Commissioner=s Decision # 1302
Décision de la Commissaire # 1302

TOPIC: C00
SUJET: C00

Application No. : 583,988
Demande n^{o} : 583,988

Commissioner=s Decision Summary

The subject application was rejected in a Final Action for lack of support for claims directed to anti-interleukin-1 receptor monoclonal antibodies. Following a review of the rejected application, the Board found that the rejected claims were too broad in view of the description and recommended that certain amendments be required in order to restrict the scope of the claims to those antibodies found to be adequately supported. Since the reasoning for finding that the rejected claims were too broad also applied to other non-rejected claims, it was recommended that the Applicant be required to restrict their scope as well. The Commissioner of Patents agreed with the Board and the Applicant was invited to make the required amendments failing which the application would be refused.

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 583,988 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 on behalf of the Commissioner of Patents. The findings of the Board and the ruling of the Commissioner are as follows:

Agent for the Applicant:

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INTRODUCTION

[1] This decision deals with a review pursuant to subsection 30(6) of the *Patent Rules* of a Final Action taken under subsection 30(4) of the *Patent Rules* on patent application 583,988.

[2] The Applicant is Immunex Corporation. The inventors are Steven K. Dower, Carl J. March, John E. Sims and David L. Urdal and the invention is entitled AInterleukin-1 Receptors.@

BACKGROUND

[3] The subject matter of the application principally relates to cytokine receptors, in particular interleukin-1 receptors (IL-1R). Interleukin-1α and interleukin 1β are polypeptides released by mammalian immune system cells which play key roles in the regulation of activation of immune system cells including T cells, B cells, natural killer cells, and many other cells involved in inflammatory responses. Their biological activities are mediated through IL-1R=s that are found in low abundance on the surface of the immune system cells and it is now known that there are two distinct types of IL-1R: Type I having a molecular weight of 82 KDa and Type II having a molecular weight of 60 KDa.

[4] The subject application generally relates to DNA molecules encoding human and murine Type I IL-1R, purified human and murine Type I IL-1R, uses of human and murine Type I IL-1R, antibodies immunoreactive with IL-1R, as well as processes for producing recombinant Type I IL-1R.

[5] Of particular importance in this case are claims directed to monoclonal antibodies immunoreactive with IL-1R. Antibodies are proteins which specifically bind to foreign antigens. Their general structures are well-known and a typical antibody is made up of four polypeptide chains (two identical Aheavy@ chains joined together at a hinge region and two identical Alight@ chains) which link together to form a complete AY@ shaped molecule carrying two Aarms.@ Each arm carries an antigen binding site at its tip. Though the general structures of antibodies are known, the unique structures of the antibody=s antigen binding sites (defined by short stretches of amino acids located in six hypervariable regions or Acomplementarity determining regions@) cannot be predicted from the structure of the antibody=s cognate antigen (to be more particular, the structure of the cognate Aepitope@ found on the antigen).

[6] Monoclonal antibodies can be made using classical monoclonal antibody production technology or Ahybridoma@ technology. This technology, pioneered by Nobel laureates Köhler and Milstein in the mid 1970=s, involves methods for making homogeneous preparations of antibodies. When immunized with an antigen, mammalian immune systems respond with cellular and humoral reactions, the net result of which is the proliferation of AB@ cells that produce a range of antibodies B all of which are immunoreactive with the antigen. Each B cell produces its own unique antibody but, prior to the development of hybridoma technology, it was difficult to obtain pure preparations of any one of these unique antibodies in appreciable quantities. Hybridoma technology involves immunizing mice with an antigen and then immortalizing the murine antibody producing cells by fusing them with murine myeloma tumour cells. The resultant hybridoma cells are then individually screened for binding activity and cloned to yield unique, Amonoclonal@, cell lines each of which is capable of producing practically limitless amounts of identical Amonoclonal@ antibodies.

PROSECUTION HISTORY

[7] The subject application was filed on November 24, 1988 and the Examiner in charge of the application issued a Final Action on October 30, 2002 at which time claim 29 of the application was rejected for lack of support under subsection 174(2) of the *Patent Rules*. Claims 1-28 and 30-52 were indicated to be in allowable form.

[8] On April 30, 2003 the Applicant replied to the Final Action and outlined arguments as to why claim 29 was compliant with the Act and Rules. The Applicant also submitted six new claims bringing the total number of pending claims to 58. The reply was accompanied by a declaration from Mr. Kenneth Schooley, a scientist employed by Immunex. On May 28, 2003 the Applicant further submitted a signed declaration, dated April 30, 2003, from Dr. John Sims, one of the inventors of the present application. The substance of the Sims= declaration was equivalent to an unsigned declaration previously submitted on June 18, 2002 in response to an earlier Office action.

[9] In the Examiner=s estimation, the Applicant=s reply to the Final Action did not overcome the objections raised in the Final Action with respect to claim 29. Additionally, the Examiner held that two newly submitted claims were directed to similar subject matter and therefore objectionable. Accordingly the application was forwarded to the Patent Appeal Board for review. At the request of the Applicant an oral hearing was held on January 23, 2008, at which time the Applicant was represented by Mr. David Schwartz of the firm Fetherstonhaugh & Co.

[10] At the hearing the Board heard additional oral submissions from the Applicant=s representative. The oral submissions were accompanied by corresponding written submissions and an affidavit from Mr. Kenneth Schooley.

THE CLAIMS AT ISSUE

[11] Rejected claim 29 is directed to a monoclonal antibody immunoreactive with IL-1R polypeptide:

> 29. A monoclonal antibody immunoreactive with IL-1R polypeptide.

[12] Two of the six new claims submitted by the Applicant in response to the Final Action also related to monoclonal antibodies and were therefore also identified by the Examiner as problematic. The two new claims are claims 54 and 58:

> 54. A monoclonal antibody immunoreactive with a polypeptide according to anyone of claims 9-13, 30-42, and 49- 50.
>
> 58. A monoclonal antibody produced by the process according to claim 57.

THE ISSUE

[13] We understand from the prosecution history that the issue before us centres on whether the description provides proper support, as required under subsection 174(2) of the *Patent Rules*, for claims to monoclonal antibodies as set forth in claims 29, 54 and 58.

LEGAL FRAMEWORK

Subsection 174(2) of the Patent Rules

[14] The subject application was filed before October 1, 1989 and, by virtue of Section 78.1 of the *Patent Act*, is governed by the *Patent Act* as it read immediately before that date. Unless otherwise indicated, references to the *Patent Act* in this recommendation refer to the Act as it read immediately prior to October 1, 1989.

