Commissioner=s Decision # 1283
Décision du Commissaire # 1283

TOPIC: B00, C00
SUJET: B00, C00

Application No.: 605,669
Demande no.: 605,669

COMMISSIONER=S DECISION SUMMARY

C.D. 1283 .... Application No. 605,669

Lack of Support (C00), Indefiniteness (B00)

The application related to a subunit polypeptide of insulin-like growth factor binding complex. Claims to nucleic acids encoding the polypeptide and claims to antibodies immunoreactive with the polypeptide were rejected by the examiner for lack of support under Rule 174(2) and also for being indefinite contrary to subsection 34(2) of the Act. The applicant submitted that the claims were fully enabled and that a person of skill in the art could obtain the claimed products using routine methods and that the claims accurately delimited the scope of the proposed monopoly. The Board relied on subsection 34(1) of the Act in its analysis and considered that compliance with that subsection demanded that the claimed subject matter be enabled and adequately described. The Board found that claimed nucleic acids were neither enabled nor described but found that the claimed antibodies, in general, were enabled and described. However, a specific claim to a monoclonal antibody, although enabled, was not considered to be adequately described. The Board found that the nucleic acid claims complied with subsection 34(2) of the Act but found that the antibody claims did not since the antibodies were defined in relation to an ill-defined target polypeptide. The Board recommended that the applicant be given the opportunity under Rule 31(c) to remediate the claims through claim cancellation and amendment in accordance with its findings, failing which it was the Board=s recommendation that the entire application be refused. The Commissioner of Patents agreed and the applicant was so informed.

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 605,669 having been rejected under Subsection 30(4) of the *Patent Rules*, the Applicant asked that the Final Action of the Examiner be reviewed. The rejection has consequently been considered 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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I. INTRODUCTION

[1] This decision deals with a request that the Commissioner of Patents review the Examiner=s Final Action on patent application 605,669.

[2] The Applicant is Central Sydney Area Health Service. The inventor is Robert C. Baxter and the invention is entitled AACID-LABILE SUB-UNIT ALS OF INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN COMPLEX.@

II. BACKGROUND

(a) The Technology

[3] By way of background information, the application teaches that peptides of the insulin-like growth factor (IGF) family resemble insulin in terms of their structure and function, producing a range of biological activities such as stimulation of glycogen synthesis and stimulation of cell differentiation. Unlike most hormones, IGFs are associated in the circulatory system with one or more binding proteins. One such protein is an acid-stable protein which has a molecular weight of 53 kilodaltons (Kd). Within this class are other acid-stable IGF binding proteins with varying molecular weights.

[4] The subject matter of the application principally relates to an acid-labile subunit (ALS) protein of IGF which binds to and stabilizes a complex between IGF and the aforementioned acid-stable 53 Kd protein (also referred to as ABP-53").

[5] The application includes claims to an ALS polypeptide, pharmaceutical compositions comprising ALS, methods of purifying ALS, methods of detecting ALS, a nucleic acid sequence encoding ALS, antibodies capable of binding ALS, and related subject matter.

(b) Prosecution History

[6] The subject application was filed on July 14, 1989 and the examiner in charge of the application issued a Final Action on March 20, 1998 in which claims 19 to 34 then pending in the application were rejected ostensibly for lack of support under Subsection 174(2) of the *Patent Rules*. The Final Action closed with an indication that the compounds covered by the claims are not described in distinct and explicit terms as required by Subsection 34(2) of the *Patent Act* as it read immediately before October 1, 1989.

[7] On September 21, 1998 the Applicant replied to the Final Action and argued that the claims on file were not open to rejection on the grounds outlined by the Examiner. No new claims were submitted.

[8] In the Examiner=s estimation, the Applicant=s reply to the Final Action did not overcome the objections raised in the Final Action. In accordance with Subsection 30(6) of the *Patent Rules*, the Applicant requested an oral hearing before the Patent Appeal Board and a review by the Commissioner of Patents. The oral hearing was held on November 8, 2007. At the hearing, the Applicant was represented by Joy Morrow, Catherine Eckenswiller, and David Schwartz of the firm Fetherstonhaugh & Co. The Patent Office was represented by Daniel Begin, Section Head and Mike De Vouge, the Examiner now responsible for the application.

