Commissioner=s Decision # 1307
Décision du Commissaire # 1307

TOPIC: A20, B20, C00
SUJET: A20, B20, C00

Application No. : 2,407,304
Demande n^{o}. : 2,407,304

Commissioner=s Decision Summary

The subject application related to antibodies specific for various receptor polypeptides and was a divisional application of a parent patent that claimed the receptor polypeptides.

The subject application was rejected in a Final Action for Aobviousness@ double patenting because the claimed antibodies were found to be not Apatentably distinct@ from the subject matter of the claims of the parent patent.

The application was also rejected for lack of support for claims directed to monoclonal antibodies specific for the receptor polypeptides and for lack of support for a claim directed to a therapeutic use of antibodies.

AObviousness@ double patenting

Held: rejection on these grounds reversed.

The claimed antibodies are not covered by the scope of the claims of the parent patent and there is no overlap between the claims.

The instant claimed subject matter does not reflect the same intended utility or the main purpose of the compounds claimed in the parent patent; the claimed subject matter is not an obvious selection of the subject matter claimed in the parent patent; and the claimed subject matter is not an obvious variation, modification or combination of the subject matter claimed in the parent patent.

Therefore, claims to an antibody specific for a polypeptide do not unduly extend the statutory monopoly provided by the parent patent on the target polypeptide through the separate protection of not Apatentably distinct@ subject matter.

Support for monoclonal antibodies

Held: rejection on these grounds reversed in part, affirmed in part.

In cases where a novel target polypeptide has been fully characterized, an applicant may validly claim monoclonal antibodies specific for the polypeptide even though the specification may not provide exemplary support, provided that the specification also satisfies the other requirements of the Act (e.g. enablement requirement of subsection 27(3) of the *Patent Act*). However, the scope of the claims in respect of the target polypeptide is one of several key considerations.

In the instant case, the rejected claims directed to monoclonal antibodies were too broad in view of the target polypeptides. Amendment was therefore required in order to restrict the scope of the claims to those target polypeptides found to be adequately supported.

Support for the utility of the claimed antibodies as anti-inflammatory agents

Held: rejection on these grounds affirmed.

The promised utility of therapeutic antibodies must be either demonstrated or based on a sound prediction. In the instant case, the promised utility was not demonstrated and the factual basis in the specification as filed did not adequately substantiate an articulable and sound line of reasoning which would validate the promised therapeutic utility.

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,407,304 having been rejected under subsection 30(3) of the *Patent Rules*, has consequently been reviewed in accordance with subsection 30(6) of the *Patent Rules* by the Patent Appeal Board and the Commissioner of Patents. The findings of the Board and the ruling of the Commissioner are as follows:

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INTRODUCTION

[1] This decision deals with a review of the Examiner=s Final Action on patent application no. 2,407,304.

[2] The Applicant is Genentech, Inc., the inventors are William I. Wood and James Lee and the invention is entitled AHUMAN PF4A RECEPTORS AND THEIR USE.@

BACKGROUND

[3] By way of background information, the application is concerned with human receptors for the platelet factor 4 superfamily (PF4A), antibodies capable of specifically binding to said receptors and the use of said antibodies as anti-inflammatory agents. According to the description, the platelet factor 4 superfamily includes ACXC@ polypeptides and AC-C@ polypeptides and comprises ten or more pro-inflammatory cytokines, including the cytokine interleukin-8 (IL-8).

PROSECUTION HISTORY

[4] The subject application is a voluntary division of subject matter from parent patent 2,105,998 and was filed with claims directed to monoclonal antibodies capable of specifically binding an isolated platelet factor 4 superfamily receptor (PF4AR) polypeptide and the use of such antibodies in therapy or diagnosis. A Pre-Final Action dated June 1, 2006 maintained an "obviousness" double patenting objection to all of the claims and also maintained objections to claims related to monoclonal antibodies (claims 5 to 7) under subsection 138(2) of the Patent Rules and subsection 27(3) of the Patent Act. In that report, the Examiner raised a separate and additional objection to claim 7 for not being compliant with subsection 138(2) of the Patent Rules and subsection 27(3) of the Patent Act on new grounds. In a response dated December 1, 2006, the Applicant submitted new claims 1 to 4, resubmitted previous claims 5 to 7 and argued that it had traversed the objections.

[5] In a Final Action dated August 27, 2007, the Examiner elaborated and maintained all the previously raised objections on the same grounds. In the February 27, 2008 response to the Final Action, the Applicant provided new claims 1 to 7, but only claim 7 was significantly amended. Again the Applicant argued that the objections were traversed. According to the Examiner, the Applicant's reply to the Final Action did not overcome the objections raised in the Final Action. Subsequently, a Summary of Reasons was forwarded to the Patent Appeal Board on May 8, 2008, a copy of which was sent to the Applicant.

[6] An oral hearing was held on February 17, 2010. At the Hearing, the Applicant was represented by Mr. John Jeffrey of the firm Dennison Associates. Ms. Rena Oulton, the Examiner in charge of the application, and Mr. Nicholas Ohan, the Section Head, were also present.

GROUNDS FOR REJECTION

[7] The claims of the instant divisional application have been objected to under subsection 36(2) of the *Patent Act* for not being Apatentably distinct@ from the subject matter of the claims of the parent patent 2,105,998. The arguments presented by the Examiner in the Final Action pertained to Aobviousness@ double patenting. The Examiner further objected to claims 5 to 7 for not complying with subsection 138(2) of the *Patent Rules* and to the specification for not complying with subsection 27(3) of the *Patent Act* with respect to monoclonal antibodies. Finally, the Examiner objected to claim 7 under subsection 138(2) of the *Patent Rules* and the specification for not complying with subsection 27(3) of the *Patent Act* with respect to therapeutic and diagnostic uses of antibodies.

THE ISSUES

[8] Having regard to the claims, the Final Action and the arguments submitted in response to the Final Action, the Patent Appeal Board is faced with two questions:

(1) Are claims 1 to 7 subject to the prohibition against Aobviousness@ double patenting in view of the parent patent 2,105,998?

(2) Does the instant specification provide sufficient support for the monoclonal antibodies encompassed by the scope of claims 5 to 7 and for the use of antibodies as anti-inflammatory

agents as defined in claim 7?

ISSUE (1): AOBVIOUSNESS@ DOUBLE PATENTING

Legal principles of Aobviousness@ double patenting

[9] *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067 (*Whirlpool*) is considered the leading authority on double patenting. Although the prohibition against double patenting is judge made law, the Supreme Court accepted in *Whirlpool* that there is an inherent prohibition against double patenting in the *Patent Act*. According to subsection 36(1) of the *Patent Act*, an inventor or applicant is only entitled to Aa@ patent for one invention. In the same decision, the Court held further that there are two branches of the prohibition on double patenting.

[10] The first branch is called Asame invention@ double patenting and the second branch is called Aobviousness@ double patenting. The first branch applies in situations where the claims are identical or conterminous.

[11] The second branch of the prohibition against double patenting is more comprehensive and applies in situations where the claims are not Apatentably distinct@. The second branch is described at para. 66 of *Whirlpool*:

> There is, however, a second branch of the prohibition which is sometimes called Aobviousness@ double patenting. This is a more flexible and less literal test that prohibits the issuance of a second patent with claims that are not Apatentably distinct@ from those of the earlier patent.

[12] The instant application is a divisional application of the parent patent 2,105,998. The statutory provisions of the *Patent Act* relevant to divisional applications are found in section 36 of the *Patent Act*.