[15] Subsection 174(2) of the *Rules* appears under the heading AForm and Contents of Applications@ and indicates that A[e]very claim must be fully supported by the description.@

[16] Canadian courts have provided little judicial interpretation of subsection 174(2) of the Rules or any of its equivalents. However in *Re Application of Ciba* (1974), Commissioner's Decision No. 208, the Board stated B after noting that it may be possible for a single sentence in the disclosure to provide sufficient support to warrant claims to some inventions B that the overriding principle was that an inventor may not validly claim what he has not described (citing *Radio Corporation of America v. Raytheon Manufacturing Co.* (1957), [1956-1960] Ex. C.R. 98 para 28, 27 C.P.R. 1 [*R.C.A.*]). Thus the question of whether the claims are Afully supported@ can be a substantive one.

[17] The concept of support was also explored in a number of Commissioner=s decisions relating to biotechnological inventions, including: *Re Institut Pasteur Patent Application* (1995), 76 C.P.R. (3d) 206, Commissioner=s Decision No. 1206 [*Pasteur*] when it considered whether there was specific Asupport@ for claims to monoclonal antibodies and hybridomas; *Re Application of Alonso* (2006), Commissioner=s Decision No. 1269 [*Alonso*] when the Board considered claims relating to monoclonal antibodies described through a deposit of a biological material; *Re Application of Yeda Research & Development Co.* (2007), 59 C.P.R. (4th) 464, Commissioner's Decision No. 1273 when the Board considered claims to nucleic acid molecules; *Re Application of Central Sydney Area Health Service* (2008), Commissioner=s Decision No. 1283 [*CSAHS*] when the Board again considered the question of specific support for monoclonal antibodies and nucleic acid molecules; and most recently in *Re Application of Sloan-Kettering Institute for Cancer Research* (2009), Commissioner=s Decision No. 1296 when the Board considered claims relating to chimeric and humanized forms of a particular monoclonal antibody.

Subsection 34(1) of the Patent Act

[18] Subsection 174(2) of the Rules, or its equivalent, is a subordinate form of legislation which cannot operate outside the *Patent Act*. As such, the concept of Asupport@ as expressed in subsection 174(2) of the *Patent Rules* brings into play subsection 34(1) of the Act, which reads as follows:

> (1) An applicant shall in the specification of his invention
> (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 appertains, 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 thereof and the best mode in which he has contemplated the application of that principle;
> (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; and
> (e) particularly indicate and distinctly claim the part, improvement or combination that he claims as his invention.

[19] Compliance with paragraphs (a) and (b) of subsection 34(1) of the Act, and by extension subsection 174(2) of the Rules, requires respectively: (i) that the specification, beyond merely providing a generalized concept for an invention, provide a correct and full written description of the invention; and separately, (ii) that the specification describe how of invention actually was, or at least how it can be, put into practice: it must be enabling. The decision in *Farbwerke Hoechst A.G. vormals Meister Lucius & Bruning v. Canada (Commissioner of Patents)* (1965), [1966] Ex. C.R. 91, aff'd, [1966] S.C.R. 604 also tells us that the claims must not exceed the invention made and that the claims must not exceed the invention which has been described in the specification.

[20] While actual physical construction of embodiments is not necessarily a strict requirement, it may be B particularly in the case of a biotechnological invention B that an invention cannot be correctly and fully described without having first obtained and then characterized a representative embodiment(s). The absence of a working example can also bring into play, as we consider it does in this case, a related aspect of Asupport@, that being the question of the utility of the claimed invention.

Authorities Particularly Relevant to Monoclonal Antibodies

[21] While the Canadian courts have never had the occasion to consider what constitutes adequate support for claims to monoclonal antibodies, the Patent Appeal Board and the Commissioner of Patents have considered the question on several occasions.

[22] At paragraph 10 of *Pasteur*, the Board placed emphasis on the words Adescribe@ and Aenable@ as used in paragraphs (a) and (b) respectively of subsection 34(1) of the Act. In addressing the two requirements presented by paragraphs (a) and (b) of subsection 34(1), the Board found that no Aspecific description@ of the claimed monoclonal antibodies or a process for their preparation was disclosed. In *CSAHS* the Board reviewed relevant Commissioner=s Decisions, including *Pasteur*, and found that, based on expert evidence, the underlying core technology of making monoclonal antibodies had matured to such a point that by the late 1980=s it was reasonable to say that a person of skill in the art would generally not experience undue burden in trying to make a monoclonal antibody immunoreactive with a given polypeptide. Nonetheless the Board did indicate at para 125 that due consideration was to be given to the facts of any given case and, in that regard, things such as the immunogenicity of the polypeptide, the scope of the claims, the presence of working examples as well as indications of success, failure and undue adaptation of known methods or undue experimentation could be considered. In considering what might constitute an adequate description of a monoclonal antibody, as distinct from a method for preparing one, the Board also relied upon the facts as they were in that case and found that a specific claim related to a monoclonal antibody was not fully supported. In respect of a claim to a monoclonal antibody, a number of considerations were found relevant,

including: whether the specification provided more than a general description of the polypeptide (which could include the description of epitopes) or provided a structural description of the paratopes (or complementarity determining regions, CDRs) of a monoclonal antibody; the scope of the claims; and the presence of actual working examples.

[23] Although decisions in other jurisdictions are not binding, they can be informative and guiding to the extent they do not contradict Canadian jurisprudence and legislation (see for example *Baker Petrolite Corp. v. Canwell Enviro-Industries Ltd.* (2002), 17 C.P.R. (4th) 478 paras 34-37). In fact, convergence of the law in jurisdictions such as the United States and the United Kingdom, and more contemporary foreign jurisprudence, has also prompted the Supreme Court to re-examine the restrictiveness with which fundamental legal tests have been interpreted in Canada (see *Apotex Inc. v. Sanofi-Synthelabo Canada Inc*., 2008 SCC 61 paras 23 and 60).

[24] Therefore in cases such as the present one where Canadian courts have provided no guidance on claims directed to monoclonal antibodies, and where there exists recent and relevant case-law from foreign jurisdictions having similar legislation, it is reasonable to take notice of both established precedents and recent decisions from other common-law jurisdictions.

[25] In *Pasteur*, the sole legal authority cited for the proposition that monoclonal antibody production technology is unpredictable was a 1985 decision of the United States Patent Office Board of Patent Appeals and Interferences: *Ex Parte Old*, 229 U.S.P.Q. 196. (Bd. Pat. App. 1985) However, the Court of Appeals for the Federal Circuit in the United States has more recently held that the production of monoclonal antibodies to a given antigen is based on well-known techniques and that the execution of those techniques by a person of skill in the art does not necessarily amount to undue experimentation (see for example *In re Wands,* 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988); *Hybritech Incorporated v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986); *The Johns Hopkins University v. Cellpro Inc.*, 47 U.S.P.Q. 2d 1705 (Fed. Cir. 1998).

[26] In terms of written description, we note that the Court of Appeal for the Federal Circuit, sitting *en banc*, has very recently re-affirmed in *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, No. 2008-1248 (Fed. Cir. 2010) that this is a requirement separate from enablement. The same court generally stated its understanding of the written description requirement as it relates to monoclonal antibodies in *Noelle v. Lederman*, 69 U.S.P.Q. 2d 1508 (Fed. Cir. 2004)[*Noelle*]:

> 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.

