Citation: Armagen Inc. (Re), 2023 CACP 8

Commissioner's Decision #1641
Décision du commissaire nº 1641
Date: 2023-03-02

TOPIC:	J80	Professional or Artistic Skill
	F00	Novelty
	O00	Obviousness
	B22	Not Supported by Disclosure
	C00	Adequacy or Deficiency of Description
	B00	Ambiguity or indefiniteness
SUJET:	J80	Aptitudes professionnelles ou artistiques
	F00	Nouveauté
	O00	Évidence
	B22	Non appuyée par la divulgation
	C00	Caractère Adéquat ou Inadéquat de la Description
	B00	Caractère ambigu ou indéfini

Application No. : 2,694,762

Demande nº 2 694 762

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,694,762 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.

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INTRODUCTION

[1] This recommendation concerns the review of rejected Canadian patent application number 2,694,762, which is entitled “Methods and compositions for increasing alpha-L-iduronidase activity in the CNS” and owned by Armagen Inc. A review of the rejected application has been conducted by a Panel of the Patent Appeal 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 under the *Patent Cooperation Treaty* and has an effective filing date in Canada of July 25, 2008. It was laid open to public inspection on February 5, 2009.

[4] The rejected application relates to the delivery of α-L-iduronidase (IDUA) across the blood brain barrier (BBB) of a subject suffering from a deficiency of IDUA in the central nervous system (CNS) by binding the human insulin receptor (HIR) with a HIR Ab-IDUA fusion antibody. This binding triggers transport across the BBB of the fusion antibody, thereby carrying into the CNS the attached replacement IDUA.

[5] The claims under review are claims 1 to 42 dated September 4, 2018 (the claims on file) that were rejected in the Final Action (FA).

Prosecution History

[6] On April 5, 2019, a Final Action was written under subsection 30(4) of the former *Patent Rules*. The Final Action states that the subject-matter of claims 1 to 27, 29 to 33 and 36 to 42 encompass subject-matter that lies outside the definition of “invention” and does not comply with section 2 of the *Patent Act.* The Final Action further states that the subject-matter of claims 28, 30 to 35 and 37 to 42 is anticipated contrary to paragraph 28.2(1)(a) of the *Patent Act* and is further obvious contrary to section 28.3 of the *Patent Act*. The Final Action also indicates

that claims 28 to 42 do not comply with section 84 of the former *Patent Rules* and the specification, insofar as it relates to the subject-matter of these claims, does not comply with subsection 27(3) of the *Patent Act*. Finally, the Final Action states that claims 12, 13, 24 and 25 are indefinite and therefore non-compliant with subsection 27(4) of the *Patent Act.*

[7] In the Response to the Final Action dated October 5, 2020, the Applicant expressed general disagreement with the positions laid out in the Final Action but nevertheless proposed an amended claims set containing proposed claims 1 to 86.

[8] On March 30, 2021, the application was forwarded to the Patent Appeal Board for review under paragraph 199(3)(c) of the *Patent Rules* along with a Summary of Reasons explaining that the rejection is maintained as the Applicant's arguments presented in the Response to the Final Action are not persuasive and that the proposed amendments presented in the Response to the Final Action do not overcome all of the defects identified in the Final Action.

[9] In a letter dated March 31, 2021, the Patent Appeal Board forwarded a copy of the Summary of Reasons to the Applicant and requested that they confirm their continued interest in having the application reviewed.

[10] In a letter dated June 11, 2021, the Applicant confirmed their interest in having the review proceed.

[11] The present Panel was formed to review the rejected application under paragraph 199(3)(c) of the *Patent Rules*. On November 15, 2022, the Panel sent a Preliminary Review letter detailing our preliminary analysis and opinion that claims 1 to 27, 29 to 33 and 36 to 42 are directed to patentable subject-matter falling within the definition of "invention" in section 2 of the *Patent Act*; that the subject-matter of claims 28, 30 to 33, 35, 37, 41 and 42 is novel; that the subject-matter of claims 34 and 38 to 40 is anticipated, contrary to paragraph 28.2(1)(a) of the *Patent Act*; that the subject-matter of claims 1 to 42 is obvious, contrary to section 28.3 of the *Patent Act*; that claims 28 to 41 suffer from overbreadth and, independently of this view, the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims; and that claims 12, 13, 24 and 25 fail to define distinctly the subject-matter

of the invention, contrary to subsection 27(4) of the *Patent Act*.

[12] In the same letter, the Panel further expressed the preliminary opinion that proposed claims 31, 32, 62 and 63 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*; that claims 66 to 86 suffer from overbreadth and, independently of this view, the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims; and that the subject-matter of proposed claims 1 to 65 is obvious, contrary to section 28.3 of the *Patent Act*.

[13] The Preliminary Review letter also provided the Applicant with an opportunity to make oral and/or written submissions.

[14] On November 28, 2022, the Applicant declined the opportunity for an oral hearing and on January 23, 2023 the Applicant indicated that there would be no written submissions.

Issues

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

- whether claims 1 to 27, 29 to 33 and 36 to 42 encompass subject-matter that lies outside the definition of “invention” and do not comply with section 2 of the *Patent Act*;
- whether the subject-matter of claims 28, 30 to 35 and 37 to 42 is anticipated, contrary to paragraph 28.2(1)(a) of the *Patent Act*;
- whether the subject-matter of claims 28, 30 to 35 and 37 to 42 is obvious, contrary to section 28.3 of the *Patent Act*;
- whether claims 28 to 42 do not comply with section 84 of the former *Patent Rules*;
- whether the specification, insofar as it relates to the subject-matter of claims 28 to 42, does not comply with subsection 27(3) of the *Patent Act*; and
- whether claims 12, 13, 24 and 25 are indefinite and do not comply with subsection 27(4) of the *Patent Act.*

[16] In addition to the claims on file, the proposed claims have also been considered.

FOLLOWING A PURPOSIVE CONSTRUCTION, WHICH CLAIMED ELEMENTS ARE ESSENTIAL?

[17] In our view, all of the elements of the claims on file are essential.

Legal Background

[18] According to *Free World Trust v Électro Santé* Inc, 2000 SCC 66 and *Whirlpool Corp v Camco Inc*, 2000 SCC 67, a purposive construction of the claims 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) and considers the specification and drawings. In addition to interpreting the meaning of the terms of a claim, purposive construction distinguishes the essential elements of the claim from the non-essential elements. Whether or not an element is essential depends on the intent expressed in or inferred from the claim, and on whether it would have been obvious to the POSITA that a variant has a material effect upon the way the invention works.

[19] In carrying out the identification of essential and non-essential elements, all elements set out in a claim are presumed essential unless it is established otherwise or where such a presumption is contrary to the claim language.

Analysis of the claims on file

The POSITA and the relevant CGK

[20] The Preliminary Review letter, on pages 7 to 8, states the following with regard to the identity of the POSITA and their expected CGK:

> The FA defines the POSITA as a research team including immunologists, clinical scientists specializing in Hurler's syndrome and IDUA deficiency, drug manufacturers and general practitioners.
>
> With respect to the relevant CGK, the FA states that it would include the role of IDUA in Hurler's syndrome and difficulties associated with delivering IDUA across the BBB. Further, and on the basis of the disclosure of US2005/0142141 (introduced as D1 in the FA), the FA submits that the CGK of the POSITA includes the use of a fusion antibody, wherein the fusion antibody comprises a) a fusion protein comprising an immunoglobulin heavy chain and an IDUA, and b) an immunoglobulin

light chain, to treat IDUA deficiency, wherein the heavy chain comprises SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, and the light chain comprises SEQ ID NO: 4, SEQ ID NO: 5 and/or SEQ ID NO: 6.