Subsection 36(1) states:

> A patent shall be granted for one invention only but in an action or other proceeding a patent shall not be deemed to be invalid by reason only that it has been granted for more than one invention. [Emphasis added]

and subsection 36(2) states:

> Where an application (the "original application") describes more than one invention, the applicant may limit the claims to one invention only, and any other invention disclosed may be made the subject of a divisional application, if the divisional application is filed before the issue of a patent on the original application. [Emphasis added]

[13] Although sharing the same monopoly duration as the parent patent, a second patent which issues as the result of the filing of a divisional application is still subject to the prohibition against double patenting (*Glaxosmithkline Inc. v. Apotex Inc.*, 2003 FCT 687, 27 C.P.R. (4th) 114 (*GSK*)). In *GSK*, Justice Kelen stated at paras. 90 and 91:

> I cannot agree with GSK that Athe sin of double patenting@ has evaporated. GSK has

> overlooked the impact that a second patent can have under the Regulations. Under paragraph 7(1)(e) of the Regulations, the Minister is prohibited from issuing the requested NOC for 24 months once the owner of a patent has applied for an order under subsection 6(1). The effect of this provision is to put in place a mandatory injunction that remains in force until either the case is disposed of or the 24-month period expires. The existence of additional patents allows the patent-holder to bring additional applications, thereby obtaining multiple injunctive periods. There is no need to look further than the case at bar for an excellent example of this practice. Even though Apotex successfully invalidated the '637 patent in 2001, the filing of this application by GSK has prohibited Apotex from bringing its product to market for the past two years.
>
> Furthermore, regardless of whether "the sin of double patenting" still exists a patent holder should not be able to receive additional patents for the same invention. Support for this position can be found in the decision of Lutfy J. (as he then was) in *Bayer Inc. v. Canada (Minister of National Health and Welfare)* (1998), 154 F.T.R. 192, 82 C.P.R. (3d) 359, aff'd (2000) 6 C.P.R. (4th) 285 (F.C.A.). Bayer had two patents, filed as divisional applications, that covered the same invention. The period of patent protection ran from the date of issue and the term of the second patent ran for an additional eighty months after the expiry of the initial patent. Bayer later made a terminal disclaimer that brought the expiry date of the second patent in line with that of the first. Bayer argued that the second patent was not invalid for double patenting because the terminal disclaimer had removed the harm of double patenting. The argument was rejected by Lufty J., who held that inventive ingenuity was still needed to support the second patent. I agree. As Binnie J. noted in *Whirlpool* at paragraph 63, subsection 36(1) of the Act states that an inventor is only entitled to "a" patent for each invention. The logical extension of this is that two inventions are required to support two patents. This is confirmed by the wording of subsection 36(2).

Analysis and findings

[14] Given the objections found in the Final Action and the claim set on file, it is clear that the claims of the instant application are not identical or conterminous with the claims of the parent patent 2,105,998. Therefore it is the second branch of the prohibition against double patenting (i.e. Aobviousness@ double patenting) that will be assessed in this Decision.

[15] Although the Examiner objected to claims 1 to 7 of the instant application as not being patentably distinct from claims 1 to 9 of the parent patent, we note that none of the claims of the parent patent relate to anti-PF4AR antibodies. Further, the Examiner=s arguments in the Final Action and the Applicant=s submissions in his response to the Final Action are limited to the comparison between polypeptides and their specific antibodies. Independent claim 1 of the instant divisional application and independent claim 1 of the parent patent are considered the broadest and the most relevant claims. For the sake of efficiency, only these claims will be considered when determining whether the presently claimed subject matter falls under the Aobviousness@ double patenting proscription. If these claims are determined to not fall under the proscription, then claims 2 to 7 will also necessarily not do so. The narrower claims need only to be assessed separately should both independent claims 1 be determined to fall under the Aobviousness@ double patenting proscription.

[16] The relevant claims are:

Claim 1 of the instant divisional (2,407,304)	Claim 1 of the parent patent (2,105,998)

1. An antibody that is capable of specifically binding an isolated platelet factor 4 superfamily receptor PF4AR polypeptide having at least an 85% amino acid sequence identity with the translated amino acid sequence of figures 2, 4 or 5.

1. An isolated platelet factor 4 superfamily receptor (PF4AR) polypeptide having at least an 85% amino acid sequence identity with the translated amino acid sequence of figures 2, 4 or 5.

[17] The following excerpts of the Final Action outline, in part, the Examiner=s position with respect to the Aobviousness@ double patenting issue:

> The anti-PF4AR antibodies recited in claims 1-4, 6 and 7 of the present divisional application are obvious in view of the PF4AR polypeptide of claims 1-9 of parent Canadian patent 2105998. The person skilled in the art having knowledge of the PF4AR polypeptide of claims 1-9 of parent Canadian patent 2105998 would have been expected to successfully prepare antibodies which specifically bind to said same PF4AR polypeptide without considerable and protracted experimentation in view of the common general knowledge of antibody production. Obtaining antibodies directed to a specific polypeptide while in possession of said specific polypeptide constituted common general knowledge at the time of the invention. Indeed, applicant has merely described how to make said antibodies and has not in fact provided any antibodies, apparently relying on the ease with which this can be done to support said hypothetical antibodies. Moreover, the contemplated anti-PF4AR antibodies of the present divisional application do not present any surprising technical effect which would render them unobvious to the skilled artisan in possession of the PF4AR polypeptide as disclosed in parent Canadian Patent 2105998. Therefore, the contemplated anti-PF4AR antibodies of the instant application are a different aspect of the same invention, and claims 1-4, 6 and 7 of the instant application and claims 1-9 of the parent Canadian Patent 2105998 cannot be granted in separate patents.
>
> ...
>
> If, as applicant argues in their correspondence of December 1, 2006, monoclonal antibody production would not involve undue experimentation, then the anti-PF4AR antibodies recited in claims 5-7 of the present divisional application are obvious in view of the PF4AR polypeptide of claims 1-9 of parent Canadian patent 2105998. Therefore, the person skilled in the art having knowledge of the PF4AR polypeptide of claims 1-9 of parent Canadian patent 2105998 would have been expected to successfully prepare antibodies which specifically bind to said same PF4AR polypeptide without considerable and protracted experimentation in view of the common general knowledge of antibody production. Obtaining antibodies directed to a specific polypeptide while in possession of said specific polypeptide constituted common general knowledge at the time of the invention. Indeed, applicant has merely described how to make said antibodies and has not in fact provided any antibodies, apparently relying on the ease with which this can be done to support said hypothetical antibodies. Moreover, the contemplated anti-PF4AR antibodies of the present divisional application do not present any surprising technical effect which would render them unobvious to the skilled artisan in possession of the PF4AR polypeptide as disclosed in parent Canadian Patent 2105998. Therefore, the contemplated anti-PF4AR antibodies of the instant application are a different aspect of the same invention, and claims 5-7 of the instant application and claims 1-9 of the parent Canadian Patent 2105998 cannot be granted in separate patents.

[18] To summarize the Examiner=s position, the claimed antibodies are considered a different aspect of the same invention and are not considered Apatentably distinct@ from the polypeptides

claimed in the parent patent since it would have been obvious for the person skilled in the art to obtain such antibodies and that person would have been able to do so without considerable and protracted experimentation.