[27] The Apast precedent@ referred to above is *Enzo Biochem v. Gen-Probe, Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) B a case in which the court acknowledged that the United States Patent Office would find compliance with the written description requirement expressed in the first paragraph of 35 U.S.C. ' 112 Afor a claim to an isolated antibody capable of binding to antigen X.@ This was accepted Anotwithstanding the functional definition of the antibody, in light of the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature.@

[28] Thus, an antibody can be described by its immunoreactivity with a fully characterized target polypeptide. That said, it should be remembered that in *Noelle* it was ultimately held that it is not legitimate to claim an antibody immunoreactive with a genus of polypeptides if only one species of the genus has been described. It is also apparently not legitimate in the United States to claim a broad family of antibodies in cases where the antigen is complex or ill-characterized and where the specification Ateaches nothing about the structure, epitope characterization, binding affinity, specificity, or pharmacological properties common to the large family of antibodies@: *In re Alonso*, 88 U.S.P.Q. 2d 1849 (Fed. Cir. 2008).

[29] The courts in the United Kingdom have also recently recognized that it generally does not require undue effort to make and identify monoclonal antibodies that are capable of specifically binding to a novel and defined polypeptide (see *Eli Lilly & Co v Human Genome Sciences Inc*, [2008] EWHC 1903 (Pat) at para 250, aff=d [2010] EWCA Civ 33 [*HGS*]). Nonetheless, if the common general knowledge and the patent specification, considered together, do not disclose a practical way of exploiting the polypeptide, or do not provide a sound and concrete basis for recognising that the polypeptide could lead to practical application in industry, claims to both the polypeptide and antibodies specifically reactive therewith may fall (*HGS* at paras 228-237). Moreover, antibody claims more specifically related to diagnostic and therapeutic applications can be found invalid for insufficiency if the realization of such products would entail the undertaking of a research programme (*HGS* at paras 252-260).

[30] Although the Technical Boards of Appeal may, depending on the facts and evidence, reach different conclusions as that of the UK courts on questions of sufficiency and industrial applicability, both strive to follow the same underlying legal principles. For example, in T 0018/09, after considering the same patent at issue in *HGS*, the Board concluded that the specification was sufficient to allow a skilled person to make antibodies, including monoclonal antibodies, to a defined polypeptide since Athe production of antibodies against a protein of known amino acid sequence does not in itself require any particular effort@ (para 19). In contrast to the findings in the UK courts, industrial applicability of both polypeptide and antibodies reactive therewith, including therapeutic antibodies, was acknowledged by the Board based on the evidence before it. In other cases, notwithstanding acknowledgement of industrial applicability of a putative novel receptor polypeptide, the European Patent Office has found insufficient disclosure in respect of claims drawn to therapeutic antibodies reactive with the putative receptor polypeptide in cases where there was no evidence in the specification that an antibody blocking the receptor would produce a therapeutic effect (see T 0604/04 at paras 24-27).

[31] A consistent theme that generally emerges from a review of foreign case law is that monoclonal antibodies immunoreactive with a defined novel polypeptide are typically claimed by reference to the polypeptide. Valid claims may issue even if no working example(s) has been provided. The question of enablement is also generally resolved in favour of the applicant/patentee in view of the maturity of monoclonal antibody production technology. Nonetheless, lack of utility/industrial applicability concerns may arise in cases where the specification and common general knowledge reveal little information of the polypeptide=s particular function or in cases where the claims specifically relate to antibodies for therapy or diagnosis. These more particular concerns may be alternatively or additionally expressed in terms of lack of enablement/lack of support/insufficiency for failure to disclose how to use (as opposed to how to make) the antibodies or expressed as requiring undue experimentation to determine their function.

THE FINAL ACTION

[32] The application has been rejected largely on authority of the decision in *Pasteur*. The Final Action also discusses the teachings of the specification in respect of monoclonal antibodies and nicely summarizes the content of several scientific articles concerned with monoclonal antibodies reactive with IL-1R which were published after the filing date of the present application. The Final Action states, in part, the following:

> The declaration [provided by the Applicant] and cited documents by Slack et al and Rogers et al show that monoclonal antibodies to IL-1R have subsequently been produced, but does not support their production either by Athe first priority date@, as stated in applicant's declaration of June 18, 2002, or by the filing date of the present application.
> . . .
> As stated in the examiner's action of December 18, 2001, Example 7 of the description, describes procedures for producing hybridoma cells and monoclonal antibodies, referring to US Patent 4,411,993 as disclosing techniques for generating monoclonal antibodies, and to Engvall et al (1971) and US Patent 4,703,004 as disclosing techniques for screening hybridomas.
> . . .
> Example 7 describes what can be done, but never states that any positive hybridoma clone producing a monoclonal antibody to IL-1R was actually produced, and the binding characteristics and utility of any monoclonal antibody produced to IL- 1R are not disclosed.
> . . .
> Applicant's declaration of June 18, 2002 states (last paragraph) that Athe teachings of the description provide a sound prediction that antibodies, including polyclonal and monoclonal antibodies, are easily formed against Il-1 R and fragments thereof, and the sound prediction is supported by the findings discussed above@. As stated earlier in this action, McMahan et al and Bomsztyk et al (referred to in Slack et al and Rogers et al respectively), both used a line of C127 cells stably expressing recombinant human type I IL-1R as immunogen in the first step of producing monoclonal antibodies to IL-1R. Rogers et al also used highly purified preparations of the murine type I IL-1R extracellular domain as immunogen. Chizzonite et al (cited in Rogers et al), used partially purified IL-R isolated from EL4 cells as immunogen. Thus publications originating with the applicant describing production of monoclonal antibodies, McMahan et al, Bomsztyk et al and Rogers et al, all include details not found in the description of the present application, use of a cell line expressing IL-1R or use of an extracellular domain of IL-1R as immunogen. Only Chizzonite et al, who do not appear to be associated with the applicant, appear to have used a method equivalent to that described in example 7.
>
> Applicant is reminded that the description of Canadian Patent 1,338,323, also referred to known methods for making monoclonal antibodies and hybridomas. The Commissioner's Decision stated that specific instruction required to make the claimed antibodies must be disclosed, and that permissible modifications of the basic method for the specific antigens disclosed must be included in addition to referring to known techniques. Example 7 does not provide anything more than general instruction. While a method for producing monoclonal antibodies was envisioned based on methods known at filing, as described in Example 7, the monoclonal antibody product of claim 29 had not been made, and its properties, characteristics and utility could only be stated in general terms, which simply

> described what the hoped for product would do, bind to IL-1R polypeptide. The description does not show by examples or broad statements that the described method was successfully used, or provide any data to illustrate the number of positive clones produced using the method. Further there is no data confirming that monoclonal antibodies which are useful products, capable of binding only with IL-1R and with sufficient concentration to be useful assays or other applications, were produced. Thus the description of the present application does not show that the described method was successfully used to produce monoclonal antibodies which are novel, useful products.

