Commissioner's Decision #1489

Décision du Commissaire n^{o} 1489

TOPICS: C00: Disclosure (Adequacy or Deficiency of Description); G00 (Utility)

SUJETS: C00 Divulgation (Caractère adéquat ou inadéquat de la description); G00 (Utilité)

Application No: 2,709,771

Demande n^{o}: 2 709 771

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,709,771 having been rejected under subsection 30(3) of the *Patent Rules*, has consequently been reviewed in accordance with paragraph 30(6)(*c*) of the *Patent Rules*. The recommendation of the Patent Appeal Board and the decision of the Commissioner are to notify the Applicant that certain claims in the application must be deleted, failing which the application will be refused.

Agent for the Applicant

DENNISON ASSOCIATES
301-133 Richmond Street West
Toronto, Ontario
M5H 2L7

INTRODUCTION

[1] This recommendation deals with a review of the rejection of patent application number 2,709,771 entitled "Compositions and methods for diagnosis and treatment of disorders involving angiogenesis." The Applicant is Genentech, Inc.

[2] Of the 26 claims in the subject application, claims 1-24 covering the use of certain antagonistic antibodies to inhibit the formation of new blood vessels in a mammal were rejected during examination, notionally for lack of support under section 84 of the *Patent Rules* and insufficient disclosure under subsection 27(3) of the *Patent Act*. A review of the rejected application has therefore been conducted by the Patent Appeal Board ("the Board") pursuant to paragraph 30(6)(*c*) of the *Patent Rules*.

[3] For the reasons that follow, we recommend that the Applicant be notified that claims 1-24 currently on file must be deleted, failing which the application should be refused.

BACKGROUND

The application

[4] Broadly speaking, the matter before us concerns antibodies. Antibodies are large polypeptides produced by the immune system in response to exposure to foreign molecules (antigens). They typically specifically bind to the foreign molecule and thereby target it for eventual elimination. Antibodies, by virtue of their size and binding capabilities, may also stimulate or inhibit a biological activity that may be carried by a target antigen, e.g., a polypeptide involved in some cellular or physiological function.

[5] The present case is concerned with certain antibodies that purportedly inhibit angiogenesis, the physiological process that generates new blood vessels.

Unregulated angiogenesis plays a role in a wide range of disorders, including: cardiovascular disease, cancer, rheumatoid arthritis, age-related macular degeneration, psoriasis and diabetic retinopathy. Inhibition of unregulated angiogenesis therefore represents a laudable goal.

[6] The subject application describes a considerable number of polypeptides, each asserted by the inventors to be associated with angiogenesis. The claims at issue concern only one such polypeptide, termed "PRO1449." Although the PRO1449 polypeptide appears to have been known per se before the date of filing, its association with angiogenesis was apparently not. By virtue of that association, the PRO1449 polypeptide represents an attractive target for inhibition of unregulated angiogenesis. The inventors accordingly claim that antagonistic antibodies reactive with the target PRO1449 polypeptide can be used to inhibit angiogenesis in a mammal.

Procedural history

[7] The subject application is a divisional application of parent application number 2,412,211, now irrevocably abandoned. The Applicant requested that the subject-matter of the subject application be divided from the parent application on July 21, 2010. However, as a divisional application, the subject application carries, as its actual filing date, the same filing date as its parent: June 20, 2001.

[8] The application currently contains 26 claims, of which claims 1-24 were rejected in a Final Action ("FA") dated December 8, 2015. The claims were rejected for lack of "support", an issued framed in the FA as non-compliance with section 84 of the *Patent Rules* and subsection 27(3) of the *Patent Act*. On June 8, 2016 the Applicant submitted a response to the FA ("R-FA"). Since the Examiner was not satisfied that the application was in condition for allowance, a Summary of Reasons ("SOR") was prepared and the matter referred to the Board for review.

[9] The present panel subsequently undertook a Preliminary Review ("PR") of the application and informed the Applicant of its preliminary views in a letter dated August 9, 2018. At that time, the Applicant was also offered an opportunity to be heard and invited to provide submissions addressing the Board's comments outlined in the PR letter. No submissions were received in response to the PR letter.

[10] An oral hearing was held on November 23, 2018 at which time the Applicant advanced oral arguments in favour of patentability of the claims at issue. Additional written submissions and supporting documentation were provided by the Applicant on December 3, 2018. No claim amendments were proposed.

ISSUES

[11] Although it is generally accepted that antibodies that simply bind to a given polypeptide can be routinely prepared and adequately described, the present case considers whether the same applies to antagonistic antibodies that bind a particular polypeptide and inhibit the physiological process of angiogenesis. In that regard, the FA and the R-FA appear to discuss one substantive issue in relation to claims 1-24 on file at the time the FA was written: "support" for the claimed subject-matter; more particularly, whether the specification provides adequate support for the antagonistic anti-PRO1449 antibodies mentioned in the claims. The issue is framed in the FA as non-compliance with section 84 of the *Patent Rules* as well as subsection 27(3) of the *Patent Act*.

[12] Although there does not appear to be a formal objection in the FA under section 2 of the *Patent Act* for lack of utility, the phrasing of the arguments in the FA and R-FA suggested to us that there may be a concern in that regard. For the sake of completeness, we addressed that issue as well at the PR stage and expressed our view, as discussed below, that the application is compliant in that respect.

[13] However, considered as a separate issue, it was our preliminary view that the subject-matter of the rejected claims— to the extent they concern antagonistic anti-PRO1449 antibodies—would be considered by the skilled person as neither being correctly and fully described nor enabled by the specification, contrary to paragraphs (*a*) and (*b*) of subsection 27(3) of the *Patent Act*. We considered any attendant issue of non-compliance with section 84 of the Rules to be subsumed within that analysis.

[14] At the hearing and in its post-hearing written submissions, the Applicant argued the application was compliant with paragraph 27(3)(*b*) of the Act because the antagonistic anti-PRO1449 antibodies mentioned in the claims are fully enabled by the specification, bearing in mind the identity of the skilled person and the common general knowledge they would possess as of the filing date of the application. Documentation was also provided in support of that argument. No arguments were advanced in relation to compliance with paragraph 27(3)(*a*) of the Act.

[15] Having heard from the Applicant and considered its latest submissions, what now follows is our final review of the outstanding issues, namely compliance with paragraphs 27(3)(*a*) and 27(3)(*b*) of the Act.