The RFA does not comment on either the identity of the POSITA or their CGK.

Having reviewed the specification as whole, as well as the disclosure of D1 and the scientific literature pertinent to the claimed subject-matter, we consider that the characterization of the POSITA found in the FA is reasonable and we adopt it for the purposes of this preliminary review.

We also agree that the role of IDUA in Hurler's syndrome and the difficulties associated with delivering IDUA across the BBB were CGK.

Although we consider that the general principle of receptor-mediated transcytosis systems for trans-BBB transport of antibody-conjugated therapeutics was CGK (as evidenced by the review article Jones and Shusta, "Blood-brain barrier transport of therapeutics via receptor-mediation", *Pharm Res.*, 24(9):1759-71, published online July 10, 2007, doi: 10.1007/s11095-007-9379-0 [*Jones and Shusta*], we consider that the specific teachings regarding the HIR Ab-IDUA fusion antibody taught by D1 and its corresponding specific heavy and light chain coding sequences is not knowledge that would have been generally known by the POSITA described above. It is therefore our preliminary view that such specific teachings of D1 were not CGK.

Finally, it is our preliminary view that the normal range of levels of IDUA enzyme activity per mg of protein for the human brain and the total amount of protein in an average human brain were CGK (as evidenced by para [00157] of the description).

[21] In the absence of submissions from the Applicant, we adopt the above characterizations of the POSITA and the relevant CGK for our final analysis.

The claims on file

[22] There are 42 claims on file. Claims 1, 16, 28 and 34 are independent claims and read as follows:

1. A fusion antibody having α-L-iduronidase activity for use in the treatment of an α-L-iduronidase deficiency in the central nervous system, wherein:

(i) the fusion antibody comprises (a) a fusion protein comprising an immunoglobulin heavy chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:1, a CDR2 defined by the amino acid sequence of SEQ ID NO:2, and a CDR3 defined by the amino acid sequence of SEQ ID NO:3, and an α-L-iduronidase, wherein the α-L-iduronidase retains at least 30% of its activity

compared to an unfused α-L-iduronidase, and (b) an immunoglobulin light chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:4, a CDR2 defined by the amino acid sequence of SEQ ID NO:5, and a CDR3 defined by the amino acid sequence of SEQ ID NO:6;

(ii) the fusion antibody binds to an extracellular domain of a human insulin receptor expressed on the Blood Brain Barrier (BBB), wherein the human insulin receptor expressed on the BBB is for delivery of the fusion antibody to the brain; and catalyzes hydrolysis of unsulfated alpha-L-iduronosidic linkages in dermatan sulfate; and

(iii) the amino acid sequence of the α-L-iduronidase is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin heavy chain; and

(iv) the fusion antibody is for peripheral administration and a dose of the fusion antibody for administration comprises between 5×10^5 and 3×10^7 units of α-L-iduronidase activity.

16. Use of a fusion antibody having α-L-iduronidase activity for the manufacture of a medicament for the treatment of an α-L-iduronidase deficiency in the central nervous system, wherein:

(i) the fusion antibody comprises (a) a fusion protein comprising an immunoglobulin heavy chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:1, a CDR2 defined by the amino acid sequence of SEQ ID NO:2, and a CDR3 defined by the amino acid sequence of SEQ ID NO:3, and an α-L-iduronidase, wherein the α-L-iduronidase retains at least 30% of its activity compared to an unfused α-L-iduronidase, and (b) an immunoglobulin light chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:4, a CDR2 defined by the amino acid sequence of SEQ ID NO:5, and a CDR3 defined by the amino acid sequence of SEQ ID NO:6;

(ii) the fusion antibody binds to an extracellular domain of a human insulin receptor expressed on the Blood Brain Barrier (BBB); wherein the human insulin receptor expressed on the BBB is for delivery of the fusion antibody to the brain; and catalyzes hydrolysis of unsulfated alpha-L-iduronosidic linkages in dermatan sulfate;

(iii) the amino acid sequence of the α-L-iduronidase is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin heavy chain; and

(iv) a therapeutically effective dose comprises between 1×10^6 and 3×10^7 units of α-L-iduronidase activity.

28. A fusion antibody having α-L-iduronidase activity for use in the treatment

of an α-L-iduronidase deficiency in the central nervous system, wherein:

(i) the fusion antibody comprises: (a) a fusion protein comprising SEQ ID NO: 10, wherein the fusion protein retains at least 30% α-L-iduronidase activity compared to an unfused α-L-iduronidase, and (b) an immunoglobulin light chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:4, a CDR2 defined by the amino acid sequence of SEQ ID NO:5, or a CDR3 defined by the amino acid sequence of SEQ ID NO:6;

(ii) the fusion antibody binds to an extracellular domain of a human insulin receptor expressed on the Blood Brain Barrier (BBB), wherein the human insulin receptor expressed on the BBB is for delivery of the fusion antibody to the brain; and catalyzes hydrolysis of unsulfated alpha-L-iduronosidic linkages in dermatan sulfate.

34. A fusion antibody having α-L-iduronidase activity for use in the treatment of an α-L-iduronidase deficiency in the central nervous system, wherein:

(i) the fusion antibody comprises (a) a fusion protein comprising an immunoglobulin heavy chain, and an α-L-iduronidase comprising SEQ ID NO: 10, or a fusion protein containing the amino acid sequence of an immunoglobulin light chain comprising a CDR1 defined by the amino acid sequence of SEQ ID NO:4, a CDR2 defined by the amino acid sequence of SEQ ID NO:5, or a CDR3 defined by the amino acid sequence of SEQ ID NO:6 and an α-L-iduronidase, wherein the α-L-iduronidase retains at least 30% of its activity compared to an unfused α-L-iduronidase; the fusion antibody binds to an extracellular domain of a human insulin receptor expressed on the Blood Brain Barrier (BBB), wherein the human insulin receptor expressed on the BBB is for delivery of the fusion antibody to the brain; and catalyzes hydrolysis of unsulfated alpha-L-iduronosidic linkages in dermatan sulfate; and

(ii) the amino acid sequence of the α-L-iduronidase is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin heavy chain or the immunoglobulin light chain.

[23] The dependent claims 2 to 15, 17 to 27, 29 to 33 and 35 to 42 define further limitations with regard to: the dose of α-L-iduronidase activity (claims 2, 3, 17, 29, 30, 36 and 37), the administration route (claims 4, 31 and 38), the timing of the delivery to the CNS (claims 5, 32 and 39), the chimeric type of the antibody (claims 6, 18, 33 and 40), the amino acid sequences of the heavy and light chains (claims 7 to 15, 19 to 27, 41 and 42) and the composition of the fusion protein (claim 35).