[19] In the response to the Final Action the Applicant submitted, in part, the following with respect to the Aobviousness@ double patenting objection:

> It is respectfully submitted however that the Examiner has applied the test for double patenting incorrectly.
> ...
> In order for two patents to be directed to the same invention, there must be substantial overlap in the claims of the patents, that is they must relate to the same art, process, machine, manufacture or composition of matter. See Apotex v. Merck; Apotex v. Sanofli; cited above. If for example, the claims of the two patents relate to different compositions of matter, then they must relate to different inventions.
>
> It is clear from the decisions of the Courts that the claims of the application must relate to the same invention. In all of the cases before the Court dealing with the issue of the same invention for two patents, all were related to the same product covered by two patents such that the claims of each patent could be infringed by the same product. If this were not the case, then there could not be double patenting. Thus for example, in Commissioner of Patents v. Farbwerke Hoechst AG, 41 C.P.R. 9, the parent patent was directed to a medical substance while the divisional application was directed to the same medical substance mixed with a pharmaceutically acceptable carrier. Similarly, in GlaxoSmithKIine Inc. v. Apotex Inc. 27 C.P.R. (4th) 114, the parent application was directed to a formulation process in which water was absent and the divisional application was directed to the same formulation process in which water was absent and microcrystalline cellulose was also absent. In Bayer Inc. v. Canada 6 C.P.R. (4th) 285, the parent application was directed to a medical substance and the divisional application was directed to the same medical substance in combination with a pharmaceutically acceptable carrier. Similarly in the other cases in which the issue of same invention has been decided namely Consolboard Inc. v. MacMillan Bloedel Saskatchewan Limited 56 C.P.R. (2nd) 145 and Whirlpool Corp. v. Camco Inc. 9 C.P.R. (4th) 129 the claims of the two patents being considered related to the same product.
>
> The Courts in the decisions discussed above have set out the tests for double patenting. As stated by the Supreme Court in the Whirlpool case, one must compare the claims of the two applications:
>
> > It is clear that the prohibition against double patenting involves a comparison of the claims rather than the disclosure, because it is the claims that define the monopoly. The question is how "identical" must be the claims in the subsequent patent to justify invalidation.
>
> Accordingly, it is respectfully submitted that the test of whether double patenting exists is whether the claims of the patents are directed to overlapping subject matter, that is are they directed to the same substance or composition of matter.
> ...
> The claims of the present application are directed to antibodies capable of binding platelet factor 4 super family receptor polypeptide. It is therefore clear that the claims of the present application are directed to a different composition of matter than that of the parent application namely, an antibody and not the PF4AR polypeptide. Accordingly, the claims of the present application could not be directed to the same invention as the invention claimed in the parent application.

> As the claims of the present application are directed to a different substance or composition of matter than the claims of the parent application, therefore the claims of the present application are not directed to the same invention as the claims of the parent application. As noted by the Court in Whirlpool the prohibition relates to "evergreening" or an improper extension of monopoly. If two patents are directed to different substances, there can be no improper extension of monopoly. Accordingly in view of all of the above, it is submitted that claims 1-4, 6 and 7 are directed to a different invention than claims 1 to 9 of the present patent. Applicant requests that this rejection be withdrawn.

[20] In summary, the Applicant principally asserts that if the claims of two patents (in this case a parent patent and its divisional application) relate to two different compositions of matter that do not overlap, then they must necessarily relate to different inventions and double patenting cannot exist. We note that the Applicant=s arguments are also based, in part, on *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.* 2006 FCA 421 and *Merck & Co. Inc. v. Apotex Inc.* 2006 FC 524 (*Merck I*), aff'd 2006 FCA 323.

[21] In *Merck I*, the Federal Court of Appeal stated the following at paras 49-50 with regard to divisional status and double patenting:

> ...
> Where, as in the present case, the various divisional applications and the parent have no overlapping claims, there is no risk that a patentee will be able to extend its patent monopoly by having two patents for the same invention.
>
> In summary, Hughes J. correctly held that an improper divisional of a patent does not, in the absence of double patenting, give rise to a loss of patent rights. I would further only note that Apotex did not appeal the Judge=s rejection of their double patenting argument and that issue is not before this panel. [Emphasis added]

[22] In view of the above, the Board needs only to determine whether Aobviousness@ double patenting would occur if the instant divisional application subsequently issued to patent.

[23] Justice Sharlow in *Pharmascience Inc. v. Sanofi-Aventis Canada Inc.*, 2006 FCA 229 stated the following at para. 67:

> ADouble patenting@ refers to certain judge made rules that have been devised to prevent the Aevergreening@ of patents. Evergreening is the undue extension of the statutory monopoly in a particular patent by means of a series of patents with obvious or uninventive additions (*Whirlpool Corp. v. Camco Inc.*, [2000] 2 S.C.R. 1067, at paragraph 37). [Emphasis added]

[24] Also in respect to double patenting, Justice Hughes in *Bristol-Myers Squibb Canada Co. v. Apotex Inc.*, 2009 FC 137 stated the following at para. 175:

> Even when the same person has received two patents the test for distinguishing one from the other is like anticipation or obviousness. One asks whether the second patent is claiming the same thing as the first (literal or co-terminus) or is the second patent claiming something that is obviously within the scope of the first. The Supreme Court of Canada has accepted both approaches as sound: see *Whirlpool Inc. v. Camco Inc.*, [2000] 2 S.C.R. 1067 at paragraphs 63 to 75. [Emphasis added]

[25] According to the passages cited above, it follows that where the claimed subject matter of a divisional application partially covers the subject matter of claims found in its issued parent patent, or where the divided subject matter is obviously within the scope of the parent claims, an undue extension of the statutory monopoly already conferred through the grant of the parent patent can occur as a result of "obviousness" double patenting.

[26] The Federal Court in *Merck & Co. v. Apotex Inc.*, (1994), 59 C.P.R. (3d) 133 (F.C.T.D.), aff'd [1995] 2 F.C. 723 (C.A.), 60 C.P.R. (3rd) 356 (*Merck II*) and the Board in *Re Application of BASF AG* (2010), Commissioner=s Decision No.1299, in *Re Application of Millennium Pharmaceuticals*, Commissioner=s Decision No.1294 and in *Re Application of Norimasa Miyairi et al.* (1976), Commissioner's Decision No.332 determined that the inherent utility or main purpose of a compound is not considered a separate invention from the compound itself but a different aspect of the same invention. To exemplify the above, the Court in *Merck II*, in considering whether the compound Enalapril7 and its use in treating hypertension were different inventions, stated the following:

> ...several or many compounds, and several compositions, and specific uses for them, [are] all aspects of the same invention. Enalapril may be the essence of each claim, but the claims, and the patent for the invention, are more than the chemical molecule of enalapril or of enalapril maleate.
>
> Inherent in the compound, and indeed in the patent, is the purpose and utility of the compound of enalapril. [Emphasis added]

[27] It is also clear from *Whirlpool* that a second patent is not justified unless the claims exhibited Anovelty or ingenuity@ over the first patent; that is, the subject matter of the claims of the second patent must be Apatentably distinct@ from the subject matter of the first patent. The Supreme Court, as an example, referred to *Commissioner of Patents v. Farbwerke Hoechst AG* [1964] S.C.R. 49 (*Hoechst*), where a dilute form of the same medicine was held to be not Apatentably distinct@ from the medicine itself.

[28] In view of the cited case law, and contrary to the Applicant=s submissions, the Board cannot conclude that the test of whether double patenting exists is simply whether the claims of the patents are directed to overlapping subject matter. The fact that claims related to the inherent utility or main purpose of a compound have not been considered by the Courts or the Commissioner to be an invention distinct from claims to the compound itself supports this finding. The patentability of a claim to a compound is thus understood to be based on the compound=s inherent utility, and a separate claim related to the same use of that compound will not be considered as being patentably distinct from the claim to the compound.

[29] Moreover, the Board finds that claims directed to different compositions of matter are not always and inevitably directed to different inventions and the Board is not convinced by the Applicant=s arguments that there can be no improper extension of monopoly if two patents are directed to different compositions of matter. The subject matter of the claims of the second patent must be Apatentably distinct@ from the subject matter of the first patent, novelty alone is not sufficient. Otherwise, such an interpretation would permit undue extension of the statutory monopoly in a particular patent by means of a series of patents with novel but obvious additions, modifications to a previously claimed composition of matter.

[30] With regard to the Examiner=s arguments to the effect that it would have been obvious for the person skilled in the art having knowledge of the PF4AR polypeptides claimed in the parent patent to obtain the instant claimed antibodies without considerable and protracted experimentation, the Board finds that such an argument provides limited assistance in answering the following critical question: would the grant of a second monopoly covering antibodies reactive with certain polypeptides unduly extend, in an obvious manner, the statutory monopoly already conferred through the prior grant of a parent patent that covers the polypeptides?

