 2021.