Essential elements

[24] The Preliminary Review letter, on page 6, states the following with regard to the

elements in the claims that the POSITA would consider to be essential:

> We consider that the POSITA reading claims 1 to 42 would understand that there is no use of language in any of the claims indicating that any of the elements are optional, or a preferred embodiment. Although some claims recite a list of alternatives, we consider that the POSITA would understand that the element represented by one of said alternatives is essential. Further, there is no indication on the record before us that any claim elements are non-essential. It is therefore our preliminary view that the POSITA would consider all of the elements of claims 1 to 42 as essential.

[25] In the absence of submissions from the Applicant, we adopt the above identification of the claim elements that are essential in this recommendation.

ARE CLAIMS 1 TO 27, 29 TO 33 AND 36 TO 42 ENCOMPASSING SUBJECT-MATTER THAT LIES OUTSIDE THE DEFINITION OF "INVENTION" AND DOES NOT COMPLY WITH SECTION 2 OF THE PATENT ACT?

[26] In our view, claims 1 to 27, 29 to 33 and 36 to 42 are directed to patentable subject-matter falling within the definition of "invention" in section 2 of the *Patent Act*.

Legal Background

[27] The definition of invention is set out 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

[28] It is well established that methods of medical treatment and surgery are not patentable subject-matter falling within the manual and productive arts and are excluded from the definition of invention as defined in section 2 of the *Patent Act* (see *Tennessee Eastman Co v Commissioner of Patents* (1970), 62 CPR 117 (Ex Ct), aff'd [1974] SCR 111). However, medical "use" claims have been considered to be directed to patentable subject-matter (see *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77).

[29] A number of lower court decisions have considered the validity of medical use

claims (*Axcan Pharma Inc v Pharmascience Inc*, 2006 FC 527; *Merck & Co, Inc v Pharmascience Inc*, 2010 FC 510; *Janssen Inc v Mylan Pharmaceuticals ULC*, 2010 FC 1123; *AbbVie Biotechnology Ltd v Canada (Attorney General)*, 2014 FC 1251 [*AbbVie*]). Upon reviewing prior decisions, the Federal Court in *AbbVie* concluded that the jurisprudence is consistent; Federal Court jurisprudence has developed the principle that:

> [A] claim directed to the exercise of professional skill or judgment is not patentable. However, a claim which does not restrict, or interfere with, or otherwise engage professional skill or judgment – including a claim for a fixed dosage and or a fixed dosage schedule or interval – is not impermissible subject matter where there is no evidence to contradict that claimed dosage. (para 114)

[30] With particular reference to the determination of patentable subject-matter in respect of medical use claims containing a dosage or dosing regimen, the current Patent notice titled "Patentable Subject-Matter under the *Patent Act*"[1] states that:

> [I]n cases where at least one of the essential elements of the actual invention limits the claimed use to a dosage, a range of potential dosages that a patient may receive, and/or a dosage regimen, regardless of whether these are fixed and/or cover a range, this fact alone is not determinative of whether the claim is patentable subject-matter. It is also necessary to consider whether the exercise of professional skill and judgment of a medical professional is part of the actual invention. For example, professional skill and judgment may be involved if a medical professional is expected to monitor or make adjustments to the treatment, or make a selection of a dosage from a claimed range (i.e., in cases where not all dosages in the range will work for all subjects within the treatment group).

Analysis of the claims

[31] The Preliminary Review letter, on pages 8 to 9, explains why we agree with the Summary of Reasons of the Examiner that the non-patentable subject-matter defect relating to claims 1 to 27, 29 to 33 and 36 to 42 should be withdrawn:

> According to the FA on page 4, these claims encompass a method of medical treatment, and therefore are not patentable, because the use of the recited fusion antibody is defined in terms of a dose which comprises a range of units of IDUA activity and said use would therefore require the skill of a medical professional to

[1] https://ised-isde.canada.ca/site/canadian-intellectual-property-office/en/patents/patent-notices/patentable-subject-matter-under-patent-act

> determine the therapeutic dose of the fusion antibody required to attain the desired therapeutic effect. The analysis presented in the FA was based on a purposive construction of the claims that was conducted according to an Office practice that is no longer in effect.
>
> The SOR states that in light of the most recent Office practice, the non-patentable subject-matter defect relating to claims 1 to 27, 29 to 33 and 36 to 42 should be withdrawn "[s]ince the specification does not appear to provide any evidence indicating that the range of doses indicated in these claims prevents, interferes with or requires the skill or judgement of a medical professional". We agree for the following reasons.
>
> One essential element common to claims 1 to 27, 29 to 33 and 36 to 42 is the use of a dose for peripheral administration of the recited fusion antibody that is expressed as a range of α-L-iduronidase activity for treating an α-L-iduronidase deficiency in the central nervous system.
>
> There is nothing in the description that indicates that the encompassed range of doses of α-L-iduronidase activity would not all work for treating an α-L-iduronidase deficiency in the central nervous system for all subjects in need thereof, or that the dose is selected based on any patient-specific features. To the contrary, the encompassed doses are based on CGK elements such as the normal range of levels of IDUA enzyme activity per mg of protein for the human brain and the total amount of protein in an average human brain (see para [00157] of the description). As such, there is no indication that selecting a dose from the claimed range would require the skill and judgment of a medical professional.
>
> Our preliminary view is therefore that claims 1 to 27, 29 to 33 and 36 to 42 are directed to patentable subject-matter falling within the definition of "invention" in section 2 of the *Patent Act*.

[32] We adopt the foregoing reasoning and conclude that claims 1 to 27, 29 to 33 and 36 to 42 are directed to patentable subject-matter falling within the definition of "invention" in section 2 of the *Patent Act*.

IS THE SUBJECT-MATTER OF CLAIMS 28, 30 TO 35 AND 37 TO 42 ON FILE ANTICIPATED?

[33] It is our view that the subject-matter of claims 28, 30 to 33, 35, 37, 41 and 42 is novel but that the subject-matter of claims 34, and 38 to 40 became available to the public in a manner that is contrary to paragraph 28.2(1)(a) of the *Patent Act*.

Legal Background

[34] Paragraph 28.2(1)(a) of the *Patent Act* sets out the requirement that the subject-matter of a claim must be novel in view of a disclosure by the applicant itself:

> The subject-matter defined by a claim in an application for a patent in Canada (the "pending application") must not have been disclosed
>
> (a) before the one-year period immediately preceding the filing date or, if the claim date is before that period, before the claim date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant, in such a manner that the subject-matter became available to the public in Canada or elsewhere;
>
> […].

[35] There are two separate requirements to show that prior art anticipates a claimed invention: there must be a prior disclosure of the claimed subject-matter and the prior disclosure must enable the claimed subject-matter to be practised by the POSITA (*Apotex Inc v Sanofi–Synthelabo Canada Inc*, 2008 SCC 61 [*Sanofi*] at paras 24 to 29 and 49).

[36] "Prior disclosure" means that the prior art must disclose subject-matter which, if performed, would necessarily result in infringement of the patent. The POSITA looking at the disclosure is "taken to be trying to understand what the author of the description [in the prior patent] meant" (see *Sanofi* at para 32). At this stage, there is no room for trial and error or experimentation by the POSITA. The prior art is simply read "for the purposes of understanding it": see *Sanofi*, at paragraph 25, citing *Synthon B.V. v SmithKline Beecham plc*, [2006] 1 All ER 685, [2005] UKHL 59.