LEGAL PRINCIPLES AND PATENT OFFICE PRACTICE

"Support" under section 84 of the Rules and the disclosure requirements of subsection 27(3) of the Act

[16] Although the FA relies on non-compliance with section 84 of the Rules as one of the grounds for rejection, we note that there is little judicial guidance on the requirements of that section, or any of its predecessor equivalents. Section 84 of the *Patent Rules* simply states that "The claims shall be clear and concise and shall be fully supported by the description independently of any document referred to in the description." Subsections 11.05 and 11.05.02 of the *Manual of*

Patent Office Practice (MOPOP) provides general guidance on compliance with Rule 84 but does not appear to include the disclosure requirements of subsection 27(3) of the Act as relevant considerations:

> A claim must be fully supported by the description as required by section 84 of the *Patent Rules*. All the characteristics of the embodiment of the invention which are set forth in the claim must be fully set forth in the description (Section 84 of the *Patent Rules*). However, since the claims included in the application at the time of filing are part of the specification (see definition of specification in section 2 of the *Patent Rules*), any matter in the originally filed claims that was not included in the description as filed may be added to the description.
>
> A claim is objected to for lack of support by the description if the terms used in the claim are not used in the description and cannot be clearly inferred from the description. Terms used in the claims and in the description must be used in the same sense.
> …
> A claim may be as narrow as the applicant wishes within the scope of the invention disclosed. It must not, however, be broader than the invention as described or supported by the description. Furthermore, a claim will fail if, in addition to claiming what is new and useful, it also claims something that is old or useless (Minerals Separation v. Noranda Mines 12 C.P.R. 99; 12 C.P.R. 182; 15 C.P.R. 133).
>
> Each claim must be read giving its words the meaning and scope which they normally have in the relevant art, unless in particular cases the description gives the words a special meaning by explicit definition. If a claim covers subject matter outside the scope of the described invention, it should be objected to for failing to satisfy the provisions of section 84 of the *Patent Rules*.

[17] A review of the prosecution indicates that the question of "support" in the present case should be addressed as a matter of non-compliance with subsection 27(3) of the Act, a ground also identified in the FA for which a wealth of jurisprudence exists. Any concern over non-compliance with section 84 of the Rules we take as being subsumed within that inquiry. The possibility that the claimed subject-matter lacks utility has been addressed as a separate issue, as the case law instructs it should be.

[18] Paragraphs 27(3)(*a*) and (*b*) of the Act outline certain disclosure requirements and demand, respectively, that the specification of a patent (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;
> . . .

[19] A determination of whether the specification complies with paragraphs 27(3)(*a*) and 27(3)(*b*) of the Act requires that three questions be answered: What is the invention? How does it work? Having only the specification, can the person of skill in the art 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 ["*Teva*"] and *Consolboard v MacMillan Bloedel* (1981), 56 CPR 2d 145 (SCC) ["*Consolboard*"]). Although the common general knowledge can be relied upon, an affirmative answer to the third question requires that the person of skill in the art 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.

[20] The relevant date for assessing compliance with subsection 27(3) of the Act is the filing date (*Teva*, *supra*, at para 90; *Idenix Pharmaceutical Inc v Gilead*

Pharmasset LLC, 2017 FCA 161 at paras 46-51), which in this case is June 20, 2001.

[21] We note that the Applicant has argued in the R-FA, with supporting reference to *Monsanto Co v Commissioner of Patents* (1972), 42 CPR 2d 161 ["*Monsanto*"], that "there is clearly no requirement in Canadian law for a patentee to provide a specific example of every aspect of an invention." We agree. However, although exemplification of all aspects of an invention is not a requirement, in our view, an inventor's disclosure of working examples of the invention is one of many valid considerations, including the common general knowledge, that can be taken into account. Although not determinative on their own, examples can provide meaningful, specific guidance to the skilled person and indicate that working embodiments can indeed be successfully produced.

Utility

[22] Section 2 of the *Patent Act* indicates that the subject-matter of a claim must be "useful": "*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."

[23] In *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36 at paras 54-55 ["*AstraZeneca*"], the Supreme Court of Canada stated the approach to be taken when determining whether a claimed invention meets the utility requirement:

> To determine whether a patent discloses an invention with sufficient utility under s. 2, courts should undertake the following analysis. First, courts must identify the subject-matter of the invention as claimed in the patent. Second, courts must ask whether that subject-matter is useful — is it capable of a practical purpose (i.e. an actual result)?

> The Act does not prescribe the degree or quantum of usefulness required, or that every potential use be realized — a scintilla of utility will do. A single use related to the nature of the subject-matter is sufficient, and the utility must be established by either demonstration or sound prediction as of the filing date (*AZT*, at para. 56).

[24] Thus, utility must be established either by demonstration or "sound prediction" as of the Canadian filing date: *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 ("*AZT*").

[25] The soundness of a prediction is a question of fact and cannot be supported by evidence and knowledge that only became available after the filing date (*AZT*, at para 56). A sound prediction has three elements (*AZT*, at para 70):

1) there must be a factual basis for the prediction;
2) the inventor must have at the date of the patent application an articulable and "sound" line of reasoning from which the desired result can be inferred from the factual basis; and
3) there must be proper disclosure of the factual basis and line of reasoning.

[26] These elements are assessed from the perspective of the person of ordinary skill in the art to whom the patent application is directed, taking into account their common general knowledge. With the exception of the common general knowledge, the factual basis and the line of reasoning must be included in the application: *Bell Helicopter Textron Canada Limitée v Eurocopter, société par actions simplifiée*, 2013 FCA 219, at paras 152 and 153.

[27] Although a prediction does not need to amount to a certainty to be sound, there must be a *prima facie* reasonable inference of utility: *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119, at para 55; *Gilead Sciences, Inc v Idenix Pharmaceuticals Inc*, 2015 FC 1156, at para 251.

[28] In *Re Application of Genentech Inc*, CD 1314, the Commissioner concluded that claims to antibodies therapeutically useful as anti-inflammatory agents failed the test for a sound prediction of utility. Although it was accepted that antibodies binding to particular novel target proteins could be made and claimed in a per se manner, it was not accepted that the information in the specification provided a factual basis sufficient for the skilled person to conclude that the antibodies would be therapeutically useful. Subsection 17.07.05 of MOPOP is to the same effect:

> In cases where the utility requires the antibody to possess not only binding capacity to the target antigen but also functional activities, such as antagonist (i.e., blocking), agonist (i.e., activating) or neutralizing activity, the description would likely require more than a disclosure of the binding capacity to the target antigen to establish utility.

[29] In addition to an analysis taken from the perspective of utility, the case law discussed immediately below indicates that it remains open to *separately* ask whether the disclosure requirements of subsection 27(3) of the Act have been met, particularly to the extent that the claims rely on antibodies with certain properties.