[33] From this we gather that the specification is considered by the Examiner to be not fully supportive of claims to monoclonal antibodies mainly because the scientific articles discussed in the Final Action establish that the claimed products were actually made only after the filing date of the present application, that they were made using protocols not disclosed in the specification and that the claimed antibodies have not been characterized.

THE APPLICANT=S SUBMISSIONS

[34] The Applicant=s arguments in favour of the patentability of the claimed subject matter are based on the following:

> (i) a written response to the Final Action accompanied by a declaration from Kenneth Schooley, a scientist employed by the Applicant;
> (ii) a second declaration, dated April 30, 2003, from Dr. John Sims, one of the inventors of the present application (this declaration was equivalent to an unsigned declaration first submitted on June 18, 2002 in response to a non-final action);
> (iii) oral submissions presented at the hearing;
> (iv) written submissions submitted at the hearing; and
> (v) an affidavit from Kenneth Schooley accompanied by supporting copies of pages from his laboratory notebooks.

[35] In the response to the Final Action the Applicant submits that claim 29 is allowable since the monoclonal antibodies defined by the claim are correctly and fully described in the specification and since the specification provides a full, enabling description of how to make and use the claimed monoclonal antibodies. The Applicant says that the substantive requirements for patentability of the claimed subject matter as provided for in subsections 34(1)(a) (written description) and 34(1)(b) (enablement) of the *Patent Act* have therefore been met. In particular the Applicant has put forward, in part, the following argument with respect to the rejection of claim 29:

> <u>The claimed monoclonal antibodies are correctly and fully described in the specification</u>
>
> Concerning Section 34(1)(a) of the *Patent Act*, Applicant respectfully submits that monoclonal antibodies are conventionally described in patent claims by their specificity e.g. Aa monoclonal antibody that is immunoreactive with protein X.@ That is, a monoclonal antibody is invariably described by the identity of the antigen to which it binds.
>
> Claim 29 recites AA monoclonal antibody immunoreactive with 1L-1R polypeptide.@ There is no dispute that A1L-1R polypeptide@ is properly described

in the specification. See, e.g. allowed claims 9-13,30-42, etc. Hence, the antigens to which the claimed monoclonal antibodies bind are fully described, and the monoclonal antibodies are therefore also fully described in conventional terms.

Applicant further respectfully submits that had monoclonal antibodies as claimed in clam 29 been prepared at the time of the instant application and described in a working example, the principal difference in the content of the instant specification would be that Example 7 would be phrased in the past rather than present tense. Thus, in the instant case, the presence or absence of a working example is clearly irrelevant to the sufficiency of the description of a monoclonal antibody under Section 34(l)(a) of the Patent Act as it read immediately before October 1, 1989. Therefore, section 34(l)(a) is satisfied.

The claimed monoclonal antibodies are fully enabled bv the specification as filed

The second requirement of section 34(1) of the *Patent Act* as it read immediately before October 1, 1989 is that the specification provide an enabling description of the claimed subject matter. That is, the specification must provide sufficient direction to enable a skilled person, in view of his or her background knowledge in the art, to make and use the invention as claimed.

Applicant respectfully submits that the instant specification fully enables the preparation and use of monoclonal antibodies immunoreactive with 1L-1R polypeptide as claimed.

This is evidenced by Mr. Schooley's attached Declaration, which clarifies and confirms that shortly after the filing date, Applicant prepared monoclonal antibodies as claimed using the techniques described in Example 7 in the specification without the exercise of undue experimentation or inventive ingenuity.

As mentioned above, Applicant emphasizes that it is not relevant to the compliance of the instant specification with section 34(l)(b) of the *Patent Act* as it read immediately before October 1, 1989 that the actual demonstration of monoclonal antibodies took place after filing. Full details of how monoclonal antibodies are made and used are contained in the application as filed. The reproduction of Example 7 post-filing is presented merely as further proof that Example 7 was indeed fully enabling at the time of filing. Whether this demonstration took place in 1986, 1989 or 2003 is immaterial.

[36] The response concludes with arguments to the effect that, while the claimed monoclonal antibodies may be useful as therapeutic agents, the skilled person would recognize that monoclonal antibodies will also find uses outside the therapeutic arena, for example, for use as reagents in assays for the presence of IL-1R. The Applicant also relies upon the doctrine of sound prediction as authority for maintaining that the specification *prima facie* fully supports claim 29 saying that the tripartite test set out in *Apotex Inc. v. Wellcome Foundation Ltd.* (2002), 21 C.P.R. (4th) 499 has been satisfied.

[37] At the oral hearing the Applicant presented the Board with written submissions outlining additional reasons why, in the Applicant=s opinion, claims 29, 54 and 58 are compliant with the

Act and the Rules. These submissions have been summarized by the Applicant as follows:

> By way of a very brief summary of the foregoing submissions, Applicant submits that the pending claims directed to monoclonal antibodies are fully supported by the patent application as filed, meet all requirements for patentability under the *Patent Act*, and should be allowed by the Office, for at least the following reasons:
>
> 1. The present application provides fully characterized IL-IR protein and a specific, detailed and enabling protocol for preparing monoclonal antibodies immunoreactive with IL-IR.
>
> 2. It is not a requirement of Canadian patent law that a claimed invention or embodiment thereof be disclosed in working examples. It is sufficient that the specification fully and correctly describe the invention in enabling terms. The present application meets these requirements. The application describes monoclonal antibodies to IL-IR using art-accepted terminology, and provides a full, enabling description of how to make such antibodies.
>
> 3. As supported by numerous scientific publications available at the time, and contrary to the conclusions reached in *Institut Pasteur*, hybridoma technology was a proven, well-established technology as of the priority date and filing date of the present application.
>
> 4. The present claims to monoclonal antibodies do not constitute "reach-through" claims. Rather the claimed monoclonal antibodies are fully and specifically defined molecules that are the expected outcome of an established and fully documented method for their production.
>
> 5. The Federal Court of Appeal has held that compliance with section 34(1) of the *Patent Act* as it read immediately before October 1, 1989 must be met by the date of publication. The present application will be published (i.e. granted) sometime in 2008 or later. The skill in the art concerning preparation of monoclonal antibodies is indisputably high in 2008.
>
> 6. Although compliance with section 34(1) has been held to be determined as of the date of publication, the Federal Court of Appeal has held that sound prediction is to be established as of the filing date. The specification as filed, by disclosing IL-IR protein and a detailed protocol for making monoclonal antibodies, in light of the knowledge in the art as of the filing date concerning the preparation of monoclonal antibodies, supports a sound prediction that monoclonal antibodies immunoreactive with IL-IR could be made in accordance with the teachings of the specification. Sound prediction does not require certainty, and no reasonable basis for doubting Applicant's prediction has been asserted.
>
> 7. Soon after the patent application was filed, Immunex Corporation produced monoclonal antibodies as claimed, using a protocol equivalent to that described in the patent application, and which in some aspects was in fact simpler and less demanding than the protocol described in the application. This demonstrates that the specification as filed is enabling and that Applicant's sound prediction was correct.
>
> 8. The *Institut Pasteur* decision, upon which the present rejections are predicated: (a) defined incorrect requirements for the description of

monoclonal antibodies; (b) failed to accurately assess the state of monoclonal antibody technology in the mid-1980s; (c) made reference to US authorities that did not reflect the state of US law at the relevant time; (d) contained an erroneous analysis concerning obviousness, failing to take into account that the relevant antigen was not then known in the prior art; and (e) erroneously concluded that the absence of cures for various diseases speaks to the unpredictability of methods for making monoclonal antibodies.