[37] The enablement requirement means that the POSITA would have been able to perform the invention as claimed without undue burden. Unlike the prior disclosure stage, at this stage the POSITA is assumed to be willing to make trial and error experiments to get it to work (see *Sanofi* at paras 26 to 27).

Analysis of the claims

[38] The Preliminary Review letter, on pages 10 to 13, identifies the prior art document D1 (US2005/0142141) that was cited in the Final Action, and offers the following

analysis [Emphasis in original]:

Prior art disclosure

We must determine if the subject-matter of claims 28, 30 to 35 and 37 to 42 on file is disclosed in the following document cited in the FA:

D1: US2005/0142141 Pardridge pub. date: June 30, 2005

In our preliminary view, D1 teaches the use of a HIR Ab-IDUA fusion antibody which comprises a) a fusion protein comprising an immunoglobulin heavy chain and an IDUA, and b) an immunoglobulin light chain, to treat IDUA deficiency in the central nervous system, wherein the heavy chain comprises SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, and the light chain comprises SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6. Said fusion antibody specifically binds to the extracellular domain of a human insulin receptor expressed on the BBB, which triggers transport of the fusion antibody across the BBB for the delivery of the fusion antibody, which includes IDUA, to the brain. D1 also teaches that the amino acid sequence of the IDUA can be covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin heavy chain or the light chain. Said fusion antibody may be for peripheral administration.

More specifically, D1 discloses in Figure 5 the following amino acid sequence of the contemplated heavy chain of the fusion antibody wherein the coding sequence of IDUA is in bold [our emphasis]:

QVQLLESGAELVRPGSSVKISCKASGYTFTNYDIHWVKQRPGQGLEWIGWIYPGD
GSTKYNEKFKGKATLTADKSSSTAYMHLSSLTSEKSAVYFCAREWAYWGQGTTVT
VSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
K**APHLVQVDAARALWPLRRFWRSTGFCPPLPHSQADQYVLSWDQQLNLAYVGA**
VPHRGIKQVRTHWLLELVTTRGSTGRGLSYNFTHLDGYLDLLRENQLLPGFELM
GSASGHFTDFEDKQQVFEWKDLVSSLARRYIGRYGLAHVSKWNFETWNEPDHH
DFDNVSMTMQGFLNYYDACSEGLRAASPALRLGGPGDSFHTPPRSPLSWGLLR
HCHDGTNFFTGEAGVRLDYISLHRKGARSSISILEQEKVVAQQIRQLFPKFADTPIY
NDEADPLVGWSLPQPWRADVTYAAMVVKVIAQHQNLLLANTTSAFPYALLSNDN
AFLSYHPHPFAQRTLTARFQVNNTRPPHVQLLRKPVLTAMGLLALLDEEQLWAE
VSQAGTVLDSNHTVGVLASAHRPQGPADAWRAAVLIYASDDTRAHPNRSVAVTL
RLRGVPPGPGLVYVTRYLDNGLCSPDGEWRRLGRPVFPTAEQFRRMRAAEDPV
AAAPRPLPAGGRLTLRPALRLPSLLLVHVCARPEKPPGQVTRLRALPLTQGQLV
LVWSDEHVGSKCLWTYEIQFSQDGKAYTPVSRKPSTFNLFVFSPDTGAVSGSYR
VRALDYWARPGPFSDPVPYLEVPVPRGPPSPGNP

Although D1 refers to the complete known human IDUA coding sequence in Table 4 (Genbank NM_000203), we note that the above IDUA coding sequence represented in Figure 5 and SEQ ID NO:48 are both missing the signal peptide and the first coding amino-terminus glutamic acid of IDUA.

The fusion antibody encompassed by claims 28, 30 to 35 and 37 to 42 comprises “a fusion protein comprising SEQ ID NO: 10”. It is our understanding that SEQ ID NO:10 represents a fusion protein comprising the heavy chain of the HIR antibody covalently linked to IDUA as described in the instant application.

Once the sequence represented in Figure 5 of D1 is aligned and compared to the sequence represented in SEQ ID NO:10 of the instant application, we note the following differences:

- the sequence found in Figure 5 is missing an IgG signal peptide at its amino-terminal end;

- positions 5, 6, 9, 13, 16 and 17 of the sequence found in Figure 5 (all part of the Framework Region (FR) 1 region) differ from the corresponding positions in SEQ ID NO:10;

- position 108 of the sequence found in Figure 5 (part of the FR4 region) differs from the corresponding position in SEQ ID NO:10;

- there is an additional Ser-Ser peptide linker between the carboxy-terminal end of the heavy chain and the fused IDUA in SEQ ID NO:10; and

- the first amino-terminus glutamic acid of IDUA is missing in the IDUA sequence portion represented in Figure 5.

In view of the above differences, it is our preliminary view that D1 does not disclose the subject-matter of claims 28, 30 to 35 and 37 to 42 insofar as they relate to a fusion antibody comprising SEQ ID NO: 10.

We further note that independent claim 34, also encompasses a fusion antibody comprising an α-L-iduronidase that is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin light chain. Having reviewed D1, it is our preliminary view that D1 describes on page 11 an embodiment of a humanized HIR Ab-IDUA fusion antibody wherein the gene encoding IDUA is fused to the region of the humanized HIR Ab light chain gene corresponding to the carboxyl terminus of a HIR Ab light chain protein comprising the light chain CDRs recited in claim 34. It is also our preliminary view that D1 discloses the additional feature recited in dependent claim 38 and that the feature recited in dependent claim 39 is inherent to the peripheral administration of HIR Ab-IDUA fusion antibody. Finally, it is our preliminary view that D1 does not disclose the dosages recited in claims 36 and 37 or a fusion antibody wherein the amino acid sequence of the

immunoglobulin light chain is at least 90% identical to SEQ ID NO:8 as encompassed by claims 41 and 42.

Enablement

Since the disclosure requirement is not met in respect of the subject-matter of claims 28, 30 to 35 and 37 to 42 insofar as the subject-matter comprises SEQ ID NO:10 or SEQ ID NO: 8 and/or the dosages of claims 36 and 37, there is no need to consider enablement of such subject-matter.

With respect to claims 34, and 38 to 40, which encompass HIR Ab-IDUA fusion antibody wherein IDUA is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin light chain, it is our preliminary view that D1 provides all the required information so that the POSITA would have been able to perform the subject-matter as claimed without undue burden.

Conclusion on anticipation

In view of the above analyses, it is our preliminary view that the subject-matter of claims 28, 30 to 33, 35, 37, 41 and 42 is novel in view of D1 and complies with paragraph 28.2(1)(a) of the *Patent Act*.

Further, it is our preliminary view that the subject-matter of claims 34, and 38 to 40 is anticipated by D1, contrary to paragraph 28.2(1)(a) of the *Patent Act*.

[39] In the absence of submissions from the Applicant, we adopt the foregoing reasoning and conclude that the subject-matter of claims 28, 30 to 33, 35, 37, 41 and 42 is novel in view of D1 and complies with paragraph 28.2(1)(a) of the *Patent Act*.

[40] Further, we conclude that the subject-matter of claims 34 and 38 to 40 is anticipated by D1, contrary to paragraph 28.2(1)(a) of the *Patent Act*.

IS THE SUBJECT-MATTER OF THE CLAIMS ON FILE OBVIOUS?