Utility under section 2 of the Act and the disclosure requirements of subsection 27(3) of the Act are separate considerations

[30] Since both the Applicant and the Examiner have discussed the concept of a "sound prediction" of utility under section 2 of the Act in a manner seemingly interwoven with the disclosure requirements of subsection 27(3) of the Act, it warrants clarifying that the Supreme Court has repeatedly indicated the two concepts are separate and distinct. In *AstraZeneca*, the Supreme Court, quoting *Consolboard*, most recently reiterated as much at para 43:

> There is a difference between the requirement in s. 2 that an invention be "useful" and the requirement to disclose an invention's "operation or use" as per s. 27(3). As explained by Dickson J. (as he then was) in *Consolboard*, the former is a "condition precedent to an invention" and

> the latter a "disclosure requirement, independent of the first": [quotation omitted]

[31] Subsection 12.04.03*c* of MOPOP (revised after the date of the FA) similarly states that the "disclosure requirement within sound prediction analysis is tied to the requirement that an invention have utility as set out in section 2 of the *Patent Act*; it does not pertain to the sufficiency of disclosure requirement set out in subsection 27(3) of the *Patent Act*." Subsection 12.05 of MOPOP also cautions against confusing the two concepts in office actions.

[32] With this in mind, we again note that the Applicant has relied on *Monsanto* in the R-FA as informative of the requirements of subsection 27(3) of the Act. However, we are not convinced that the decision is of assistance to the Applicant because *Monsanto* primarily concerned the doctrine of sound prediction under section 2, not the separate disclosure requirements of subsection 27(3) of the Act. In the words of the Supreme Court, *Monsanto* related to "a patent that included claims to numerous chemical compounds to inhibit premature vulcanization of rubber, but only three of the claimed compounds had actually been prepared and tested before the date the application was filed" (*AZT*, para 58). In our view, the decision does not stand for the proposition that an invention whose utility has been soundly predicted necessarily satisfies the separate requirements of subsection 27(3) of the Act. We would say the same is true in the case of *Burton Parsons Chemical Inc v Hewlett-Packard (Canada) Ltd* (1975), 17 CPR (2d) 97 which the Applicant has also cited in the R-FA (page 13, first paragraph) in support of the patentability of the claims at issue. That case appears to concern the breadth of claims, again considered as a matter of utility, not the requirements to correctly and fully describe the invention and enable its production and use.

ANALYSIS

The claims

[33] There are 26 claims on file, of which claims 1-24 stand rejected. They concern antagonistic anti-PRO1449 antibodies for use in inhibiting angiogenesis in a mammal. The PRO1449 polypeptide and parts thereof are defined in the claims by reference to an amino acid sequence, SEQ ID NO. 374, as well as through reference to a DNA molecule that encodes it, deposited under ATCC accession number 203243. Claim 1 is representative of the claims at issue:

> An antagonist of a polypeptide having:
>
> (a) the amino acid sequence shown in Figure 374 (SEQ ID NO:374);
> (b) the amino acid sequence encoded by the full-length coding sequence of the DNA deposited under ATCC accession number 203243;
> (c) the amino acid sequence of the polypeptide shown in Figure 374 (SEQ ID NO:374), lacking its associated signal peptide;
> (d) the amino acid sequence of an extracellular domain of the polypeptide shown in Figure 374 (SEQ ID N0:374), with its associated signal peptide; or
> (e) the amino acid sequence of an extracellular domain of the polypeptide shown in Figure 374 (SEQ ID N0:374), lacking its associated signal peptide,
>
> wherein the antagonist is an antagonist antibody which binds to an amino acid sequence of (a) - (e) of said polypeptide and inhibits the ability of said polypeptide to induce angiogenesis for use in inhibiting angiogenesis in a mammal.

[34] For reasons that will become apparent in our analysis below, it warrants mentioning that parts (a) and (b) of the claim, and to a lesser extent part (c), refer to virtually the entirety of the PRO1449 polypeptide. The claim thereby indicates to the person of skill in the art (whose nature is more fully considered below) that

antibodies supposedly reactive with various regions of the whole polypeptide, including portions that appear to be inaccessible to antibodies, are within the scope of the claim. By contrast, parts (d) and (e) inform the skilled person that these parts of the claim are appropriately limited to antibodies reactive only with the polypeptide's extracellular domain, a region presumably outwardly exposed on or near the cell's surface and therefore more readily available for binding to an antibody, in line with the skilled person's genuine understanding of an antibody's expected binding behaviour.

[35] Again taken from the perspective of the skilled person, it is also notable that the claim ends with an indication that the antagonistic anti-PRO1449 antibodies are "*for use* in inhibiting angiogenesis *in a mammal*", meaning the Applicant makes no claim to antagonistic antibodies per se. Although the claimed invention is thus limited to their "use" in inhibiting angiogenesis, such antibodies still must do so in a mammal, i.e., *in vivo*.

Enablement under paragraph 27(3)(*b*) of the Act

The person of ordinary skill in the art and their relevant common general knowledge

[36] Although the identity of the skilled person and their common general knowledge bear on all issues discussed in this review, in this case, the particular question of compliance with paragraph 27(3)(*b*) of the Act hinges to a great extent on a balanced assessment of the two considerations. Bearing in mind that the specification provides limited explicit guidance and does not disclose the actual preparation of the antibodies of the claims, the ordinary skilled person must rely on their common general knowledge to supplement the specification and thereby produce such antibodies without exercising inventive effort or engaging in undue experimentation.

[37] Production of antagonistic anti-PRO1449 antibodies can be said to involve two aspects:

1) A first aspect that involves the production and *in vitro* screening of antibodies that simply bind to the PRO1449 polypeptide; and

2) A second aspect that involves further screening of those antibodies that bind the PRO1449 polypeptide to identify any that may be antagonistic and potentially useful for inhibiting angiogenesis in a mammal, i.e., *in vivo*.

[38] There is no dispute regarding the first aspect since, as outlined below, we agree with the Applicant that it would entail the skilled person applying their common general knowledge to the PRO1449 polypeptide. We do not agree, however, that the same would be true of the second aspect.

The Board's preliminary views on the skilled person and the common general knowledge

[39] In the PR letter, we first identified the person of ordinary skill in the art and the common general knowledge they would be expected to possess. We agreed with the Applicant's submission that the skilled person would be a composite of "a molecular immunologist with experience in monoclonal antibody production, immunoassays and a clinical immunologist specializing in angiogenesis" (R-FA, page 16, last paragraph). Such a person was said to possess the following common general knowledge:

- knowledge of commonplace methods to prepare and screen antibodies that are capable of binding to a given polypeptide; and
- knowledge that angiogenesis:
    - is a complex process that occurs primarily during embryonic development;
    - occurs on a limited basis in adult mammals, e.g., during hair growth and wound healing; and
    - when left unregulated, is responsible for a number of disorders.