9. The patent application at issue in *Institut Pasteur* claimed monoclonal antibodies to any HIV-2 protein, glycoprotein, or peptide, and did not disclose, isolate or otherwise characterize such immunogens. Further, the application simply stated that the broad class of monoclonal antibodies claimed could be prepared by "traditional techniques". There was no evidence that such antibodies ever were made. In contrast to *Institut Pasteur*, the present application claims monoclonal antibodies to IL-IR, a particular protein that is fully characterized in the present application, and a detailed and specific protocol for making the monoclonal antibodies is provided in the application. The record establishes that these monoclonal antibodies were made shortly after filing. Accordingly, in view of the differences in the two technologies (HIV -2 monoclonal antibodies versus IL-IR monoclonal antibodies) and the relevant technical teachings of the two patent applications, the findings in *Institut Pasteur* do not apply to the present application.

[38] The Applicant has provided declarations from two of its employees, Kenneth Schooley and Dr. John Sims one of whom, Dr. Sims, is also an inventor of the present application. These declarations state that anti-monoclonal antibodies to IL-1R may be, and in fact were, prepared using procedures substantially similar to those outlined in a prophetic example (example 7) provided in the specification.

[39] The Applicant has also supplied an affidavit from Kenneth Schooley B then employed as a research associate in Immunex=s hybridoma laboratory B that describes how he actually made monoclonal antibodies to human IL-1R using conventional techniques consistent with those outlined in example 7. The affidavit compares his procedure with the steps proposed in example 7. The affidavit is notarized and is accompanied by copies of relevant pages from his laboratory notebooks which indicate that he started his procedures on November 16, 1988 (*i.e.*, eight days before the present application was filed) at which time mice were immunized with cells expressing high levels of human IL-1R. By March 1989 he apparently was in possession of a murine hybridoma cell line, termed AHuIL-1RM1@, that is capable of producing monoclonal antibodies to human IL-1R.

Post-filing Scientific Articles

[40] The Applicant and the Examiner have referred to several scientific articles that were published after the filing date of the application and which all disclose the preparation of monoclonal antibodies to IL-1R. These articles are:

(i) Slack *et al.* (1993). Independent Binding of Interleukin-la and Interleukin-18 to Type I and Type I1 Interleukin-1 Receptors. *J. Biol. Chem.* 268: 2513-2524;
(ii) Rogers *et al.* (1992). Interleukin 1 participates in the development of anti-Listeria

responses in normal and SCID mice. *Proc. Natl. Acad. Sci USA* 89: 1011-1015;
(iii) McMahan *et al.* (1991). A novel IL-1 receptor, cloned from B cells by mammalian expression, is expressed in many cell types. *EMBO J.* 10: 2821-2832;
(iv) Spriggs *et al.* (1990). Induction of an Interleukin-1 Receptor (IL-1R) on Monocytic Cells. *J. Biol. Chem.* 265: 22499-22505;
(v) Bomsztyk et al. (1989). Evidence for different interleukin 1 receptors in murine B- and T-cell lines. *Proc. Natl. Acad. Sci USA* 86: 8034-8038; and
(vi) Chizzonite *et al.* (1989). Two high-affinity interleukin 1 receptors represent separate gene products. *Proc. Natl. Acad. Sci. USA* 86: 8029-8033

[41] Articles (i) through (v) originate in whole or in part with the Applicant whereas article (vi) is of independent origin. Of the articles that originate with the Applicant, articles (i), (iii) and (iv) mention an anti-IL1R monoclonal antibody termed either AM1" or AhuIL-1RM1" in apparent reference to the same murine anti-human IL-1R antibody described by Schooley in his affidavit.

ANALYSIS AND FINDINGS

[42] The more general question of whether the claims directed to monoclonal antibodies are fully supported leads us to consider several interrelated aspects: whether such antibodies are enabled; whether they have been adequately described; and whether they are useful.

Enablement

[43] In considering the question of enablement we note that both the Examiner and the Applicant have referred to *Pasteur*. In *CSAHS* the state of monoclonal antibody production technology in the late 1980=s was examined in light of evidence provided by a professor Goding: the author of a publication cited as authority in *Pasteur* for the finding that monoclonal antibody production technology was unpredictable and required particular teachings in order to enable the skilled person to make monoclonal antibodies to a given polypeptide. However, based on the evidence of professor Goding to the contrary, it was concluded in *CSAHS* that *Pasteur* need not be rigidly followed and relied upon as authority for the proposition that a claim to a monoclonal antibody is not enabled merely because the application fails to set out a detailed protocol or because the specification does not provide evidence of enablement in the form of the actual preparation of a monoclonal antibody. What emerged from *CSAHS* (paragraph 125) was a list of factors that may be useful when asking whether claims to monoclonal antibodies are enabled:

(i) whether there is a description of the polypeptide and knowledge of its real or expected immunogenicity (see for example *Goding*, subsection 2.6.1, pp. 28-29, for a discussion on features of an antigen which control antigenicity);
(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.

Scope of Enablement

[44] In this case, of the factors listed above, an examination of the scope such a claim in respect of the polypeptide itself is critically important.

[45] In respect of the term AIL-1R@ as used in claim 29 for example, we note that the specification broadly defines the term as encompassing Aproteins which are capable of binding Interleukin-1 (IL-1) molecules@ (see the ADefinitions@ section on page 9, lines 14-18). Since claim 29 does not qualify the term AIL-1R@, the skilled person would interpret it to encompass all types of IL-1R polypeptides.

[46] A review of the scientific articles discussed by the Examiner and the Applicant during prosecution reveals that there are apparently two distinct types of IL-1R polypeptides: Type I and Type II. Type I receptors are found predominantly on T-cells and fibroblasts, have an apparent molecular weight in native form of approximately 82 KDa whereas type II receptors are found on B-cells and T-cells and have a molecular weight in native form of about 60 KDa. Although both Type I and Type II share the ability to bind IL-1 molecules and are members of the same superfamily, it is apparent, as explained below, that they are antigenically different.