[41] In our view, the claims on file define subject-matter that would have been obvious to the POSITA in view of information that was publicly available before the claim date.

Legal Background

[42] Section 28.3 of the *Patent Act* requires that the subject-matter of a claim not be

obvious to the person skilled in the art:

> 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 or, if the claim date is before that period, before the claim 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.

[43] In *Sanofi*, the Supreme Court of Canada states 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?

Analysis of the Claims

[44] Although the Final Action only identifies claims 28, 30 to 35 and 37 to 42 as being directed to subject-matter that would have been obvious, we have also considered whether claims 1 to 27, 29 and 36 suffer from obviousness and, in accordance with subsection 86(9) of the *Patent Rules*, we gave the Applicant notice of this assessment and corresponding preliminary conclusion in the Preliminary Review Letter. We also introduced the prior art document Crow et al., "Biochemical and histopathological studies on patients with mucopolysaccharidoses, two of whom

had been treated by fibroblast transplantation", *J Clin Pathol.* 36(4):415 to 30, 1983 as D2. The relevant passages are found on pages 14 to 17 of the Preliminary Review Letter:

> The POSITA and the relevant CGK
>
> The POSITA and the relevant CGK have been identified above as part of the purposive construction of the claims. Although in this context the information forming the relevant CGK is identified using the publication date, this information is also considered CGK at the claim date and is therefore relevant for assessing obviousness.
>
> Identify the inventive concept of the claim in question or, if that cannot readily be done, construe it
>
> In this assessment, we take into account all of the essential elements of the claims. In our preliminary view, the combination of essential elements of independent claims 1, 16, 28 and 34 represent their inventive concepts as well.
>
> Our preliminary view is also that the elements of the dependent claims relating to the dose of α-L-iduronidase activity, the administration route, the timing of the delivery to the CNS, the chimeric type of the antibody, the amino acid sequences of the heavy and light chains and the composition of the fusion protein, as set out above, are part of the respective inventive concepts of dependent claims 2 to 15, 17 to 27, 29 to 33 and 35 to 42.
>
> 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
>
> The FA cites the same document D1 for obviousness.
>
> In our preliminary view, the main differences between the subject-matter of the claims on file and the disclosure of D1 are: i) a specified dose of the fusion antibody for peripheral administration defined in terms of units of activity of IDUA (claims 1 to 27, 29 to 33 and 36 to 42); and/or ii) the amino acid sequence recited in SEQ ID NO:10 of the instant application within the fused heavy chain of the fusion antibody (claims 15 and 27 to 42) and/or iii) the amino acid sequence recited in SEQ ID NO:8 of the instant application within the fusion antibody (claims 41 and 42).
>
> Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

The Federal Court of Appeal has reminded at para 65 of *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76, that the instant step of the obviousness analysis is concerned with whether bridging the difference between the prior art and a second point constitutes steps that require any degree of invention:

> It may be helpful to keep in mind that the obviousness analysis asks whether the distance between two points in the development of the art can be bridged by the Skilled Person using only the common general knowledge available to such a person. If so, it is obvious. The first of those points is the state of the prior art at the relevant date. References in the jurisprudence to "the inventive concept", "the solution taught by the patent", "what is claimed" or simply "the invention" are attempts to define the second point.

In the present case, what must be considered is whether it would have required any degree of invention from the POSITA, based on the disclosure of D1 and the relevant CGK, to use the HIR Ab-IDUA fusion antibody disclosed in D1 at a dose of units of activity of IDUA encompassed by the claims on file to treat an α-L-iduronidase deficiency in the central nervous system and whether the presence of SEQ ID NO:10 or SEQ ID NO:8 in a contemplated fusion antibody is otherwise indicative of inventiveness.

It is our preliminary view that it would not have required any degree of invention from the POSITA to determine with routine experimentation a replacement dose of IDUA activity to be delivered to the brain given that the normal range of levels of IDUA enzyme activity per mg of protein for the human brain and the total amount of protein in an average human brain were CGK (or otherwise known from Crow et al., "Biochemical and histopathological studies on patients with mucopolysaccharidoses, two of whom had been treated by fibroblast transplantation", *J Clin Pathol.* 36(4):415 to 30, 1983 [D2], cited in the instant description at para [00157]).

With regard to the presence of the amino acid sequence set forth in SEQ ID NO:10 in the contemplated fusion antibody, we have already identified above the differences with the heavy chain of the HIR Ab-IDUA fusion antibody disclosed in D1. In summary, the amino acid sequence set forth in SEQ ID NO:10 includes an additional IgG signal at the amino-terminal end, an additional Ser-Ser peptide linker between the carboxy-terminal end of the heavy chain, an additional amino-terminus glutamic acid in the IDUA sequence portion as well as single amino acid differences in the FR1 (6 differences) and FR4 (1 difference) regions.

It is our preliminary view that the POSITA would understand that these differences are outside the heavy chain antigen-binding variable region and outside the IDUA substrate binding/catalytic regions. Further, the POSITA would not consider that these differences are associated with any relevant surprising

> or unexpected effects in view of their CGK and/or the teachings of the instant description and thus, these differences do not support that the presence of the amino acid sequence set forth in SEQ ID NO:10 in the contemplated fusion antibody is inventive *vis-à-vis* the HIR Ab-IDUA fusion antibody taught by D1.
>
> We further considered an alternate embodiment of claims 34 to 42, specifically a fusion antibody comprising an α-L-iduronidase that is covalently linked to the carboxy terminus of the amino acid sequence of the immunoglobulin light chain comprising the recited light chain CDRs. As mentioned above, it is our preliminary view that D1 describes a fusion antibody comprising an α-L-iduronidase that is covalently linked to the carboxy terminus of the amino acid sequence of an immunoglobulin light chain comprising the light chain CDRs recited in claim 34.
>
> Having considered the additional limiting features of the dependent claims, we are of the preliminary view no ingenuity would have been required from the POSITA in respect of the dose of α-L-iduronidase activity (claims 2, 3, 17, 29, 30, 36 and 37), the administration route (claims 4, 31 and 38), the timing of the delivery to the CNS (claims 5, 32 and 39), the chimeric type of the antibody (claims 6, 18, 33 and 40), the recited percentage of identity with the amino acid sequences of the heavy and light chains (claims 7 to 15, 19 to 27, 41 and 42) and the composition of the fusion protein (claim 35).
>
> Conclusion on obviousness
>
> Therefore, it is our preliminary view that the subject-matter of claims 1 to 42 on file would have been obvious to POSITA as of the relevant date, in view of either D1 and the CGK or D1, D2 and the CGK, contrary to section 28.3 of the *Patent Act*.

[45] In the absence of submissions from the Applicant, we adopt the foregoing reasoning and conclude that the subject-matter of claims 1 to 42 would have been obvious to POSITA as of the relevant date, in view of either D1 and the CGK or D1, D2 and the CGK, contrary to section 28.3 of the *Patent Act*.

DO CLAIMS 28 TO 42 LACK SUPPORT, IS THE DESCRIPTION INSUFFICIENT UNDER SUBSECTION 27(3) OF THE *PATENT ACT* AND IS THE JUDICIALLY-CREATED DOCTRINE OF OVERBREADTH APPLICABLE TO CLAIMS 28 TO 42?

[46] In our view, claims 28 to 41 suffer from overbreadth and, independently of this view, the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of claims 28 to 41.