[40] We also agreed with the Applicant's argument in relation to the first point, i.e., that as of the relevant date, "the preparation of monoclonal antibodies employed routine workshop techniques and did not require the exercise of inventive ingenuity" (R-FA, page 17). A number of references reflective of the common general knowledge were relied upon in support of that submission, including:

- *Monoclonal Antibodies: Basic Principles, Experimental and Clinical Applications in Endocrinology*, Editors, G. Forti, et al., Raven Press, 1986 [the "*Forti*" textbook];
- *Monoclonal Antibodies*, Editors, J. Moulds and S. Masouredis, American Association of Blood Banks, 1989;
- *Monoclonal Antibodies*, Editors, J. H. Peters and H. Baumgarten, Springer-Verlag, 1992;
- *A Practical Guide to Monoclonal Antibodies*, J. Eryl Liddell and A. Cryer, John Wiley & Sons, 1991;
- *Immunohistochemistry II*, Edited by A. C. Cuello, John Wiley & Sons, 1993 [the "*Cuello*" textbook]; and
- *Handbook of Immunochemistry*, Miroslav Ferencik, Chapman & Hall, 1993.

[41] A number of other apparently commonplace references discussed in the specification were also considered, including:

- *Monoclonal Antibodies: A Manual of Techniques*, H. Zola, CRC Press, Inc., 1987 (referred to on page 87, lines 34-35); and
- G. Kohler & C. Milstein, *Continuous cultures of fused cells secreting antibody of predefined specificity*, Nature, 256:495-497, 1975 (referred to on page 111, line 32).

[42] In the PR letter, we therefore agreed that the record supports the conclusion that the primary aspect of producing the antibodies of the claims involving the production and *in vitro* screening of antibodies that specifically bind to the PRO1449 polypeptide would be a matter of routine. We were not satisfied, however, that the record supports the same conclusion in respect of the second aspect that further involves *in vivo* screening to identify antibodies that may also be antagonistic and potentially useful for inhibiting angiogenesis in a mammal. It was our preliminary view that such antibodies would be regarded by the skilled person as special or remarkable in nature, therefore requiring additional disclosure concerning their screening and identification.

[43] In the case of antibodies that antagonize and inhibit the *in vivo* biological activity of a polypeptide that appears to function as part of a complex angiogenesis mechanism, we were not satisfied that the necessary and particular screening steps were commonplace and routine. It appeared to us that methods to identify such antibodies could not be satisfactorily described to the skilled person in general terms. Rather, the required screening methods would appear to the skilled person to be specialized in nature and accordingly would need to be described to that person in specific terms that align with the eventual antagonistic and inhibitory application of the antibodies "in a mammal", as the claims explicitly require. In that regard, we noted that the references provided by the Applicant indicate as much:

> The results show that it is relatively easy to obtain antibody-producing hybridomas and that the properties of the purified antibodies depend strongly on the screening method. The ideal situation is, therefore, to use a screening procedure which is as close as possible to the actual assay method for which the antibody is intended. [page 8 of the *Forti* textbook]
>
> For the final selection of clones, highly sensitive assay systems are required and should be developed before the subcloning procedures are

> performed. It is essential that these tests are performed in agreement with the intended application of monoclonal antibodies, e.g. in tissue sections if they are wanted for immunohistochemistry. [page 117 of the *Cuello* textbook; emphasis added]

[44] We therefore concluded in our PR letter that the production of anti-PRO1449 antibodies of the type mentioned in the claims which inhibit angiogenesis in a mammal was not entirely a matter of the application of the common general knowledge to that particular polypeptide.

The Applicant's latest submissions on the skilled person and the common general knowledge

[45] At the oral hearing and in its latest submissions of December 3, 2018, the Applicant pointed to additional documentation regarding the nature of the skilled person and their common general knowledge, all of which we agree is relevant. However, we disagree with the Applicant's suggestion that simply further elaborating on the common general knowledge as it exists in this case necessarily means producing the antibodies of the claims would have been a matter of routine.

[46] In its latest submissions, the Applicant indicated that the skilled person, considered as a clinical immunologist specializing in angiogenesis, would be familiar with other polypeptides well known to be associated with angiogenesis, notably, a polypeptide known as "vascular endothelial growth factor" (VEGF), its receptors, as well as antibodies reactive with these polypeptides. These molecules are discussed in the Background portion of the specification (page 7, lines 15-21) with reference to several scientific articles and patent documents:

> Anti-VEGF neutralizing antibodies suppress the growth of a variety of human tumor cell lines in nude mice (Kim *et al*., Nature, 362: 841-844 (1993); Warren *et al*., J. Clin. Invest., 95: 1789-1797 (1995); Borgström *et al*., Cancer Res., 56: 4032-4039 (1996); Melnyk *et al*., Cancer Res., 56: 921-924 (1996)) and also inhibit intraocular angiogenesis in models

> of ischemic retinal disorders. Adamis *et al*., Arch. Ophthalmol., 114: 66-71 (1996). Therefore, anti-VEGF monoclonal antibodies or other inhibitors of VEGF action are promising candidates for the treatment of solid tumors and various intraocular neovascular disorders. Such antibodies are described, for example, in EP 817,648 published Jan. 14, 1998 and in WO98/45331 and WO98/45332 both published Oct. 15, 1998.

[47] Of these references, the article by Kim et al. (Nature, 362: 841-844, 1993 - "*Kim 1993*") stands out as being an early report of an anti-angiogenesis antibody termed "A4.6.1." An earlier article by the same group of researchers reported more preliminary results on the same antibody (see Kim et al., Growth Factors, vol. 7: 53-64, 1992 – "*Kim 1992*"). Certain *in vivo* assays and tumour cell lines used to identify the A4.6.1 antibody as anti-angiogenic are described in both articles.