[47] The two types of receptors and their differences are generally discussed by McMahan *et al.* (*EMBO J.* 10: 2821-2832, 1991) in the introduction portion:

> One species of receptor, of Mr - 80 000, which has been thought to be the predominant form found on T cells and fibroblasts, has been well characterized, and cDNA clones isolated. However, IL-I receptors on cells or cell lines representative of B cells, monocytes, neutrophils, bone marrow cells and hepatoma cells differ in size and/or antigenicity from the receptors found on T cells and fibroblasts . In B cells and monocytes, this clearly is not a consequence of post-translational modification; rather, the IL-1 receptor on these cells is the product of a different gene. Here we report the isolation from human and murine B cells of cDNA clones encoding a novel IL-1 receptor, and some characteristics of the receptor proteins encoded by these clones. We propose to call this new receptor the type II IL-I receptor, to distinguish it from the previously cloned p80 or type I receptor.[emphasis addded; citations omitted]

[48] The publication by McMahan *et al.* (originating with the Applicant) appears to be the first published description of recombinant murine and human Type II receptors. Moreover, McMahan *et al.* report (see page 2821 under the AResults@ section) that the cloning of a Type II receptor was facilitated by several improvements to the method used in the present application to clone the murine Type I receptor. These facts indicate to us that further inventive work was done in developing a method which could be used to clone Type II receptors.

[49] We also note that the abstract of Bomsztyk *et al.* (*Proc. Natl. Acad. Sci USA* 86: 8034-8038, 1989) indicates that a monoclonal antibody which binds to a Type I receptor does not bind to a Type II receptor:

> In this study we used a B-lymphoid cell line, 70Z/3, and T-lymphoid cell line, EL-4 6.1 C10, to explore further the differences that exist between IL-1 receptors on cells of B and T lineage. We show that a monoclonal antibody against the [Type I]

> IL-1 receptor on EL-4 cells **does not bind** to the [Type II] IL-1 receptor on 70Z/3 cells. This finding suggests that there are structural differences in the extracellular domains of the IL-1 receptors on the two cell lines.
>
> . . .
>
> Lastly, a probe containing the entire coding region of the murine T-cell IL-1 receptor hybridized under high stringency conditions with mRNA from EL-4 cells but not with mRNA from 70Z/3 cells. Taken together, the observations made in this study suggest that major structural differences exist between the IL-1 receptors on B and T lymphocytes. [emphasis added]

[50] To enable the full scope of claim 29 it is apparent that the skilled person would first have to isolate or otherwise obtain a Type II IL-1 receptor. However, the task of obtaining a Type II IL-1 receptor is not something we see as involving routine experimentation in view of the following facts:

(i) the specification indicates that considerable experimentation was done in order to secure a DNA clone encoding a Type I murine IL-1 receptor;

(ii) that sequence information derived from the murine clone was subsequently used to clone a highly similar Type I human IL-1 receptor;

(iii) there are no teachings (for example in the form of the identification and at least partial characterization of putative clones) in the specification that DNA sequence information derived from either the murine or human Type I IL-1 clones was used, or could be used, to clone antigenically dissimilar Type II receptors;

(iv) there are no indications that cloning methods other than those that rely on DNA sequence similarity could be alternatively used to isolate Type II IL-1 receptor B to the contrary, there are indications (see Bomsztyk *et al.* and McMahan *et al.*) that methods relying on antigenic similarities between the two types of receptors would not have been successful;

(v) it appears that inventive work was used by the Applicant to subsequently isolate and characterize a Type II receptor; and

(vi) IL-1 α and β were themselves known and characterized before the filing of the present application yet the state of the art with respect to their receptors was apparently still evolving.

[51] This leads us to conclude that claim 29 is not enabled across its scope since it inappropriately encompasses monoclonal antibodies directed to Type II IL-1 receptors. The skilled person would not have been able to make antibodies to a Type II receptor without first isolating one in order to use it as an immunogen. It does not appear that the use of a Type I receptor, as disclosed in the present specification, as an immunogen would generate a monoclonal antibody immunoreactive with a Type II receptor. Lastly, we are not convinced that the state of the art, even as of today, has generally advanced to such a point that the skilled person would be able to overcome the particular obstacles mentioned above without exercising inventive effort.

[52] In respect of monoclonal antibody claims 54 and 58 we note that they too suffer from the same problem since they broadly encompass B at least in part through reference to other claims B an unqualified AIL-1R@ polypeptide.

[53] Thus we are not satisfied that the enablement requirement of subsection 34(1) has been met in this case.

Enablement: Other Considerations

[54] The question arises out of necessity after having inspected other claims on file (see below under APost-Hearing Correspondence@) whether the monoclonal antibody claims would be considered to be enabled if they had been, or could be, appropriately limited by reference to those IL-1 receptor polypeptides properly disclosed, *i.e.*, Type I receptor polypeptides. In our view the answer to this question is yes.

[55] In this case, the skilled person upon reading the specification would understand that the murine and human IL-1R Type I polypeptides described in the specification are large 82 KDa receptor molecules found on the cell surface and would appreciate that receptor molecules such as these would be immunogenic. It is further apparent that the specification teaches molecular cloning of mammalian Type I IL-1R polypeptides and their recombinant expression in a variety of cell types B something which greatly facilitates the preparation of immunogen to be subsequently used to make monoclonal antibodies. As such we accept that preparation and availability of such antigens in this case is not a significant issue.

[56] It has been established that it is possible to generate anti-Type I IL-1R monoclonal antibodies: see for example the scientific articles (e.g. Chizzonite *et al., Proc. Natl. Acad. Sci. USA* 86: 8029-8033, 1989) discussed during prosecution and the affidavit submitted by the Applicant in the name of Kenneth Schooley. Though these documents post-date the filing date of the present specification, they can be taken as indicators that the specification was enabling, even as early as the filing date, since there are no indications that the post-filing work involved undue experimentation or undue adaptation of methods generally already known to the skilled person. More to the point, the affidavit of Kenneth Schooley, who approximates the person skilled in the art, indicates that once the antigen was in hand the development of an anti-Type I IL-1R monoclonal antibody immediately followed and that its production proceeded in a straightforward manner. A comparison of the steps outlined in example 7 of the present specification with the steps followed by Schooley indicates that they are strikingly similar. Furthermore, there are no indications that Schooley=s success was a chance outcome. In fact, it is apparent that others, *i.e.,* Chizzonite et al., were able to independently generate their own anti-IL-1R monoclonal antibodies once they too were in possession of a Type I IL-1R antigen. The scientific articles also collectively indicate that researchers were repeatedly successful in developing monoclonal antibodies of various type (murine, rat, hamster) that are immunoreactive with different mammalian Type I IL-1R polypeptides.

[57] The Final Action expresses the following particular concerns related to the nature of the antigenic material subsequently used by others:

> . . . publications originating with the applicant describing production of monoclonal antibodies, McMahan et al, Bomsztyk et al and Rogers et al, all include details not found in the description of the present application, use of a cell line expressing IL-1 R or use of an extracellular domain of IL-1 R as immunogen.