[31] To answer this question, a comparison between the scope covered by the claims of the instant divisional application and the claims of the parent patent must be performed in order to determine whether Aobviousness@ double patenting would occur if the instant divisional application were to issue to patent. During the Hearing, the Applicant submitted that, although related by the PF4AR polypeptides, there is no overlap between the instant claims and the parent claims and thus, no single type of product, whether antibody or polypeptide, could infringe the claims of both the instant divisional application and the parent patent. Antibodies capable of binding to said PF4AR polypeptides are what is claimed in the instant divisional application, not the polypeptides *per se* as in the granted parent patent. Finally, it is clear from pages 32 to 35 of the description that the claimed antibodies have intended uses that are fundamentally different from those of the target PF4AR polypeptides claimed in the parent.

[32] The Board therefore agrees with the Applicant that the instant claimed subject matter is not covered by the scope of the claims of the parent patent and that there is no overlap between the claims. Yet, as stated above, this finding alone is not necessarily sufficient to illustrate the absence of Aobviousness@ double patenting because it does not take into account the fact that non-overlapping claims could cover not Apatentably distinct@ subject matter. However, this concern does not arise in this case because the Board also finds as follows: firstly, that the instant claimed subject matter does not reflect the same intended utility or the main purpose of the compounds claimed in the parent patent; and secondly, that the instant claimed subject matter is not an obvious variation, modification or combination of the subject matter claimed in the parent patent in the sense of *Hoechst*, wherein the same compound was simply diluted. In summary, the subject matter of the instant claims is not covered by the scope of a claim granted in the parent patent nor obviously within the scope of a claim granted in the parent patent.

[33] For these reasons, in this case, the Board finds no double patenting if a patent issued for the instant claimed subject matter, because it would not extend the statutory monopoly provided by the parent patent.

ISSUE (2): SUPPORT FOR MONOCLONAL ANTIBODIES AND FOR THE CLAIMED THERAPEUTIC USES OF ANTIBODIES

[34] The claims at issue (in bold) and the independent claims from which they ultimately depend, or refer to, read as follows:

1. An antibody that is capable of specifically binding an isolated platelet factor 4 superfamily receptor PF4AR polypeptide having at least an 85% amino acid sequence identity with the translated amino acid sequence of figures 2, 4 or 5.

2. An antibody that is capable of specifically binding the PF4AR polypeptide of figures 2, 4 or 5.

5. The antibody of any one of claims 1 to 4 which is a monoclonal antibody.

6. A composition comprising the antibody of any one of claims 1 to 5 and a pharmaceutically acceptable carrier.

7. An antibody of any one of claims 1 to 5 for use as an anti-inflammatory agent.

Legal principles and authorities regarding support, sufficient description and enablement of monoclonal antibodies

[35] In the Final Action, claims 5 to 7 have been held not compliant with subsection 138(2) of the *Patent Rules* and subsection 27(3) of the *Patent Act*.

[36] Subsection 138(2) of the *Patent Rules* reads as follows:

> Every claim must be fully supported by the description.

and subsection 27(3) of the *Patent Act* reads as follows:

> 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;
>
> (c) in the case of a machine, explain the principle of the machine and the best mode in which the inventor has contemplated the application of that principle; and
> (d) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions.

[37] The concept of Asupport@ found in subsection 138(2) of the *Patent Rules* in conjunction with the provisions of subsection 27(3) of the *Patent Act* have been considered in a number of biotechnology Commissioner=s Decisions, including *Re Application of Central Sydney Area Health Service* (2008), Commissioner=s Decision No.1283 (*CSAHS*) and *Re Application of Sloan-Kettering Institute for Cancer Research* (2009), Commissioner=s Decision No.1296 (*Sloan-Kettering*).

[38] In *CSAHS* and *Sloan-Kettering*, it was determined that compliance with paragraphs (a) and (b) of subsection 27(3) of the *Patent Act* or its prior equivalents requires two things: (i) the specification must provide a correct and full written description of the claimed invention that may require going beyond echoing the language of the claims in the description (the written description requirement); and (ii) the specification must teach how the invention can be successfully put into practice over the entire scope of the claims by the person skilled in the art without the exercise of inventive ingenuity or considerable and protracted experimentation (the enablement requirement).

[39] The disclosure of specific working examples for every embodiment of an invention that may fall within the scope of the claims is not necessarily required to fulfill the requirements of subsection 138(2) of the *Patent Rules* and subsection 27(3) of the *Patent Act*. On the other hand, one cannot validly claim what he has not invented and such principle is illustrated in *Farbwerke Hoechst AG v. Canada (Commissioner of Patents*), [1966] Ex. C.R. 91 aff=d, [1966] S.C.R. 604, when Justice Thurlow said at para. 20:

> There are two fundamental limitations to the extent of the monopoly which an inventor may validly claim. One is that it must not exceed the invention which he has made, the other is that it must not exceed the invention he has described in his specification.

[40] Being Ain possession@ of an invention is not narrowly limited to mean a physical possession, but the lack of actual physical possession of a given invention is a consideration that cannot necessarily be overlooked in every case. In the case of compounds, different types of information provided in an application would indicate that an applicant was Ain possession@ of the claimed invention, including the description of physical and chemical properties and functional characteristics.

[41] The question of how much information is required in the specification in order to support claims to monoclonal antibodies has not yet been before the Canadian courts. However, the Board in *CSAHS* examined claims directed to monoclonal antibodies, antibodies that were not

described by the Applicant beyond their ability to specifically bind a partially characterized target polypeptide (i.e. only a short N-terminal amino acid sequence of the target polypeptide was disclosed). The Board found, that in 1989, a date prior to the laid open date of the instant application, the core steps for producing a monoclonal antibody were well-known and reliable. Thus, considerable and protracted experimentation would generally not be required from the person skilled in the art in order to make a monoclonal antibody capable of binding a given polypeptide. The Board also listed different considerations useful in determining whether the specification is enabling in respect of monoclonal antibodies capable of binding to a polypeptide:

> (i) whether there is a description of the polypeptide and knowledge of its real or expected immunogenicity;
> (ii) whether the scope of an antibody claim in respect of the polypeptide is appropriate;
> (iii) the availability and/or ease of production of the polypeptide;
> (iv) whether a monoclonal antibody was actually prepared;
> (v) whether there are indications of success or failure on record;
> (vi) whether there are indications on record which suggest a requirement for undue experimentation or undue adaptation of the known core steps of preparing a monoclonal antibody; and
> (vii) whether there are indications on record which suggest irreproducibility of an actual or proposed method of preparing a monoclonal antibody.

[42] Based on the facts of that case, the Board concluded in *CSAHS* that the description of the polypeptide found in the specification did not provide an adequate written description of a monoclonal antibody specific for the polypeptide. In respect of what constitutes an adequate written description of a monoclonal antibody, a number of considerations were found to be pertinent:

> (i) whether there is a more than merely a general description of the polypeptide, including an explicit description of specific epitopes on the polypeptide;
> (ii) whether there is a description of a paratope of a monoclonal antibody;
> (iii) whether the scope of an antibody claim in respect of the polypeptide is appropriate;
> (iv) whether the applicant was in physical possession of a monoclonal antibody; and
> (v) whether the applicant was in a position to provide a biological deposit of a hybridoma producing a monoclonal antibody at the time of filing.

Foreign legal authorities and practices relevant to monoclonal antibodies

[43] We remain mindful that decisions in other jurisdictions are not binding, but as the Supreme Court of Canada found in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, such decisions can be instructive and guiding. Further, little pertinent guidance can be found in the Canadian jurisprudence. Moreover, at the Hearing the Applicant referred to the positions of leading foreign patent offices on monoclonal antibodies to support his own. It follows that the Board feels compelled to consider foreign legal authorities and practices relevant to monoclonal antibodies.

[44] Before the laid open date of the instant application, the United States Court of Appeals for the Federal Circuit held *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988) that one skilled in the art, if in possession of a given antigen would have been able to use routine and well-known

methods to prepare an antibody specific to said antigen, without necessarily facing undue experimentation. The Court stated:

> The PTO concedes that the methods used to prepare hybridomas and to screen them for high-affinity IgM antibodies against HBsAg were either well known in the monoclonal antibody art or adequately disclosed in the '145 patent and in the current application. This is consistent with this court's recognition with respect to another patent application that methods for obtaining and screening monoclonal antibodies were well known in 1980.