[48] The Applicant also referred us to a number of books and monographs reflective of the common general knowledge in the field of angiogenesis, including assays that that were known as of the relevant date for testing for angiogenesis:

- *Angiogenesis in Health and Disease, Basic Mechanisms and Clinical Applications*, Edited by G.M. Ruubanyi, Marcel Dekker Inc., 2000;
- *Advances in Organic Biology, Coronary Angiogenesis*, Volume 7, Edited by E. Bittar & K. Rakusan, JAI Press Inc., 1999 ["*Bittar & Rakusan*"];
- *Methods in Molecular Medicine, Angiogenesis Protocols*, volume 46, Edited by J. C. Murray, Humana Press, 2001 ["*Angiogenesis Protocols*"]; and
- *Advances in Experimental Medicine and Biology, Angiogenesis from the Molecular to Integrative Pharmacology*, Volume 476, Edited by M.E. Maragoudakis, Kluwer Academic/ Plenum Publishers, 2000.

[49] Since the skilled person may consider a protein's location (i.e., membrane-bound versus soluble) relevant to preparation of antagonistic antibodies, there was also

discussion at the oral hearing regarding antagonistic antibodies to VEGF, a soluble protein, and whether there was any teaching in the specification regarding membrane-bound proteins, which the PRO1449 polypeptide apparently is. The Applicant accordingly located and cited three articles in its submissions of December 3, 2018 to establish that an antibody, termed "DC101", that binds to the membrane-bound receptor molecule for VEGF, and which inhibits tumour angiogenesis, was also commonly known:

- M. Prewett et al., *Anti-vascular Endothelial Growth Factor Receptor (Fetal Liver Kinase 1) Monoclonal Antibody Inhibits Tumor Angiogenesis and Growth of Several Mouse and Human Tumors*, Cancer Research, 59:5209-5218, 1999 ["*Prewett*"];
- L. Angelov et al., *Inhibition of Angiogenesis by Blocking Activation of the Vascular Endothelial Growth Factor Receptor 2 Leads to Decreased Growth of Neurogenic Sarcomas*, Cancer Research, 59, 5536-5541, 1999; and
- G. McMahon, *VEGF Receptor Signaling in Tumor Angiogenesis*, The Oncologist, 2000: 5 (supplement 1) 3-10.

[50] Having reviewed the documentation most recently identified by the Applicant, the common general knowledge can therefore be further detailed as follows:

- The VEGF polypeptide was well-known to be associated with angiogenesis, was well characterized, and was known to have a number of biological activities, such as promoting the growth of vascular endothelial cells and acting as a permeability factor (see for example *Bittar & Rakusan*, pages 25-57);
- VEGF receptors had been identified and characterized (see for example *Bittar & Rakusan*, pages 25-57);
- Two antagonistic anti-angiogenic antibodies, both associated with VEGF, had been identified, tested and shown to have activity: the A4.6.1 antibody

that binds to VEGF itself (see *Kim 1992* and *Kim 1993*); and, the DC101 antibody that binds to a VEGF receptor (see *Prewett*); and

- A variety of *in vitro* and *in vivo* angiogenesis assays were known (see for example *Angiogenesis Protocols*) and *in vivo* assays had been used to identify the two known antagonistic antibodies.

Conclusions drawn from the common general knowledge

[51] In its submissions of December 3, 2018, the Applicant suggested on the basis of the documents provided that, as of the relevant date, the common general knowledge had advanced to the point that the second aspect of producing antibodies of the type mentioned in the claims, like the first aspect, was well known and a matter of routine:

> It is well known in the art that whether a specific example of an antagonistic antibody was provided in the application or if it was only based on sound prediction, the effort of one of skill in the art to produce the invention would be the same. In either case, the animal would have to be immunized, the spleens harvested and the cell fusion undertaken. The resultant clones would be distributed in multi-cell plates to grow. The cell culture fluid in each of the wells would then be screened first for binding antibodies to the relevant polypeptide, in this case PR01449. Those wells which have significant binding would then be screened for antagonistic antibody activity using one of the assays as known in the common general knowledge as set out in the art cited above, in particular *Angiogenesis Protocols*. Those wells which demonstrated antagonistic antibody activity would be sub-cloned to arrive at the desired antibody. These are all standard workshop techniques that have been practiced for decades by those of skill in the art and do not require undue experimentation or the practice of inventive ingenuity. [submissions of December 3, 2018, page 21, last paragraph; emphasis added]

[52] We disagree. In our view, the existence of two antagonistic anti-angiogenesis antibodies, directed either to the well-characterized VEGF polypeptide or its receptor, does not establish that the common general knowledge had advanced as of the relevant date to the point that it would have been a matter of routine for the skilled person to produce antibodies that bind to other targets and which would have similar inhibitory properties.

[53] In the cases of the known antibodies, it appears that considerable work had been done by researchers in the course of their identification, including fully characterizing the biological activities of their targets, followed by production of antibodies that simply bound to them. Ultimately, certain known *in vivo* angiogenesis screening assays were used by researchers to identify some antibodies as anti-angiogenic. However, the use of *in vivo* assays for the screening of anti-angiogenic antibodies does not appear to have been commonplace, given that only two such antibodies had been identified.

[54] The documents of record therefore indicate: (1) that it was possible for researchers to produce and identify antagonistic anti-angiogenesis antibodies to a well-characterized angiogenesis target, or one of its receptors, by undertaking experimentation and screening; and, (2) that the history of that particular work was commonly known. In our view, the documents do not indicate that it was a matter of routine for the *ordinary* skilled person, devoid of insight and dispossessed of the inventive faculty, to replicate the success of the earlier researchers in the case of some other putative target polypeptide simply identified as being associated with angiogenesis.

Conclusion on enablement

[55] For the reasons set out below, we are of the opinion that the antibodies of claims 1-24 are not enabled by the specification, contrary to paragraph 27(3)(*b*) of the Act. More particularly, having heard from the Applicant and considered its latest submissions, we conclude that the ordinary skilled person could not have relied on

their common general knowledge and the limited direction provided by the specification to produce the antibodies of the claims. Producing such antibodies would appear to have required the exercise of inventive effort and/or the undertaking of undue experimentation.

The PR letter

[56] In the PR letter, we expressed our preliminary view that the record, as it was at the time, did not support the conclusion that claims 1-24 are enabled by the specification, contrary to paragraph 27(3)(*b*) of the Act. We formed that opinion for a number of reasons:

1) the reasons provided and the conclusions reached in the FA appeared reasonable;
2) although the skilled person could rely on their common general knowledge to produce antibodies that simply bound the PRO1449 polypeptide, the same was not true when it came to identifying antagonistic anti-PRO1449 antibodies that would be capable of inhibiting angiogenesis *in vivo*;
3) the specification does not provide teachings particular to the production of the antibodies of the claims and the example provided in the specification dealing particularly with the PRO1449 polypeptide does not provide guidance on antagonistic antibody production;
4) the Applicant's later filed application, which the Applicant submitted as evidence of enablement, discloses details of antibody screening assays performed *in vitro* and *in vivo* which are absent from the present specification and which appear to be of the type the skilled person would regard as instructive and enabling of the claimed subject-matter; and
5) the claims broadly encompass antagonistic antibodies supposedly reactive with seemingly any portion of the polypeptide, including portions that appear to be inaccessible *in vivo*.