Legal Background

[47] One of the grounds for rejection mentioned in the FA, lack of support, relies on section 84 of the former *Rules* (now section 60) as legislative authority. It is our understanding that the concern over lack of support under section 84 of the former *Rules* gave rise to a corresponding ground for rejection under subsection 27(3) of the *Patent Act* for lack of description and enablement of the claimed subject-matter. Of the two legislative provisions, the latter one has enjoyed extensive consideration by the courts. For the purposes of the instant case, we have therefore proceeded by considering only this latter requirement; any concern over non-compliance with section 84 of the former *Rules* we take as being subsumed within that inquiry.

[48] Paragraphs 27(3)(a) and (b) of the *Patent Act* require, respectively, that the specification of an invention (1) describe the invention, and (2) set out the steps for its production and use:

> The specification of an invention must:
>
> a) correctly and fully describe the invention and its operation or use as contemplated by the inventor;
>
> b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;
>
> […].

[49] A determination of whether the specification complies with paragraphs 27(3)(a) and 27(3)(b) of the *Patent Act* requires that three questions be answered: What is the invention? How does it work? Having only the specification, can the POSITA produce the invention using only the instructions contained in the disclosure? see: *Teva Canada Ltd v Novartis AG*, 2013 FC 141 citing *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 and *Consolboard v MacMillan Bloedel* [1981], 56 CPR 2d 145 (SCC) [*Consolboard*]. Although the CGK can be relied upon, an affirmative answer to the third question requires that the POSITA not be called upon to display inventive ingenuity or undertake undue experimentation: *Aventis Pharma Inc v*

Apotex Inc, 2005 FC 1283; *Mobil Oil Corp v Hercules Canada Inc*, [1995] FCJ No 1243; *Merck & Co v Apotex Inc*, [1995] 2 FC 723.

[50] In *Consolboard*, at pages 154 to 155, the Supreme Court referred to the textbook *Canadian Law and Practice Relating to Letters Patent for Inventions* (1969, 4th ed.) from which it quoted H.G. Fox as saying “the inventor must, in return for the grant of a patent, give to the public an adequate description of the invention with sufficiently complete and accurate details as will enable a workman, skilled in the art to which the invention relates, to construct or use that invention when the period of the monopoly has expired”.

[51] The principles and authorities laid out above primarily relate to the concept of sufficiency (or insufficiency).

[52] Another related concept is overbreadth (or overclaiming). The concept of overbreadth stems from subsections 27(3) and 27(4) of the *Patent Act*, and is a consequence of the bargain theory (see *Western Oilfield Equipment Rentals Ltd v M-I LLC*, 2021 FCA 24, at paras 129 and 130). Overbreadth may overlap with other grounds of invalidity but overbreadth is a distinct ground of invalidity. For example, it has often been said that overbreadth and insufficiency are the two sides of the same coin. Where a claim is broader than the description, it may fail for overbreadth, but it may also fail because the description does not adequately describe how to put it into practice.

[53] Overbreadth could be found because a claim is broader than the invention disclosed in the specification or it is broader than the invention made. To determine whether a claim is overbroad, it must be assessed whether the claim reads fairly on what the patent application discloses in the description and the drawings or whether the claim is too wide and claims more than what was invented. In this regard, this determination does not require that the patent application describe all possible embodiments of the claims as the claims may be broader than the embodiments disclosed in the description, which are considered examples of what is protected by the patent’s monopoly (see *Angelcare Canada Inc v Munchkin Inc*, 2022 FC 507, at para 452). However, there is a limit to how much broader the claims can be relative to the described embodiments (see *Les Laboratoires Servier v Apotex Inc,* 2019 FC 616, para 209).

[54] As mentioned above, overbreadth and insufficiency are often compared to the two sides of the same coin and therefore considerations such as what is exactly encompassed by the scope of the claims and what is disclosed in the description are relevant to both inquiries. If the claims don't read fairly on what the patent application discloses in the description and the drawings, then the claims may encompass subject-matter that is more than what was invented or adequately disclosed.

[55] Further, it is not enough for the disclosure to teach how to make the preferred embodiment. The disclosure must teach the POSITA to put into practice all the claimed embodiments of the invention, and without exercising inventive ingenuity or undue experimentation (see *Seedlings Life Science Ventures, LLC v Pfizer Canada ULC*, 2021 FCA 154, at para 68).

Analysis of the claims

[56] The Preliminary Review letter, on pages 19 to 21, explains how in our preliminary view claims 28 to 41 suffer from overbreadth and how the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims:

> As framed in the Final Action on page 5, the specification, insofar as it relates to claims 28 to 42 and the encompassed fusion antibody light chain defined by a single CDR sequence, does not comply with subsection 27(3) of the *Patent Act* because it fails to correctly and fully describe the use of any fusion antibodies that mimic the endogenous ligand in order to access the CNS via receptor-mediated transport other than a fusion antibody having all three specific light chain CDRs disclosed in the description [Emphasis in original]:
>
> > The description fails to support all of the fusion antibodies encompassed by claim 28. Additionally, with respect to claim 34, the fusion antibody is defined as comprising any fusion protein containing the amino acid sequence of an immunoglobulin light chain comprising the amino acid sequence of CDR1, CDR2 <u>or</u> CDR3. Therefore, claim 34 appears to encompass fusion proteins which do not necessarily comprise SEQ ID NO: 10 as well as fusion proteins in which only a single CDR of an immunoglobulin light chain is defined. Consequently, these claims still encompass fusion antibodies which lack support in the description. As stated in the Office Actions of March 13, 2015, April 7, 2016, April 11, 2017 and March 2, 2018, the description discloses that only "<u>certain</u> ECD-specific antibodies may mimic the endogenous ligand and thereby

> traverse a plasma membrane barrier..." (page 10, lines 1-2). Therefore, the description teaches that not all HIR Abs which bind to the ECD of the HIR mimic the endogenous ligand and transverse a plasma membrane barrier. As currently formulated, these claims encompass the use of fusion antibodies which do not mimic endogenous ligand and transverse a plasma membrane barrier, which is not supported in the description. In order for the subject matter of these claims to fall within the bounds of adequate support, the immunoglobulin heavy and light chains which bestow on the antibody the ability to bind to an extracellular domain of a human insulin receptor expressed on the blood brain barrier AND to transverse a plasma membrane barrier need to be defined in the claims.

The RFA does not contest or otherwise comment on the above views but nevertheless proposes amendments to delete claims 28 to 42 on file. We will consider the proposed claims in a separate section below.

Having reviewed the description and the drawings, we understand that the application discloses relevant exemplary embodiments wherein a HIR Ab-IDUA fusion antibody comprising specific CDR sequences (see Fig. 3) is constructed, produced and tested *ex vivo* with Hurler fibroblasts as well as tested *in vivo* with brain delivery experiments. As in the FA, we also note that the description teaches on pages 9 to 10 that only certain antibodies specific for the extracellular insulin binding domain of the insulin receptor (ECD) may mimic the endogenous ligand and thereby traverse a plasma membrane barrier via transport through the human BBB insulin receptor.