[45] More recently, the same Court made clear in *Noelle v. Lederman*, 69 U.S.P.Q. 2d 1508 (Fed. Cir. 2004) (*Noelle*) that the disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of a monoclonal antibody claimed by its binding affinity to that antigen when the Court stated:

> The court adopted the USPTO Guidelines as persuasive authority for the proposition that a claim directed to Aany antibody which is capable of binding to antigen X@ would have sufficient support in a written description that disclosed Afully characterized antigens.@ Synopsis of Application of Written Description Guidelines, at 60, available at http://www.uspto.gov/web/menu/written.pdf (last visited Jan. 16, 2003).
>
> Therefore, based on our past precedent, as long as an applicant has disclosed a Afully characterized antigen,@ either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. [Emphasis in original]

[46] However it is also clear in the United States that the scope of a claim to a monoclonal antibody that is described by its capacity to bind a given antigen must be commensurate with the polypeptide that has actually been fully characterized and it is not acceptable that the claims encompass uncharacterized antigens or ill-characterized antigens: *In re Alonso*, 88 U.S.P.Q. 2d 1879 (Fed. Cir. 2008). Moreover, in *Noelle* the Court indicated that there are limitations regarding what can be considered legitimate claim scope with respect to the target antigen that provides the necessary written description to the claimed monoclonal antibody when it was stated that:

> This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the >799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the Afully characterized@ antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown.

[47] Therefore, in view of the manner in which antibodies are made and described, it is generally accepted in the United States that if one provides a particular novel protein sequence, one would also have been Ain possession@ of its corresponding monoclonal antibodies even if none had actually been prepared.

[48] Of equal interest are the opinions of the Courts in the United Kingdom and the Technical Boards of Appeal of the European Patent Office. Authorities from these jurisdictions also recognize that it generally does not require undue effort to produce and isolate monoclonal antibodies that are capable of specifically binding a novel polypeptide: *Eli Lilly & Co v Human Genome Sciences Inc*, (2008) EWHC 1903 (Pat), aff=d (2010) EWCA Civ 33 (*HGS*) and T 0018/09. However, UK courts and Technical Boards of Appeal may find insufficient disclosure and/or lack of industrial applicability in respect of claims directed to subject matter relating to diagnostic and therapeutic applications of monoclonal antibodies in cases where there is no evidence in the specification that an antibody would produce the desired therapeutic effect (see *HGS* and T 0604/04, the latter involving the corresponding European Patent Application of the instant case) or in cases where the production of diagnostic or therapeutic monoclonal antibodies necessitates considerable and protracted experimentation that amounts to a research programme (see *HGS*).

[49] The UK *Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the Intellectual Property Office* explains *HGS* as follows:

> Similarly, claims to antibodies that may have therapeutic or diagnostic potential are unsupported if a role for the target protein in a specific disease has not been identified. In [*HGS*] Kitchin J found the claims to therapeutic and diagnostic uses of antibodies were insufficient as the application provided no data concerning expression, tissue distribution or protein levels in tissues or bodily fluids, or even the standard expression level of Neutrokine-α in humans. Kitchin considered that a skilled person wanting to develop a therapeutically or diagnostically useful antibody to Neutrokine-α would face a substantial research programme with an uncertain outcome. However, claims to antibodies specific to Neutrokine- α were allowed as it would not be an undue burden to a person skilled in the art to generate such antibodies.

[50] Common guidance and teaching with regards to monoclonal antibodies can be gathered from foreign authorities such as those cited above. In the presence of a working example or not, monoclonal antibodies claimed as capable of specifically binding a given novel polypeptide are generally considered to be adequately supported if the specification provides the polypeptide. In the United States the written description requirement of their statute is satisfied when the antigen is fully characterized. In the absence of any indication to the contrary, and conditional on the provision of an enabling specification with respect to the key starting material (i.e. the target antigen), the enablement requirement for the production of monoclonal antibodies is also generally satisfied in leading jurisdictions because monoclonal antibody production technology has been predictable and reliable since at least the late 1980's. When therapeutic applications are specified in monoclonal antibody claims, concerns related to lack of Asupport@ can arise if the specification fails to disclose sufficient guidance as to how to use the contemplated therapeutic antibody in the encompassed therapeutic applications or if the specification does not provide a sound and credible association between the function(s) of the target polypeptide and a given condition or disease such that the contemplated monoclonal antibody would be expected to produce the desired therapeutic effect.

[51] Similar support requirements for therapeutic uses also exist in Canada. For example, the disclosure requirements as set out in subsection 27(3) of the *Patent Act* form an integral part of the doctrine of sound prediction inasmuch as the specification must disclose the underlying facts and the line of reasoning that support the predicted therapeutic uses. The burden of disclosure with regard to sound prediction has been clarified in *Eli Lily Canada Inc. v. Apotex Inc.*, 2009 FCA 97, 78 C.P.R. (4th) 388, at paragraphs 14 and 18:

> &14 YIn sound prediction cases there is a heightened obligation to disclose the underlying facts and the line of reasoning for inventions that comprise the prediction.
>
> [Y]
>
> &18 The appellant argues that in requiring the complete disclosure of the factual basis underlying the sound prediction (i.e. requiring data to substantiate the invention), the Federal Court Judge has changed the disclosure requirements as set out in subsection 27(3) of the Patent Act, R.S.C. 1985, c. P-4. I respectfully disagree. In AZT, the Supreme Court, with obvious reference to subsection 34(1) of the Patent Act (the predecessor to subsection 27(3)), held that where the claimed invention had not yet actually been reduced to practice, the patent must provide a disclosure such that a person skilled in the art, given that disclosure, could have as the inventors did, soundly predicted that the invention would work once reduced to practice. Significantly, in AZT, the Court went on to state that the disclosure requirements had been met given that both the underlying facts (the test data) and the sound line of reasoning (the chain terminator effect) were in fact disclosed (AZT, para. 70). [underlining added]

Analysis and findings

[52] The Examiner=s position in the Final Action with regards to the claimed monoclonal antibodies and the lack of sufficient support and enablement in the specification for said products and their use in therapy of a condition or a disease can be summarized as follows:

- Exemplary support is required for claims to monoclonal antibodies as novel products and applicant cannot claim monoclonal antibodies or a composition relating to same that have not been produced or characterized in any manner.

- The Applicant addressed the Examiner=s arguments in the response to the Final Action. In summary the Applicant submitted the following:

- As a general principle, there is no requirement in the *Patent Act* and *Rules* or in Canadian Law that a specific example for every aspect of an invention be provided in the specification.

- The *Pasteur* decision does not stand for a general proposition that products must be specifically exemplified in the application, but rather, that the specification need only provide clear directions to those of skill in the art such that the teaching of the specification would enable them to make and use the invention without undue experimentation.

- Based upon the teaching of the disclosure, especially on pages 31 to 32, the person skilled in the art can make and use the invention without considerable and protracted experimentation or the exercise of inventive ingenuity since the specification provides clear direction and teaching to allow the person skilled in the art to produce the desired monoclonal antibodies.

(a)(i) Compliance of the monoclonal antibody claims with the enablement requirement of subsection 27(3) of the Patent Act

[58] In *CSAHS,* the Board found that in 1989, a date prior to the laid open date of the instant application, the core steps for producing a monoclonal antibody were well-known and reliable and thus, considerable and protracted experimentation would generally not be required from the person skilled in the art in his attempt to make a monoclonal antibody capable of binding a given antigen. As indicated above at paragraph 41, the Board also listed different considerations useful in determining whether the specification is enabling in respect of monoclonal antibodies capable of binding to a polypeptide.