[57] We will deal with each point in turn.

[58] Point (1) acknowledges that the reasons and conclusions expressed in the FA appeared reasonable:

> In conclusion, as the present application does not identify any antagonist antibody of PR01449, the skilled person would have to perform undue experimentation to find antibodies that can antagonize PR01449. Moreover, undue experimentation is also required from the skilled person to determine, among all possible antagonist antibodies found, which ones are actually able to efficiently inhibit angiogenesis in a mammal. In view of this, the examiner considers that the claimed use of any PR01449 antagonist antibody for inhibiting angiogenesis does not have support in the description.
>
> In view of this, it follows that the description does not comply with subsection 27(3) of the *Patent Act*. [FA, page 3]

[59] Turning to point (2), concerning the common general knowledge, we acknowledged the Applicant's submission found in the R-FA (page 23, second full paragraph) that "one of ordinary skill in the art utilizing their common general knowledge as well as the teaching of the specification could readily produce the antagonistic antibodies as claimed without the exercise of inventive ingenuity or undue experimentation." In that regard, we noted the Applicant's reliance on pages 9-10, 50, 84-89, 95-96, 111-119, 138, 141-143 and 150 of the specification, as well as Examples 11 and 24, which the Applicant argued would provide the skilled person with clear direction and teaching on the production, screening and use of antagonistic anti-PRO1449 antibodies:

> The guidance which would be required in the present case to those of skill in the art based upon the direction given in the above noted cases would be directed to the screening of the hybridoma clone for the desired antibody. In the present application, the applicant has given clear direction and teaching to those of skill in the art on the production,

> screening technique and use of the antagonistic antibodies on pages 9-10, 50, 84-89, 95-96, 111-119, 138,141-143 and 150 [R-FA, page 20, second paragraph]
>
> . . .
>
> To obtain antibodies that specifically bind to PR01449, a skilled artisan could use a variety of approaches taught by the present specification, including hybridoma methods, as described in Example 11. To identify antagonist antibodies, a skilled artisan could use a screening assay, for example, an assay utilizing the chicken embryonic eye model described in Example 24. Such a task would not be unduly burdensome, because only antibodies that specifically bind to PR01449 would be screened, and positive results obtained in this assay would provide factual evidence to a skilled artisan that the identified antagonist antibody would inhibit angiogenesis in a mammal. Therefore, based on the guidance provided by the present specification as filed, for example, at pages 51-54, 94-97, 111-119, and in Example 11, a skilled artisan could readily produce antagonist antibodies of PR01449 for use in inhibiting angiogenesis in a mammal, as is presently claimed. [R-FA, page 21, first full paragraph]

[60] We then reviewed the entirety of the specification, including the passages of the specification cited by the Applicant. We agreed that the passages referred to by the Applicant reflect commonly known techniques that could be used by the skilled person to develop antibodies that simply bind to the PRO1449 polypeptide, i.e., as a first aspect of antibody production. However, we did not agree that the passages accurately reflected what would be expected in terms of the ensuing second aspect involving additional screening to identify those antibodies that may exhibit anti-angiogenic properties *in vivo*.

[61] For instance, pages 89-90 appear to simply describe commonplace *in vitro* antibody binding studies, while pages 111-119 and Example 11 similarly appear to reflect the common general knowledge as it relates to antibody production. The passages thus appear generic in their description and seem to apply to any one of

the myriad of purported angiogenic "PRO" polypeptides disclosed. The cited passages therefore did not appear to be particularly informative of the production of the anti-PRO1449 antibodies of the claims. Furthermore, the production of the anti-PRO1449 antibodies of the claims which inhibit angiogenesis *in vivo* did not appear to be entirely a matter of the application of the common general knowledge to that particular polypeptide. In addition to the existing common general knowledge, it appeared that additional, specific, guidance on the production of antagonistic anti-PRO1449 antibodies would be required of the specification since the common general knowledge had not sufficiently advanced.

[62] Regarding point (3), which deals with the teachings particular to the PRO1449 polypeptide, we noted that the specification is limited to six sentences in Example 24. That example first discusses gene expression studies whose results the skilled person would arguably regard as consistent with the notion that PRO1449 is associated with angiogenesis. Then described are studies done using a chicken embryo eyeball model that the Applicant argued is an example of an *in vivo* screening assay that could be used to identify the antibodies of the claims. We disagreed.

[63] It was our view that the single sentence of Example 24 to which the Applicant refers would not be regarded by the skilled person as a screening assay for antagonistic anti-PRO1449 antibodies that inhibit angiogenesis in a mammal. It describes the injection of a DNA molecule encoding the murine orthologue of PRO1449 into the eyeball of a chicken embryo followed by observation of the induction of angiogenesis:

> Following electroporation of the mouse orthologue of PR01449 into the choroid layer in the eyes of chicken embryos, new vessel formation was observed in the electroporated eye (top right), but not in the control side from the same embryo (top left), or an embryo that was electroporated with a control cDNA (bottom right) (Figure 377).

[64] Notably absent from the passage is any mention of antibody screening or inhibition of angiogenesis.

[65] In the PR letter we further acknowledged the Applicant's submission in the R-FA that "the Examiner is applying an incorrect and unreasonable standard by apparently requiring that the present application identify 'all the possible antibodies that can antagonize PR01449' and determine which of these can 'efficiently inhibit angiogenesis and treat a mammal.'" We reviewed the FA and observed that that it simply and correctly points out that the specification does not disclose the actual preparation of an antibody of the type mentioned in the claims. As a matter of general principle, we agreed that exemplification of all aspects of an invention is not required. However, it was our view that an inventor's disclosure of a working example(s) of the invention, or lack thereof, is a valid consideration. A working example can provide the skilled person with specific and meaningful guidance and indicate that useful embodiments can indeed be produced. The specification's failure in that respect we took as a factor that supported our preliminary view that the application is non-compliant with paragraph 27(3)(*b*) of the Act.