[58] However, we are not convinced that the alleged omission of these details is enough of a concern to conclude that the claims are not enabled. In fact, it is apparent that the specification discloses the actual construction, expression and purification of an extracellular domain of a Type I IL-1R (see Example 9). The specification also discloses the use of mammalian cell lines expressing IL-1R (see for example page 15, line 19 to page 16, line 4). Finally, we note that

example 7 explicitly contemplates the use of transfected mammalian cells expressing IL-1R and recombinant IL-1R (which is understood by reference to page 9, lines 18-20 to specifically include truncated and soluble forms of IL-1R) as immunogenic material to be used to generate monoclonal antibodies. Thus, even without the benefit of the Schooley affidavit we would say that we are satisfied that the skilled person would have been able to make anti-Type I IL-1R monoclonal antibodies relying only on the specification.

[59] Therefore, if the claims are appropriately limited by reference to Type I IL-1 receptor polypeptides, they can be considered enabled.

Written Description

[60] In the written submissions provided at the hearing the Applicant commented as follows:

> Applicant believes that the sole issue in this case is whether, at the time of the application, the state of the art concerning the preparation of monoclonal antibodies was sufficiently advanced such that the person skilled in the art could have made monoclonal antibodies based on the teachings of the specification without an unreasonable degree of experimentation.

[61] Although we agree that the specification would have enabled the skilled person to make monoclonal antibodies to a mammalian Type I IL-1R polypeptide (even as early as the time of filing), the question of whether the specification provides a Aspecific description@ of the claimed monoclonal antibodies remains. The notion of Aspecific description@ of a monoclonal antibody as expressed in the Final Action stems from the decision in *Pasteur*. In the written submissions provided at the hearing the Applicant has disputed what constitutes a specific description:

> First, Applicant disagrees with the Commissioner's conclusion [in *Pasteur*] that a description of monoclonal antibodies as neutralizing or binding with the antigen is not a specific description. Indeed, Applicant submits that binding of the antibody to the antigen is the ***very property*** of the monoclonal antibody that is central to describing the antibodies. [emphasis in original]

> Antibodies are complex biomolecules whose tertiary structure is generally known. It is not necessary to know the exact chemical structure of the antibody, such as its amino acid sequence, to make an antibody, to use the antibody or to describe the antibody properly.

> A monoclonal antibody (or any antibody) is principally useful because it specifically binds to a particular antigen. It is a routine and accepted practice to define and claim a monoclonal antibody by its ability to bind a specified antigen. [emphasis added]

[62] Although binding reactivity is a key property of monoclonal antibodies we do not necessarily see that it is the only relevant property or consideration. In fact the Applicant appears to acknowledge that it is acceptable to define and claim a monoclonal antibody by reference to a Aspecified antigen.@

[63] In *CSAHS* the Board considered a claim reciting a monoclonal antibody immunoreactive with a polypeptide characterized in part by a partial amino acid sequence and indicated at paragraph 135 that certain factors could be considered when asking whether the specification

provides an adequate written description of a monoclonal antibody capable of binding to a polypeptide:

(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.

[64] To the extent that guidance from other jurisdictions may be helpful, we again note that in other jurisdictions, as long as an applicant has fully characterized an antigen, claims to a monoclonal antibody immunoreactive with that specified antigen are generally permitted provided of course that the specified antigen and antibody meet the other requirements of patentability (see *HGS*, T 0018/09, T 0604/04, *supra*). *Noelle*, *supra* explains that, so long as the specification discloses 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 a monoclonal antibody by its binding affinity to that fully characterized antigen. Although the physical preparation of working embodiments is not a strict requirement in other jurisdictions, considerations beyond an indication of binding functionality may apply. The skilled person would also recognize that antibodies can be described in terms such as their avidity/affinity, ability to compete with other antibodies, as well as their pharmacological, inhibitory and neutralizing properties.

Written Description and Claim Scope

[65] As discussed above, claims 29, 54 and 58 use the term AIL-1R@ in an unqualified manner and they encompass Type II receptors. This brings into question the scope of claims 29, 54 and 58 in terms of written description for reasons similar to those expressed in *Noelle*, which, although not binding, is informative. In *Noelle* the court found that claims (whether specific or generic) which related to monoclonal antibodies immunoreactive with a human form of a cell surface antigen were problematic notwithstanding the disclosure of a monoclonal antibody immunoreactive with a murine form of the antigen B the reason being that the specification did not sufficiently describe or fully characterize the human antigen and one cannot define an unknown by its binding affinity to another unknown. Likewise in the present case, we find that the specification does not adequately describe or characterize a Type II receptor polypeptide and do not find that the characterization of Type I receptors translates into an adequate characterization of monoclonal antibodies immunoreactive with a Type II IL-1 receptor.

Written Description: Other Considerations

[66] For the same reasons stated in paragraph 54, the question arises whether the claimed antibodies would be considered to be properly described if they had been, or could be, appropriately limited by reference to Type I receptor polypeptides. In our view the answer to this question is yes.

[67] A specific structural description of a monoclonal antibody can be accomplished by providing particular structural information of the antigen binding regions, *i.e.* the complementarity determining regions (CDRs). Likewise it is possible to structurally describe a corresponding

epitope (although the task is more involved in the case of a three dimensional conformational epitope as opposed to the simpler case of a linear epitope). But it is not possible to deduce structural information of one from the other. However, there is specific and meaningful functional identity (specific immunoreactivity) between the two B a fact that is exploited during the apparent routineness of the preparation of monoclonal antibodies. In situations where the antigen is small it can be seen that the epitope may effectively or entirely equate to the antigen itself. In cases where the antigen is a more complex large polypeptide, possession of isolated pure polypeptide as well as provision of its structure effectively puts one in possession of all possible epitopes, whether they be conformational or linear. Thus the skilled person would appreciate that monoclonal antibodies can be adequately described based on a combination of a structural description of the antigen, functional identity between the antibody and antigen, and knowledge of predictable production methods.

[68] Since Canadian courts endorse consistency with other common-law jurisdictions on broader legal principles to the extent the case-law and legislation permits, and since the present case involves narrower issues related to a particular type of technology, we therefore accept the principle established in other jurisdictions that in cases where the antigen is a novel polypeptide and has been fully characterized, for example by complete amino acid sequence, a pioneering applicant can then claim monoclonal antibodies that are immunoreactive with the polypeptide without the applicant actually having made or deposited a specific embodiment. Such a claim would embrace, as subgenus of sorts, antibodies implicitly (or explicitly in the case of claim 58 for example) defined in relation to well-known monoclonal antibody production methods, which methods are understood to yield numerous species of monoclonal antibodies. Such a claim would not necessarily need to be restricted to any one species of monoclonal antibody since the skilled person would appreciate that there is neither commonality amongst the particular structures of the monoclonal antibodies= binding regions (CDRs) nor a predictable structural relationship between such binding regions and their target epitopes.