[59] In the present case, the following facts emerge. The entire amino acid sequences of the polypeptides set forth in Figures 2, 4 and 5 have been described and said polypeptides would reasonably be expected to be immunogenic. The specification demonstrates that the polypeptide set forth in Figure 2 is a human receptor for interleukin-8 (IL-8). The polypeptides set forth in Figures 4 and 5 have respectively 34% and 36% of identity with the polypeptide of Figure 2 but their respective biological functions are not disclosed in the specification. No monoclonal antibody has been prepared.

[60] The Final Action refers to a publication by Seaver (Genetic Engineering News, Aug. 1994, vol. 14, p. 10) as support for the proposition that obtaining useful specific monoclonal antibodies is a difficult process. The passage quoted from Seaver in the Final Action is concerned with the production and selection of Asuperior@ antibodies that can be used in diagnostic kits. That passage reads in part:

> Defining what makes a superior antibody is difficult. Simply put, this antibody binds the antigen and does not bind interfering substances in the clinical range of clinical sample matrices encountered. Out of 6-10 good antibodies that have passed all other selection criteria, only one will give these superior results with clinical specimens.

[61] While the article is of interest, we are not satisfied that it constitutes information sufficient to convince a person skilled in the art that the production of monoclonal antibodies would amount to undue experimentation. It merely indicates that results would be obtained and that Asuperior@ results would require further work. We also note that the Applicant has referred to several textbooks in response to the Final Action which more convincingly establish that production of monoclonal antibodies was, in general, a well-known and predictable art even as of the publication date of the application.

[62] Having in mind the conclusions reached in *CSAHS* with regard to the enablement requirement for monoclonal antibodies, the facts as they are in the present case, the statements made in the Final Action and the Applicant=s submissions, the Board finds that at the laid open date of the instant application, the core steps for producing a monoclonal antibody were well known and reliable. Provision of the polypeptides set forth in Figures 2, 4 and 5 would enable the skilled person to use them as the key starting material for the production of monoclonal antibodies. Thus, considerable and protracted experimentation would not be required from the person skilled in the art in order to make monoclonal antibodies capable of binding the particular polypeptides described in the figures.

[63] However, it appears that the scope of the claims in respect of the target polypeptide merits

particular attention. The scope of claims 5 to 7 is not restricted to a monoclonal antibody capable of specifically binding the PF4AR polypeptide of Figure 2, 4 or 5 when these claims ultimately depend on claim 1. Claims 5 to 7 encompass monoclonal antibodies specific for PF4AR polypeptides other than the PF4AR polypeptides of Figures 2, 4 and 5. Such PF4AR polypeptides have an 85% amino acid sequence identity with one of the PF4AR polypeptides of Figures 2, 4 and 5. Regarding the biological activity/function of the encompassed PF4AR polypeptides, page 5 of the description defines the term "PF4AR" as follows:

> The term "PF4AR" is defined as a polypeptide having a qualitative biological activity in common with the polypeptides of Figs. 2, 4, or 5. PF4AR qualitative biological activity is defined as any one of (1) immunological cross-reactivity with at least one epitope of a polypeptide set forth in Figs. 2, 4, or 5: (2) the ability to specifically bind to a member of the PF4 superfamily; or (3) any effector or functional activity of the Figs. 2, 4 or 5 polypeptides as found in nature, including their ability to bind any ligands other than superfamily members. Immunologically cross-reactive as used herein means that the candidate polypeptide is capable of competitively inhibiting the binding of a PF4AR to polyclonal antibodies or antisera raised against a PF4AR.

[64] Taking into account the passage cited above, the full breadth of the claims encompasses monoclonal antibodies specific for target PF4AR polypeptides that have the ability to specifically bind a member of the PF4 superfamily that is not one of the ligands specific for the polypeptides of Figures 2, 4 and 5. In other words, the scope of the claims encompasses hypothetical and uncharacterized human platelet factor 4 superfamily receptors that are functionally unrelated to the human IL-8 receptor found in Figure 2 and functionally unrelated to the alleged human platelet factor 4 superfamily receptors found in Figures 4 and 5 whose ligands are not even disclosed.

[65] Finally, the Board is not satisfied that the use of the particular polypeptides of Figures 2, 4 and 5 as immunogens would suffice to produce a monoclonal antibody specific for each and every PF4AR polypeptide encompassed by the scope of the claims. In our view, the skilled person would be required to engage in undue experimentation to practise the invention over the entire scope of the claims. The Applicant could have claimed monoclonal antibodies capable of specifically binding only those polypeptides for which it had obtained an adequate level of characterization. Instead, the Applicant chose to broadly claim monoclonal antibodies which potentially bind any of what has been very broadly defined as a human platelet factor 4 superfamily receptor in the description, including receptors that have yet to be discovered.

[66] In view of the above, the Board finds that the specification does not enable the person skilled in the art to practice the alleged invention over the entire breadth of claims 5 to 7 because of their overly broad scope with respect to the target antigen of the claimed monoclonal antibody. It follows that the specification, insofar as it relates to claims 5 to 7, does not comply with the enablement requirement of subsection 27(3) of the *Patent Act*. Claims 5 to 7 have been found to be too broad with respect to the target antigen essentially because of the scope of independent claim 1 and hence, claim 1 necessarily suffers from the same defect. However, it appears that if the antibody recited in these claims were to be restricted to an antibody capable of specifically binding the particular PF4AR polypeptide of Figure 2, 4 or 5, the specification would comply with the enablement requirement of subsection 27(3) of the *Patent Act*.

(a)(ii) Compliance of the monoclonal antibody claims with the written description requirement of subsection 27(3) of the Patent Act

[67] During the Hearing, the Applicant addressed *CSAHS* wherein the Board considered the question of specific support for monoclonal antibodies and the written description requirement of subsection 34(1) of the Act [now subsection 27(3) of the *Patent Act*]. Like the instant case, *CSAHS* dealt with a situation where a monoclonal antibody was claimed in absence of exemplary support in the description. The Applicant particularly referred to the list of factual considerations useful in determining whether the specification provides an adequate written description of a monoclonal antibody capable of binding to a polypeptide introduced above at paragraph 42.

[68] The Applicant submitted that requiring an explicit description of very specific epitopes on the polypeptide goes beyond what the person skilled in the art would consider as a proper written description for the monoclonal antibody specific for the polypeptide. According to the Applicant, so long as the specification discloses the well-characterized antigen, such as the polypeptides of Figures 2, 4 and 5 for which the full amino acid sequences are provided, a monoclonal antibody capable of specifically binding to said antigen is sufficiently described. To support this submission, the Applicant provided evidence that commercially available monoclonal antibodies are often described in relation to their binding partner, not necessarily and universally by a specific epitope recognized on said binding partner. It was further submitted that Applicant=s position is consistent with the law and positions taken at both the United States Patent & Trademark Office and European Patent Office. In addition, the Applicant submitted that the present case can be distinguished from the case before the Board in *CSAHS* because the target antigen in *CSAHS* was not fully characterized (i.e. only characterized by a partial N-terminal amino acid sequence), unlike the polypeptides of the instant application.

[69] As stated above, the guidance found in other jurisdictions is not binding but nevertheless informative and is helpful for the analysis in the instant case. In the United States the disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of a monoclonal antibody claimed by its binding affinity to that antigen (see *Noelle*, *supra*). The positions taken by leading patent offices are consistent with the fact that commercially available monoclonal antibodies and monoclonal antibodies mentioned in the scientific literature are typically described solely in relation to their target antigen. It is also apparent that considerations beyond the binding function of the claimed monoclonal antibody, such as the level of characterization of the target antigen, should be taken into account to establish the appropriateness of the proposed monopoly.

[70] The characterization of an antigen through the disclosure of its complete structure reasonably conveys that an applicant is in possession of a Afully characterized@ antigen. Such facts can be distinguished from the facts examined in *CSAHS*. In *CSAHS*, the target antigen was not fully characterized with respect to all the epitopes bound by the monoclonal antibodies covered by the scope of the claims. The Board finds that it is possible, in cases where a novel polypeptide has been fully characterized, that an applicant may validly claim monoclonal antibodies specific for the polypeptide even though the specification may not provide exemplary support, provided that the specification also satisfies the other requirements of the Act (e.g. enablement requirement of subsection 27(3) of the *Patent Act*).