[66] Regarding point (4), concerning the Applicant's later filed application, we also acknowledged the argument (page 21 of the R-FA, last sentence bridging to the top of page 22) that it provides evidence that "confirms the sound prediction in the present application that antagonist antibodies to PR01449 can be generated and used to inhibit angiogenesis in a mammal, as presently claimed." We noted that the later filed W02007/106915 application (the '915 application) to which the Applicant refers was published about six years after the relevant date for assessing compliance with subsection 27(3) of the Act. We also noted that the '915 application discloses details of antibody screening assays performed *in vitro* and *in vivo* which are absent from the present specification and which appear to be of the type the skilled person would regard as instructive and enabling of the claimed subject-matter.

[67] Lastly, in relation to point (5) and the breadth of the claims, we noted that the claims, as evidenced by their reference in part (a) of claim 1 to the entire PRO1449 polypeptide, broadly encompass antagonistic antibodies supposedly reactive seemingly with any portion of the polypeptide, including portions that appear to be inaccessible *in vivo* to antibodies, e.g., its signal, intracellular or non-exposed portions. It was our view that the lack of specificity in the claims as regards the particular portion(s) of the PRO1449 polypeptide to which useful antagonistic antibodies should be prepared is a further indication of the lack of detail and appropriate level of guidance in the specification.

The Applicant's latest submissions

[68] To a considerable extent, the Applicant's latest submissions of December 3, 2018 reiterate arguments previously made in the R-FA and considered by us at the preliminary review stage. What stands out in the latest submissions is the identification of additional documents that reflect the common general knowledge. In relation to the question of enablement, the Applicant relies on the common general knowledge, when understood to include the existence of two anti-angiogenesis antibodies and angiogenesis assays, to emphasize that the claimed invention is enabled:

> The guidance which would be required in the present case to those of skill in the art based upon the direction given in the above noted cases would be directed to the screening of the hybridoma clone for the desired antibody. In the present application, the applicant has given clear direction and teaching to those of skill in the art on the production, screening technique and use of the antagonistic antibodies on pages 9-10, 50, 84-89, 95-96, 111-119, 138, 141-143 and 150. <u>In addition, as set out above, the assay methods for angiogenesis are part of the common general knowledge</u>.

> Accordingly, Applicant submits that there is no requirement in Canadian law for a patentee to provide a specific example of every aspect of an invention. Rather, based upon the demonstration of the role of PRO 1449 in angiogenesis, what is required is that the description must provide sufficient detail to enable a person skilled in the art using only the teaching of the disclosure along with their common general knowledge at the relevant date to prepare the invention.
>
> In the application, the applicant provides a clear and unequivocal direction to those of ordinary skill in the art on how to practice the invention as claimed in the claims utilizing the teaching of the specification and their common general knowledge. [submissions of December 3, 2018, page 21, first three paragraphs; emphasis added]

[69] However, as explained above in relation to our discussion of the common general knowledge particular to this case, we are of the opinion that further elaborating on it does not lead to the conclusion that producing and identifying the antibodies suitable for use in the claimed invention is entirely a matter of routine, notably, in relation to *in vivo* screening of antibodies for anti-angiogenesis properties.

[70] We note that the Applicant has again pointed to its other application (the '915 application), filed six years after the relevant date, as evidence that the antibodies of the claims can be obtained:

> Additionally, post-filing evidence confirms the sound prediction in the present application that antagonist antibodies to PR01449 can be generated and used to inhibit angiogenesis in a mammal, as presently claimed. For example, later filed W02007/106915 (the "'915 publication") discloses completion of experiments demonstrating an anti-angiogenic effect of anti-PR01449 antagonist antibodies. Example 1 of the '915 publication discloses the production of three monoclonal antibodies against PR.01449 (EGFL7) using hybridoma methods (see the '915 publication, e.g., at page 56, line 30 to page 57, line 5). Further,

> Example 1 of the '915 publication discloses that each of these antibodies specifically blocked cell adhesion and cell migration in a cell culture model of angiogenesis (page 57, lines 6-17). Example 2 of the '915 publication discloses that administration of anti-PR01449 antagonist antibodies blocked revascularization of tumors in conjunction with anti-VEGF therapy (page 60, lines 9-14). Thus, consistent with the teachings of the present specification, antagonist antibodies of PR01449 can be obtained and used to inhibit angiogenesis in a mammal, as is presently claimed. [submissions of December 3, 2018; page 22, last paragraph bridging to the top of page 23]

[71] Having again considered the '915 application, we are of the opinion that it does not support the Applicant's position. We do not dispute that antibodies of the type mentioned in the claim were indeed produced. Nor do we dispute that they would be useful. However, the relevant question is whether, as of the relevant date, the skilled person could have routinely obtained them by relying only on the teachings of the specification and their common general knowledge. The question is not, as the '915 application indicates, whether experienced researchers could have made such antibodies six years after the relevant date only after undertaking experiments to further characterize the PRO1449 polypeptide, identify suitable *in vitro* screening assays and ultimately undertaking, with some difficulty, *in vivo* screening.

[72] Regarding *in vitro* assays, the '915 application indicates that the Applicant undertook experiments after the relevant date that shed light on an aspect of the PRO1449 polypeptide's mechanism of action, in that it promotes endothelial cell adhesion and migration—a consideration seemingly taken into account when suitable secondary *in vitro* assays for antagonistic anti-PRO1449 antibodies were actually identified and pursued:

> It has previously been shown that [PRO1449] coated on culture plates promotes human umbilical vein endothelial cell (HUVEC) adhesion,

> although the strength of adhesion was significantly weaker than other cell-adhesion molecules such as fibronectin and collagen (Parker et al., Nature 428: 754-58 (2004)). Accordingly, we performed experiments to determine whether [anti-PRO14449] Mabs 4F11, 10G9, and 18F7 could block cell adhesion to [PRO1449] coated plates. [See the '915 application, page 57, lines 7-11. Note that the Applicant is a co-publisher of the "Parker" article of 2004]

[73] It is telling—but perhaps not surprising, given that the present specification reveals little in the way of PRO1449's mechanism of action—that such assays are not identified in the specification as relevant to the PRO1449 polypeptide.