Although the description on page 14 teaches that methods to produce variants of the disclosed HIR Ab-IDUA fusion antibody exist, it does not disclose alternative sets of CDRs that would effectively mimic the ligand insulin. On the basis of the record before us, it is our preliminary view that: i) the CGK regarding HIR specific antibodies does not include commonly known alternatives to the HIR humanized antibody and encoding sequences thereof disclosed in the instant description; and ii) the POSITA would not be aware of any other set of CDRs capable of mimicking the binding of the endogenous ligand insulin.

In light of the above considerations, it is our preliminary view that claims 28 to 41 on file do not read fairly on what the patent application discloses in the description and the drawings with respect to a HIR Ab-IDUA fusion antibody comprising CDR sequences that differ from the specific CDR sequences recited in Fig. 3.

Further, and on the basis of the same considerations, it is our preliminary view that the specification fails to teach the POSITA how to put into practice all the claimed embodiments of the invention without exercising undue experimentation to identify alternative CDR sequences capable of mimicking the binding of the endogenous ligand insulin. These gaps are not filled by the CGK.

> Conclusions on insufficiency under subsection 27(3) of the *Patent Act* and overbreadth
>
> Our preliminary conclusions are that; i) claims 28 to 41 on file suffer from overbreadth and, independently of this view, ii) the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of claims 28 to 41.

[57] Although not explicitly stated in the Preliminary Review Letter, it is our view that the scope of claim 42 does not encompass heavy or light chain CDR sequences that differ from the specific CDR sequences recited in Fig. 3.

[58] In the absence of submissions from the Applicant, we adopt the foregoing reasoning and conclude that; i) claims 28 to 41 suffer from overbreadth and, independently of this view, ii) the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of claims 28 to 41.

ARE CLAIMS 12, 13, 24 AND 25 INDEFINITE FOR BEING DIRECTED AT REDUNDANT SUBJECT-MATTER IN VIEW OF CLAIMS 10, 11, 22 AND 23 AND HENCE FAILING TO CLEARLY DEFINE A DIFFERENCE IN SCOPE RELATIVE TO EACH OTHER?

[59] In our view, claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

Legal Background

[60] Subsection 27(4) of the *Patent Act* states that "[t]he 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".

[61] In *Minerals Separation North American Corp v Noranda Mines Ltd*, [1947] Ex CR 306 at 352, 12 CPR 99, the Court emphasized 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

[62] The Preliminary Review letter, on page 22, explains how in our preliminary view claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*:

> According to the FA on page 5, claims 12, 13, 24 and 25 are indefinite because they are directed to the same subject-matter claimed in claims 10, 11, 22 and 23 respectively:
>
> > Claim 12 appears to be directed towards the same subject matter as claim 10 when claim 10 depends on claim 7. Similarly, claim 13 appears to be directed towards the same subject matter as claim 11 when claim 11 depends on claim 8, claim 24 appears to be directed towards the same subject matter as claim 22 when claim 22 depends on claim 19, and claim 25 appears to be directed towards the same subject matter as claim 23 when claim 23 depends on claim 20.
>
> The RFA does not contest or otherwise comment on the above views but nevertheless proposes amendments to delete claims 12, 13, 24 and 25 on file. We will consider the proposed claims in a separate section below.
>
> Having reviewed claims 12, 13, 24 and 25 as well as claims 10, 11, 22 and 23, we agree with the FA. We are of the preliminary view that the lack of differentiation between claim 12 and claim 10, between claim 13 and claim 11, between claim 24 and claim 22 and between claim 25 and claim 23 makes the subject-matter of these claims redundant and fails to clearly define a difference in scope.
>
> Conclusion on indefiniteness
>
> Given the lack of clear differentiation of scope, it is our preliminary view that claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

[63] In the absence of submissions from the Applicant, we adopt the foregoing reasoning and conclude that claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

THE PROPOSED CLAIMS DO NOT REMEDY THE DEFECTS

[64] As indicated above, with the Response to the Final Action the Applicant submitted proposed claims 1 to 86.

[65] New proposed independent claims 1 to 21 and 35 to 54 recite a fixed amount of α-L-iduronidase activity. New proposed dependent claims 22 to 34 and 55 to 65 define further limitations with regard to the dose of α-L-iduronidase activity, the administration route, the timing of the delivery to the CNS, the chimeric type of the antibody, and/or the amino acid sequences of the heavy and light chains.

[66] New proposed independent claims 66, 74 and 78 are directed to a fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB, wherein said receptor is not the insulin receptor. New proposed dependent claims 67 to 73, 75 to 77 and 79 to 86 define further limitations with regard to the dose of α-L-iduronidase activity, the administration route, the timing of the delivery to the CNS and/or the chimeric type of the antibody.

[67] According to the Summary of Reasons on page 2, proposed claims 31, 32, 62 and 63 are indefinite and the subject-matter of proposed claims 66 to 86 is not supported by the description.

[68] The Preliminary Review letter considered these alleged defects as well as whether the proposed claims address the obviousness defect that we had identified with respect to the claims on file. Pages 22 to 26 of that letter explain our preliminary view that proposed claims 31, 32, 62 and 63 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*, that proposed claims 66 to 86 suffer from overbreadth, that the specification would not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of proposed claims 66 to 86 and that the subject-matter of proposed claims 1 to 65 would have been obvious to the POSITA as of the relevant date:

ANALYSIS OF THE PROPOSED AMENDMENTS

During the review, the Panel may consider proposed amendments and determine whether such amendments would constitute necessary amendments under subsection 86(11) of the *Patent Rules*.

With the RFA the Applicant submitted a proposed claims set comprising claims 1 to 86 wherein new independent claims 1 to 21 and 35 to 54 now recite a fixed amount of α-L-iduronidase activity. New dependent claims 22 to 34 and 55 to 65 define further limitations with regard to the dose of α-L-iduronidase activity, the administration route, the timing of the delivery to the CNS, the chimeric type of the antibody, and/or the amino acid sequences of the heavy and light chains.

New independent claims 66, 74 and 78 are directed to a fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB, wherein said receptor is not the insulin receptor. New dependent claims 67 to 73, 75 to 77 and 79 to 86 define further limitations with regard to the dose of α-L-iduronidase activity, the administration route, the timing of the delivery to the CNS and/or the chimeric type of the antibody.

According to the SOR on page 2, proposed claims 31, 32, 62 and 63 are indefinite and the subject-matter of proposed claims 66 to 86 is not supported by the description.

We have considered these alleged defects as well as whether the proposed claims address the obviousness defect that we have identified above with respect to the claims on file.

Are proposed claims 31, 32, 62 and 63 indefinite for being directed at redundant subject-matter in view of proposed claims 29, 30, 60 and 61 and hence failing to clearly define a difference in scope relative to each other?

Having reviewed proposed claims 31, 32, 62 and 63 as well as proposed claims 29, 30, 60 and 61, we agree with the SOR. We are of the preliminary view that the lack of differentiation between claim 31 and claim 29, between claim 32 and claim 30, between claim 62 and claim 60 and between claim 63 and claim 61 makes the subject-matter of these claims redundant and fails to clearly define a difference in scope.

Conclusion on indefiniteness

Given the lack of clear differentiation of scope, it is our preliminary view that proposed claims 31, 32, 62 and 63 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

Do proposed claims 66 to 86 lack support, is the description insufficient under subsection 27(3) of the *Patent Act* and is the judicially-created doctrine of overbreadth applicable to claims 66 to 86?