[69] However, the lack of actual physical possession of a hybridoma producing a monoclonal antibody is a consideration that cannot necessarily be overlooked in every case. Preparation and characterization may be required, for example, in cases where the antigenic material is complex (see for example *Alonso*, *supra*) or in cases where the antigen, although being novel in its entirety, is revealed upon complete characterization to possess substructures or epitopes common to a known antigen B something indicating that monoclonal antibodies immunoreactive with the novel antigen could be either inherently known, by virtue of cross-reactivity with the known antigen, or obvious. Moreover, claims reciting therapeutic or diagnostic antibodies or claims reciting antibodies with special attributes would require correspondingly detailed support.

[70] In the present case we find that the specification provides considerable description of novel Type I IL-1 receptors. In fact, such receptors from two species have been characterized in terms of complete amino acid sequence, maturation sites, glycosylation sites, molecular weights, conserved cysteine residues, as well as their intracellular, extracellular and transmembrane domains and their confirmed interleukin binding functionality. DNA sequences encoding such receptors have also been provided B something which allows for their production in high quantities through recombinant means.

[71] Therefore, notwithstanding the absence of a working example, and presupposing that the claims can be limited to Type I IL-1 receptors, we would consider monoclonal antibodies generally claimed as immunoreactive with such receptors to be adequately described.

Utility

[72] The claims were rejected for lack of support under subsection 174(2) of the Rules, and as a related aspect of that objection, the Final Action alluded to concerns with respect to support for the utility of the claimed monoclonal antibodies:

> [t]he monoclonal antibody product of claim 29 had not been made, and its properties, characteristics and utility could only be stated in general terms, which simply described what the hoped for product would do, bind to IL-1R polypeptide
> . . .
> Further there is no data confirming that monoclonal antibodies which are useful products, capable of binding only with IL-1R and with sufficient concentration to be useful assays or other applications, were produced.

[73] If anti-Type I IL-1 receptor monoclonal antibodies are enabled and can be made without undue experimentation, as is the case here, it follows that they would not be considered hoped-for products and that they would necessarily possess, because of the nature of the production method, the ability to bind to the immunizing antigen. As such, the soundness of their predicted utility is self-evident since: enablement is acknowledged; therapeutic antibodies, particular diagnostic antibodies, pharmaceutical compositions or antibodies with more special attributes are not claimed; and the skilled person would appreciate that a monoclonal antibody has at least one utility, for example, in assays or for immunopurification of IL-1 receptor polypeptides. Thus, in the present case an expression of utility stated in general terms is sufficient.

[74] Moreover, *Consolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd.*(1981), 56 C.P.R. (2d) 145 (S.C.C.) informs us that, so long as utility would be apparent to the skilled person, neither the description nor the claims need explicitly mention the utility of a novel product claimed as such. Unlike the situation in *HGS*, we do not have here a putative polypeptide whose function and utility has been identified simply by *in silico* analysis. Rather we have in this case receptor polypeptides whose function has been identified and confirmed and we note that no concerns in respect of the utility of the claimed polypeptides themselves have been raised.

POST-HEARING CORRESPONDENCE

[75] We have found that the claims directed to monoclonal antibodies, as they presently read, broadly encompass monoclonal antibodies immunoreactive with Type II IL-1 receptors. Having found that such receptors to be neither enabled nor adequately described in the specification, claims encompassing monoclonal antibodies immunoreactive with Type II receptors are too broad.

[76] Claims 29, 54 and 58 having been found to be too broad since they encompass Type II IL-1R polypeptides which have neither been described nor enabled, the Board found that other claims may also suffer from the same defect. For example, claim 51 B which is drawn to Aan antibody immunoreactive with IL-1R polypeptide@B suffers from the same defects as the monoclonal antibody claims since it too encompasses a Type II IL-1R polypeptide. That being the case, Board felt compelled to point out to the Applicant, before reaching any final conclusions, that other claims on file may also be problematic. In order to avoid the issuance of a patent with other claims of potentially questionable scope, while affording the Applicant the opportunity to address our concerns, and to operate in an expedient manner, it was considered appropriate to

inform the Applicant and give the Applicant the opportunity to address these concerns at the review stage. Accordingly, the Applicant was informed of the Board=s concerns with claims directed to polypeptides in a letter dated November 25, 2008.

[77] The Applicant responded to the Board=s letter on August 24, 2009 proposing claim amendments that would restrict the claims, whether directed to polypeptides or monoclonal antibodies, to Type I IL-1 receptors by incorporating features which would appropriately distinguish between the two types.

CONCLUSIONS

[78] In summary, the Board concludes that claims 29, 54 and 58 are too broad and do not comply with Subsection 174(2) of the Rules and Subsection 34(1) of the Act since they encompass monoclonal antibodies immunoreactive with polypeptides (Type II IL-1 receptors) which have neither been described nor enabled. However, it appears that claim amendments can be made which will appropriately limit the scope of, not only the rejected claims, but other claims suffering from the same defects. If such amendments are made we would consider the rejection to be overcome.

RECOMMENDATIONS

[79] It is our recommendation that, in accordance with paragraph 31(c) of the *Patent Rules*, the Commissioner inform the Applicant that the proposed amendments to claims 4, 6, 11, 12, 13, 14, 15, 16, 21, 23, 24, 25, 26, 28, 29, 30, 33, 47, 49, 50, and 51 outlined in the Applicant=s correspondence dated August 24, 2009 are required for compliance with the Act and Rules. In so doing, claims 54 and 58 would be remedied as well since these claims refer to overly-broad claims 11-13, 30, 33, 49 and 50 which themselves would be appropriately limited through the proposed amendments.

[80] We further recommend that:

(i) the Applicant be invited to make only the above amendments within three months from the date of the Commissioner=s decision;

(ii) the Applicant be advised that, if the above amendments and only the above amendments, are not made within the specified time, the Commissioner intends to refuse the application; and

(iii) the Applicant be advised that, if the above amendments and only the above amendments, are made within the specified time, the Commissioner will consider the outstanding issues to have been addressed.

Ed MacLaurin Mark Couture Paul Fitzner

Member Member Member

COMMISSIONER=S DECISION

[81] I concur with the findings and recommendation of the Patent Appeal Board.

[82] In accordance with paragraph 31(c) of the *Patent Rules*, I hereby inform the Applicant that the proposed amendments to claims 4, 6, 11, 12, 13, 14, 15, 16, 21, 23, 24, 25, 26, 28, 29, 30, 33, 47, 49, 50, and 51 outlined in the Applicant=s correspondence dated August 24, 2009 are required for compliance with the Act and Rules.

[83] 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.

[84] If the above amendments, and only the above amendments, are made within three months from the date of this decision I will consider the outstanding issues to have been addressed.

Mary Carman

Commissioner of Patents

Dated at Gatineau, Quebec
this 17 day of May, 2010