[74] In relation to *in vivo* screening assays, which is a critical step in the present case, we note that the '915 application discloses that the Applicant appears to have encountered difficulties in that regard. Based on favourable results from its *in vitro* assays, the '915 application indicates that the Applicant then undertook *in vivo* experiments examining the anti-tumour properties (and, by inference, anti-angiogenic activity) of the same monoclonal antibodies (see Example 2 of the '915 application). Susceptible mice were injected with each of five tumour cell lines (A673, Colo205, Fo5, H1299, and MDA-MB231) and then administered anti-PRO1449 antibodies, either alone or in combination with an anti-VEGF antibody that became available only after the relevant date. Notably, the antibodies, when used singly, did not produce an inhibitory effect in three of the cell lines[1], including the commonly known A673 line described in the *Kim 1993* article to identify the first anti-angiogenic antibody. Inhibition was observed in only two of the cell lines, maximally when used in combination with the anti-VEGF antibody (see figures 6-9). On that basis, it is difficult to imagine that the skilled person would not have encountered similar difficulties if they were to have

1: From page 59, lines 29-31 of the '915 application: "We first tested the MAbs in the Colo205 model (human colorectal cancer) and the A673 model (human rhabdomyosarcoma model). We did not observe an effect in these models with the Mabs in PBS as single agents." From page 59, line 44 of the '915 application: "We did not observe an effect in the Fo5 model."

attempted performing such *in vivo* assays some six years earlier, without the benefit of the insights disclosed in the ‘915 application.

[75] Lastly, there is the matter of the breadth of the claims, a concern raised in our PR letter yet not addressed in the Applicant’s submissions. In the PR letter, we explained that the claims “broadly encompass antagonistic antibodies supposedly reactive with seemingly with any portion of the [PRO1449] polypeptide, including portions that appear to be inaccessible in vivo to antibodies, e.g., its signal, intracellular or non-exposed portions.” It was our view that “the lack of specificity in the claims as regards the particular portion(s) of the PRO1449 polypeptide to which useful antagonistic antibodies should be prepared is a further indication of the lack of detail and appropriate level of guidance in the specification.”

[76] To continue that theme, we note that the ‘915 application, unlike the present application, provides clear indications that anti-angiogenic antibodies bind a certain region of the PRO1449 polypeptide. According to the Applicant: “We observed that each of the Mabs bound to the EMI portion of [PRO1449]” (page 58, lines 40-41 of the ‘915 application). We are therefore not prepared to accept that the skilled person would regard the claims as enabled across their scope.

Correct and full description under paragraph 27(3)(*a*) of the Act

[77] In the PR letter, we explained that paragraph (*a*) of subsection 27(3) of the Act requires that the specification correctly and fully describe the invention — a requirement separate from the enablement requirement of paragraph (*b*).

[78] We noted that the specification does describe the PRO1449 polypeptide and its involvement in angiogenesis. However, it was our preliminary opinion that the skilled person would not regard such descriptions as being correct and full insofar as antagonistic antibodies that inhibit angiogenesis in a mammal are concerned. The antibodies of claims 1-24 are not those that simply bind to the PRO1449

polypeptide. Since they appear to be special or remarkable in their nature, it seemed to us appropriate that they be described in correspondingly meaningful terms. Yet the specification appears to merely provide bald statements that reflect only the desired attributes of antibodies of the claims. Accordingly, it was our preliminary view that the specification does not comply with paragraph 27(3)(*a*) of the Act.

[79] The Applicant's submissions of December 3, 2018 did not specifically address this issue. We therefore now conclude that the specification does not comply with paragraph 27(3)(*a*) of the Act insofar as claims 1-24 are concerned.

Utility

[80] In the PR letter, we accepted that the claimed subject-matter would possess utility and the application therefore complies with section 2 of the Act. We addressed the issue for the sake of completeness because the phrasing of the arguments in the FA and R-FA suggested to us that there may be a concern in that regard, even though no formal objection appeared in the FA. We noted that although the specification does not indicate demonstration of the claimed use, the FA appears to admit that a *prima facie* reasonable inference of utility exists and that the claimed invention satisfies the requirements of a sound prediction of utility under section 2 of the Act, per the Supreme Court's *AZT* decision:

> According to [the *AZT* decision], the soundness of a prediction is a question of fact. The factual basis for the prediction in the present application is the disclosure of a causal link between PR01449 (protein of SEQ ID NO 374) and angiogenesis. From this fact, one of skill in the art would readily agree that antagonists of PR01449 would inhibit angiogenesis. [FA, page 3, second paragraph]

[81] At the same time, we noted that the FA discusses the soundness of the predicted utility while also pointing to considerations suggesting the antibodies of the

claims have not been adequately described and enabled, as subsection 27(3) of the Act separately requires:

> Although the application describes the intended use of antagonistic antibodies, such antagonistic antibodies have not actually been prepared by applicant as of the filing date of the instant application. It is not clear how the literal description of the predicted antagonistic antibodies and their predicted utility in inhibiting angiogenesis can represent a sound prediction that such antibodies would actually possess anti-angiogenic activities.
>
> …
>
> In conclusion, as the present application does not identify any antagonist antibody of PRO1449, the skilled person would have to perform undue experimentation to find antibodies that can antagonize PRO1449. [emphasis added]

[82] Our approach was therefore to decouple any question of utility from the separate issue of non-compliance with subsection 27(3) of the Act.

[83] Per the Supreme Court's decision in *AstraZeneca*, we addressed the question of utility by first identifying the subject-matter of the invention as claimed and then considering whether it is useful — is it capable of a practical purpose?

[84] The subject-matter of representative claim 1 can be paraphrased as "an antagonist antibody which binds to a PRO1449 polypeptide and inhibits the ability of the polypeptide to induce angiogenesis for use in inhibiting angiogenesis in a mammal." In the PR letter, it was our view that the skilled person would understand that a molecule inhibitory against a target polypeptide, claimed for use in inhibiting the target polypeptide in a mammal, would self-evidently be an invention capable of a practical purpose with regard to inhibiting angiogenesis.

[85] We therefore conclude that the claimed subject-matter possesses utility.

CONCLUSIONS AND RECOMMENDATIONS

[86] For the reasons set out above, we are of the opinion that the specification complies neither with paragraph (*a*) nor with paragraph (*b*) of subsection 27(3) of the *Patent Act* insofar as claims 1-24 are concerned. We recommend that the Applicant be notified, in accordance with subsection 30(6.3) of the *Patent Rules*, that amendment of the application to delete claims 1-24 is considered necessary for compliance with the Act and Rules. If the amendment is not made within three months from the issuance of this decision, we recommend that the application be refused under section 40 of the Act.

Ed MacLaurin Member	Marcel Brisebois Member	Stephen MacNeil Member

COMMISSIONER'S DECISION

[87] I concur with the conclusions and recommendation of the Patent Appeal Board. In accordance with subsection 30(6.3) of the *Patent Rules*, I hereby notify the Applicant that amendment of the application to delete claims 1-24 is considered necessary for compliance with the Act and Rules. If the amendment is not made within three months from the issuance of this decision, I intend to refuse the application under section 40 of the Act.

Johanne Bélisle
Commissioner of Patents

Dated at Gatineau, Quebec,

This 1st day of August , 2019