[71] However, cases where the target antigen is not considered fully characterized or where the contemplated monoclonal antibodies recite particular functional characteristics or attributes

that go beyond the simple interaction with the target antigen (e.g. a monoclonal antibody having an agonistic activity, an antagonistic activity, specificity for a particular epitope of interest or a remarkable high affinity constant) may require correspondingly detailed support. For example, a representative embodiment, a biological deposit, characterization of the paratope of the monoclonal antibody and/or further detailed characterization of the functional domain of the target antigen would assist in providing the full and correct description of an invention when very particular monoclonal antibody species are claimed.

[72] The instant specification provides an adequate written description of the polypeptides of Figures 2, 4 and 5. The structures of these particular polypeptides are fully characterized by the provision of the entire amino acid sequences. The Board finds that the Applicant has indicated possession of all the putative epitopes carried by these particular polypeptides and, by extension, correctly and fully described the genus of the corresponding generic monoclonal antibodies.

[73] The Board has already established that the scope of claims 5 to 7 encompasses monoclonal antibodies capable of specifically binding a very large genus of polypeptides, including polypeptides that are not fully characterized and polypeptides that are not necessarily functionally related to the polypeptide of Figure 2, 4 or 5. Like the situation in *Noelle* wherein the Court found that a human form of a fully characterized murine antigen was not sufficiently characterized to provide an adequate written description for the corresponding monoclonal antibody, the specification in the instant case purports to describe an unknown by its binding affinity to many other unknowns since the claims encompass monoclonal antibodies capable of specifically binding polypeptides other than those defined in Figure 2, 4 or 5, which we considered to be the only ones fully characterized.

[74] In view of the above, the Board finds that the specification does not correctly and fully described the invention encompassed by claims 5 to 7 because, once again, of their overly-broad scope with respect to the target antigen. Any finding concerning the scope of claims 5 to 7 with regard to the target polypeptides of the recited antibodies necessarily also applies to independent claim 1. Similar to our findings on the question of enablement, the specification, insofar as it relates to these claims, would comply with the written description requirement of subsection 27(3) of the *Patent Act* if the target antigens of the encompassed antibodies were to be restricted to the particular PF4AR polypeptides of Figures 2, 4 and 5.

(b) Support for the utility of the claimed antibodies as anti-inflammatory agents

[75] The description indicates on page 2, lines 3 to 4 that, based on their binding capacity, anti-PF4AR antibodies are useful for assays and for purifying PF4AR polypeptides. We further note that exhibit B submitted with a declaration dated February 24, 2010 contains numerous data sheets for various types of commercially available antibodies. These data sheets indicate that antibodies can be typically used in *in vitro* applications such as western blotting, immunohistochemistry and flow cytometry. Thus, the skilled person would accept that the antibodies of claim 1 or 5 (i.e., whether monoclonal or otherwise) would have at least one soundly predicted utility. However, claim 7 relates to therapeutic antibodies that act as anti-inflammatory agents. The passage between page 32, line 38 and page 33, line 2 of the description states the following with regard to such a use:

> PF4AR antibodies that are PF4 antagonists are useful as anti-inflammatory agents or in

> the treatment of other PF4 superfamily-mediated disorders.

[76] It is clear from the above passage that the antibodies contemplated for the claimed therapeutic use would need to possess, not only a binding capacity to the target antigen, but also an antagonistic (i.e. blocking) activity that interferes with the interaction of the target PF4AR polypeptides and their respective ligands so as to inhibit an inflammatory response. It is worth noting that the objection raised by the Examiner refers to antibodies in general and therefore the concern relates to antibodies whether polyclonal or monoclonal. To decide whether the specification supports the heightened *in vivo* therapeutic utility indicated in claim 7 requires us to address further considerations.

[77] Introduced above, Decision T 0604/04 of the Boards of Appeal of the European Patent Office is of particular interest to the instant case since it involved the corresponding European patent application. With respect to claims related to therapeutic antibodies specific for the PF4AR polypeptide of Figure 2, 4 or 5, the Boards stated:

> The patent in suit provides no evidence at all that an antibody blocking the receptor would thereby produce a useful physiological effect of therapeutic potential.
>
> Document (22) (page 320, right-hand column) teaches that the PF4-related proteins are mediators of the inflammatory response which have some activities that are overlapping; for example, Table 3 shows that the ability of being a chemoattractant for neutrophils which is associated with the inflammatory response is shared by many chemokines (IL-8, βTG, PF4). Thus, unless experimentally demonstrated, it is not evident that the blocking of the receptor for any one specific chemokine with monoclonal antibodies would, on its own, necessarily result in a therapeutic effect. Consequently, the mere disclosure of a monoclonal antibody against the polypeptides of Figure 4 or 5 without identifying a diseased state caused by the "misfunctioning" of these polypeptides is not sufficient to acknowledge a use in therapy for the monoclonal antibody. For these reasons, it is concluded that the requirements of Article 83 EPC are not fulfilled in respect of the subject-matter of claims 21 and 22.

[78] Notwithstanding the absence of any indication that a monoclonal antibody specific for a polypeptide as defined in either Figure 2, 4 or 5 had actually been prepared, at the conclusion of the Opposition Proceedings that triggered the decision in T 0604/04 a new patent specification was issued with claims to a monoclonal antibody that is capable of specifically binding a PF4AR polypeptide as defined in Figure 4 or 5. However, no claims related to therapeutic applications for those antibodies were issued.

[79] We note that in T 0604/04 the Technical Board of Appeal was procedurally bound to not take issue with claims related to therapeutic applications of antibodies specifically immunoreactive with the polypeptide defined in Figure 2.

[80] Although we are not bound by the decision of the Technical Board of Appeal, we share concerns similar to those raised in the EPO with respect to claims related to therapeutic antibodies. Unlike the European Board of Appeal we may further address concerns that might arise in respect of claims related to therapeutic applications of antibodies not only to the polypeptides defined in Figure 4 or 5, but also in respect of antibodies to the polypeptide defined in Figure 2 and also in respect of any type of antibody, whether polyclonal or monoclonal.

[81] To begin with, we note that antagonist antibodies with anti-inflammatory activity (i.e. particular antibodies possessing the utility promised in claim 7) have not been provided by way of example. The promised utility had not been demonstrated as of the filing date. Thus, the Applicant must rely on the doctrine of sound prediction in order to support claims related to antibodies having a therapeutic utility.

[82] Based on *Apotex Inc. v. Wellcome Foundation Ltd*, 2002 SCC 77, [2002] 4 S.C.R. 153 (*Wellcome*), an invention that relies on sound prediction must satisfy three requirements:

(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.

[83] In our view, in order for the subject matter of claim 7 to successfully pass the test for sound prediction, the instant specification must provide a proper disclosure such that the person skilled in the art, given that disclosure, would have soundly predicted that the encompassed antibodies would have antagonistic activity towards their respective targets and would accept that such antibodies would be useful as anti-inflammatory agents once put into practice.

[84] In the instant specification, the underlying facts regarding the prediction of antibodies capable of blocking the activity of the PF4AR polypeptides are limited to the general description of all the putative epitopes carried by the PF4AR polypeptides of Figures 2, 4 and 5 and the intrinsic binding ability of an antibody. The ligands of the PF4AR polypeptides of Figures 4 and 5 are unknown and there is no information about where exactly IL-8 interacts with the PF4AR polypeptide of Figure 2.