As framed in the SOR on page 2, the specification, insofar as it relates to proposed claims 66 to 86 and the encompassed fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB other than the insulin receptor, does not comply with subsection 27(3) of the *Patent Act*:

The description discloses a fusion antibody that binds to an extracellular domain of the human insulin receptor expressed on the Blood Brain Barrier (BBB) (see figures and examples). However, a fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB, wherein said receptor is *not* the insulin receptor, is not supported in the description.

It follows that the specification as it relates to proposed claims 66-86 does not comply with subsection 27(3) of the *Patent Act.* The description fails to describe a fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB, wherein said receptor is not the insulin receptor.

The RFA on pages 1 to 2 states that support for the subject-matter of proposed claims 66 to 86 can be found in the application as filed for example paragraphs [0060] and [0061]. Paragraphs [0060] and [0061] read as follows:

> The BBB has been shown to have specific receptors, including insulin receptors, that allow the transport from the blood to the brain of several macromolecules. In particular, insulin receptors are suitable as transporters for the HIR Ab-IDUA fusion antibodies described herein. The HIR-IDUA fusion antibodies described herein bind to the extracellular domain (ECD) of the human insulin receptor.
>
> Insulin receptors and their extracellular, insulin binding domain (ECD) have been extensively characterized in the art both structurally and functionally. See, e.g., Yip et al (2003), *J Biol. Chem*, 278(30): 27329-27332; and Whittaker et al. (2005), "*J Biol Chem*, 280(22):20932-20936.The amino acid and nucleotide sequences of the human insulin receptor can be found under GenBank accession No. NM_000208.

We understand from the cited passage above and the application as a whole that the application's disclosure with regard to fusion antibodies covalently linked to IDUA is limited to fusion antibodies that bind to the extracellular domain of the human insulin receptor. Also relevant is the description teaching that only certain antibodies specific for the insulin receptor may mimic the endogenous ligand and thereby traverse a plasma membrane barrier via transport through the human BBB insulin receptor.

Although the above cited passage supports that the BBB has specific receptors other than insulin receptors that allow the transport from the blood to the brain of several macromolecules, it does not teach or disclose fusion antibodies capable of targeting such other specific receptors and that otherwise mimic the endogenous ligand in order to access the CNS via receptor-mediated transport.

The review article *Jones and Shusta* introduced above supports that the use of an anti-transferrin antibody for receptor-mediated transport of therapeutics to the CNS was commonly known and, in our preliminary view, CGK. However, all reported studies concerned the use of a monoclonal antibody conjugated to a therapeutic cargo that is not a fusion antibody and that is not covalently linked to the therapeutic cargo, unlike the claimed embodiments.

In light of the above considerations, it is our preliminary view that proposed claims 66 to 86 do not read fairly on what the patent application discloses in the description and the drawings with respect to a fusion antibody that binds to an extracellular domain of any receptor expressed on the BBB. The human insulin receptor antibody covalently linked to α-L-iduronidase is the only fusion antibody disclosed in the specification that mimics the endogenous ligand and thereby traverses the plasma membrane barrier via transport in order to be used in the treatment of an α-L-iduronidase deficiency in the central nervous system.

Further, and on the basis of the same considerations, it is our preliminary view that the specification fails to teach the POSITA how to put into practice all the claimed embodiments encompassed by proposed claims 66 to 86 without exercising undue experimentation to produce any and all fusion antibodies that bind to an extracellular domain of any receptor expressed on the BBB other than the insulin receptor and that mimic the endogenous ligand in order to access the CNS via receptor-mediated transport. These gaps with respect to the encompassed fusion antibodies are not filled by the CGK.

Conclusions on insufficiency under subsection 27(3) of the *Patent Act* and overbreadth

Our preliminary conclusions are that; i) the proposed claims 66 to 86 suffer from overbreadth and, independently of this view, ii) the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of proposed claims 66 to 86.

Is the Subject-matter of Proposed Claims 1 to 65 Obvious?

We have already expressed above our preliminary view that the subject-matter of the claims on file is obvious and does not comply with section 28.3 of the *Patent Act*. We consider that the obviousness analysis of the claims on file equally applies to proposed claims 1 to 65 as the subject-matter of proposed claims 1 to 65 is encompassed by one or more of claims 1 to 42 on file and we already expressed the

> preliminary view that no ingenuity would have been required from the POSITA in respect of identifying an effective replacement dose of α-L-iduronidase activity or in respect of any of the additional recited features.
>
> Conclusion on obviousness
>
> Therefore, it is our preliminary view that the subject-matter of proposed claims 1 to 65 would have been obvious to POSITA as of the relevant date, in view of either D1 and the CGK or D1, D2 and the CGK, contrary to section 28.3 of the *Patent Act*.

[69] In the absence of submissions from the Applicant, we adopt the foregoing reasoning and conclude that the proposed amendments do not meet the requirements of a necessary amendment under subsection 86(11) of the *Patent Rules*.

CONCLUSIONS

[70] We have determined that:

- claims 1 to 27, 29 to 33 and 36 to 42 are directed to patentable subject-matter falling within the definition of “invention” in section 2 of the *Patent Act*;
- the subject-matter of claims 28, 30 to 33, 35, 37, 41 and 42 is novel in view of D1 and complies with paragraph 28.2(1)(a) of the *Patent Act*;
- the subject-matter of claims 34, and 38 to 40 is anticipated by D1, contrary to paragraph 28.2(1)(a) of the *Patent Act*;
- the subject-matter of claims 1 to 42 would have been obvious to POSITA as of the relevant date, in view of either D1 and the CGK or D1, D2 and the CGK, contrary to section 28.3 of the *Patent Act*;
- claims 28 to 41 suffer from overbreadth and the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims; and
- claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

[71] Further, it is our view that the proposed claims submitted with the Response to the Final Action would not overcome the obviousness defect and/or otherwise introduce new defects. Therefore, the proposed claims are not considered a necessary amendment for compliance with the *Patent Act* and *Patent Rules* as

required by subsection 86(11) of the *Patent Rules*.

RECOMMENDATION OF THE BOARD

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

- the subject-matter of claims 34, and 38 to 40 is anticipated, contrary to paragraph 28.2(1)(a) of the *Patent Act*;
- the subject-matter of claims 1 to 42 is obvious, contrary to section 28.3 of the *Patent Act*;
- claims 28 to 41 suffer from overbreadth and the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims; and
- claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

Marcel Brisebois	Mary Murphy	Christine Teixeira
Member	Member	Member

DECISION OF THE COMMISSIONER

[73] I concur with the findings of the Board and its recommendation to refuse the application on the grounds that:

- the subject-matter of claims 34, and 38 to 40 is anticipated, contrary to paragraph 28.2(1)(a) of the *Patent Act*;
- the subject-matter of claims 1 to 42 is obvious, contrary to section 28.3 of the *Patent Act*;
- claims 28 to 41 suffer from overbreadth and the specification does not comply with the requirements of subsection 27(3) of the *Patent Act* with respect to the subject-matter of these claims; and
- claims 12, 13, 24 and 25 fail to define distinctly the subject-matter of the invention, contrary to subsection 27(4) of the *Patent Act*.

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

Konstantinos Georgaras
Commissioner of Patents

Dated at Gatineau, Quebec

this 2nd day of March, 2023.