[85] It is common knowledge in the art that when a purified protein is used to immunize an animal, certain epitopes will be immunodominant because they are most easily recognised by the immune system. The immunodominant epitopes are strongly immunogenic and induce high-affinity antibodies that dominate the immune response. Therefore, even though a given protein contains numerous epitopes, the majority of the raised antibodies may be specific for only a few of them. It follows that a collection of antibodies produced against a target receptor polypeptide using the well-known core steps of antibody production would not necessarily contain an antibody for each and every putative epitope or contain an antibody that possesses an antagonizing activity toward the target receptor. In addition, a specific functional characteristic such as an antagonizing activity is subject to the binding of a particular epitope by an antibody such that ligand binding is physically blocked by the antibody. Inevitably, said particular epitope must be essential to the receptor=s interaction with its ligand and must be available for binding.

[86] Factual data regarding epitopes essential to the function(s) of a target polypeptide may provide the person skilled in the art with enough information such that an antagonistic activity for the corresponding antibody would be soundly predictable. However, and as stated above, the underlying facts regarding the prediction of antibodies capable of blocking the activity of the PF4AR polypeptides are limited to the structural description of the PF4AR polypeptides of Figures 2, 4 and 5. Therefore, the Board finds that the factual basis is limited to antibodies that possess a binding capacity to the target antigen and that fact does not by itself substantiate an articulable line of reasoning to soundly predict that the encompassed antibodies would also antagonize the activity of their respective targets.

[87] Assuming for the moment that the specification had disclosed the production of effective antagonist antibodies specific to the PF4AR polypeptides of Figures 2, 4 and 5, we turn now to the promise that such antagonist antibodies would be effective as anti-inflammatory agents.

[88] With respect to the use of an antagonist antibody specific for the particular PF4AR polypeptide of Figure 2 and having an anti-inflammatory activity, the factual basis includes the fact that IL-8, the ligand of the PF4AR polypeptide of Figure 2, has pro-inflammatory activities. However, the following is found on page 31, line 34 to page 32, line 3 of the description and also forms part of the factual basis:

> Murphy et al. (supra) describe a receptor having a high degree of homology to the receptor of Fig. 2. The Murphy et al. characterized their receptor in recombinant oocytes as being a "low affinity" receptor for IL-8 and having little capability to bind MGSA, thus suggesting that it plays a minor role in IL-8 and MGSA biological activity in vivo. Our studies, however, have shown that the Murphy et al. receptor exhibits IL-8 affinity as high or higher than the receptor of Fig. 2 and that as well it shows high affinity (about 1-10nM) for MGSA. Thus, antagonism of the IL-8 and/or MGSA response of lymphoid cells will likely require that both receptors be inhibited or blocked. [Emphasis added]

[89] Therefore, it appears that blocking the activity of the polypeptide of Figure 2 with a specific antibody may not be sufficient to inhibit IL-8-induced inflammatory responses since a second high affinity receptor for IL-8 exists.

[90] The polypeptides of Figures 4 and 5 have 34% and 36% of identity with the polypeptide of Figure 2 respectively. With respect to their respective biological function(s), the following is found on page 35, lines 16 to 27 of the description:

> The polypeptides set forth in Figs. 4 and 5 are believed to represent receptors for different and as yet undetermined members of the PF4 superfamily (which includes both the C-C and CXC subfamilies). Like the IL-8 receptor of Fig. 2 they are members of the G-protein-coupled superfamily and bear greater similarity to the IL-8 receptor than other receptors. In preliminary experiments, recombinant cells bearing these receptors do not respond to Rantes, MCP1, IL-8 or MGSA, although they may ultimately be shown to bind other members of the PF4 superfamily or presently unknown ligands. However, whether or not the Figs. 4 or 5 polypeptides bind to members of the PF4 superfamily, the
> polypeptides are useful for preparing antibodies for diagnostic use in determining the tissue distribution of the receptors and thus as an immunohistochemical diagnostic for such tissues, in particular as a diagnostic for monocytic cells or PBLs since it is known that such cells express the receptors of Figs. 4 and 5.

[91] Therefore, the specification admits that the PF4AR polypeptides of Figures 4 and 5 may or may not play a critical role in the inflammatory response. An immune response is a complex cascade of sequential and simultaneous biological events wherein many molecules such as cytokines and chemokines have independent but overlapping pro-inflammatory activities, wherein the exact nature of the cytokines and/or chemokines involved depends, amongst others, on the triggering agent and the cell population(s) involved at a given step of the inflammatory response. Unlike the situation for the polypeptide defined in Figure 2, the ligands that bind to the purported receptor polypeptides defined in Figure 4 or 5 have not been disclosed. Taking these facts into account there is insufficient information in the instant

specification suggesting the involvement of the PF4AR polypeptides of Figures 4 and 5 in an inflammatory response process wherein an antibody specific for said polypeptides could be therapeutically active.

[92] Further, the instant disclosure provides neither *in vitro* or *in vivo* data relating to an antibody specific for the PF4AR polypeptide of Figure 2, 4 or 5 with anti-inflammatory activity nor enough information to infer that a single one of the encompassed antibodies would have the desired anti-inflammatory activity.

[93] In summary, the factual basis would not lead the skilled person to conclude that the binding and/or blocking of any one of the PF4AR polypeptides of Figures 2, 4 and 5 with a specific antibody would, on its own, necessarily results in an inhibition of inflammation.

[94] The Board finds that there is no factual basis in the specification at the filing date to substantiate or warrant an articulable and sound line of reasoning for validating the promised utility of an antibody specific for the PF4AR polypeptide of Figure 2, 4 or 5 for use as an anti-inflammatory agent. It also follows that the instant specification does not provide a sufficient disclosure with regard to the utility promised in claim 7 and consequently the requirements of the tripartite test for sound prediction have not been met.

CONCLUSIONS

[95] The Board concludes that the instant claims 1 to 7 do not unduly extend the statutory monopoly provided by the parent patent 2,105,998 through the separate protection of not Apatentably distinct@ subject matter and thus, there is no Aobviousness@ double patenting between the present divisional application and the parent patent.

[96] The Board concludes that claims 5 to 7 do not comply with subsection 138(2) of the *Patent Rules* and that the specification, insofar as it relates to these claims, does not comply with subsection 27(3) of the *Patent Act*. Claims 5 to 7 encompass monoclonal antibodies which have neither been adequately described nor enabled because of their overly broad scope with respect to their respective target antigens. However, it appears that amendments can be made which will properly limit the scope of the rejected claims. By incorporating the restrictions of claim 2 with respect to the target polypeptide to the subject matter of claim 1, the scope of the claims would be appropriately reduced to encompass monoclonal antibodies capable of specifically binding the polypeptides fully characterized in the specification. If such amendments are made, we would consider the rejection to be overcome.

[97] Finally and with respect to the use of the antibody recited in claim 7 as an anti-inflammatory agent, the Board concludes that the instant application fails to satisfy the test of the sound prediction principle, including the disclosure criterion, and thus the specification does not comply with subsection 27(3) of the *Patent Act* with respect to the claimed subject matter and said subject matter does not comply with subsection 138(2) of the *Patent Rules*.

RECOMMENDATIONS

[98] The Board recommends to the Commissioner that:

(1) The Examiner's rejection of claims 1 to 7 for Aobviousness@ double patenting, be

reversed;

(2) The Examiner's rejection under subsection 138(2) of the *Patent Rules* and under subsection 27(3) of the *Patent Act* of the use of an antibody in therapy of claim 7, be upheld; and

(3) The Applicant be informed in accordance with paragraph 31(c) of the *Patent Rules*, that the following amendments, and only the following amendments, of the application are necessary for compliance with the *Patent Act* and *Patent Rules*:

a) deletion of claim 7, and

b) amendment of claim 1 to incorporate the restriction of claim 2 with respect to the target polypeptide.

Marcel Brisebois Ed MacLaurin Serge Meunier

Member Member Member

COMMISSIONER=S DECISION

[99] I concur with the findings and recommendation of the Patent Appeal Board. Accordingly, I invite the applicant to make the above amendments, and only the above amendments, within three months from the date of this decision, failing which I intend to refuse the application.

Mary Carman
Commissioner of Patents

Dated at Gatineau, Quebec
this 1st day of November, 2010