[9] At the hearing the Board heard additional oral submissions from the Applicant=s representatives. The oral submissions were accompanied by corresponding written submissions as well as two affidavits.

(c) The Claims in Dispute

[10] The contentious claims read as follows:

19. A recombinant nucleic acid sequence encoding the acid-labile subunit (ALS) of insulin-like growth factor (IGF).

20. A recombinant nucleic acid sequence according to claim 19, wherein said acid- labile subunit (ALS) has the following partial N-terminal amino acid sequence:
Gly
Asp Pro Gly Thr Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys
Ala
wherein said first amino acid may be Gly or Ala.

21. An expression vector containing the DNA sequence of claim 20.

22. A host cell, which is a prokaryotic or eukaryotic cell, transformed with the expression vector of claim 21

23. The recombinant nucleic acid sequence of claim 19 which is cDNA.

24. Acid-labile subunit (ALS) when produced by the host cell of claim 22.

25. An antibody reagent capable of binding to acid-labile subunit (ALS) of insulin-like growth factor (IGF) binding protein.

26. An antibody reagent according to claim 25 which is a monoclonal or polyclonal antibody.

27. An antibody reagent according to claim 25 or 26 which is labelled with one or more reporter groups.

28. An antibody reagent according to claim 27, wherein the reporter group is selected from fluorescent groups, enzymes or colloidal groups.

29. A nucleic acid isolate comprising nucleic acid encoding the sequence:
Gly
Asp Pro Gly Thr Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys
Ala
wherein said first amino acid may be Gly or Ala.

30. A nucleic acid isolate comprising nucleic acid encoding residues 1-5, 2-7, 5-9, 7-11, 8-14,11-15,13-17,3-9, 2-8, 4-10, 6-12, 8-14, 10-16, 12-18, 1-6, 3-9, 5-11, 7-13, 9-15, 11-17, 4-9, 6-11, 8-13,10-15, or 12-17 of acid-labile subunit (ALS), wherein the amino acid residues of acid-labile subunits (ALS) are numbered from the N-terminus of the amino acid sequence as defined in claim 1.

31. The nucleic acid isolate of claim 29 further comprising a replicable vector.

32. The nucleic acid isolate of claim 30 further comprising a replicable vector.

33. The nucleic acid isolate of claim 29 further comprising nucleic acid encoding a secretion signal ligated to the 5' end of nucleic acid encoding the sequence:
Gly
Asp Pro Gly Thr Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys Ala
Ala
wherein said first amino acid may be Gly or Ala.

34. A host cell transformed with the isolate of any one of claims 29 to 33.

[11] At the hearing, the Applicant=s representatives indicated that claim 19 would be deleted and that it was no longer in dispute.

(d) The Issues

[12] Having regard to the claims on file at the time the Final Action was written, the Board must review the prosecution and determine whether claims 20 to 34 lack support under Subsection 174(2) of the *Patent Rules* and determine whether they define the claimed subject matter in distinct and explicit terms as required by Subsection 34(2) of the *Patent Act*.

III. THE POSITION OF THE EXAMINER AND APPLICANT

(a) The Position of the Examiner

[13] The Examiner stated the following, in part, in the Final Action:

> Claims 19 to 34, directed to nucleic acids, expression vectors, transformed host cells, and antibody reagents, lack support from the disclosure and do not comply with Subsection 174(2) of the Patent Rules. Applicant has only isolated and partially purified ALS. Applicant has not prepared nucleic acids, vectors, transformed cell, or antibodies and is therefore not entitled to claim these products.
>
> Applicant has argued that the methodologies available to prepare the products defined in the claims are well known to persons skilled in the art. Applicant is referred to Commissioner's Decision #1206 (re: Canadian patent 1,338,323, issued 14 May 1996), which dealt with the issue of support for claims to monoclonal antibodies and hybridomas which had not been prepared but which were considered by the applicant to be predictable. The decision states that "the Applicant does not show by examples or broad statements the steps that were successfully used to produce hybridomas secreting monoclonal antibodies that are capable of binding only with the specific antigen. Had any hybridomas and monoclonal antibody for certain antigens been prepared, then it would have been arguable that other hybridomas and monoclonal antibodies which were claimed but unprepared or prepared but untested, could be allowable in view of the" sound prediction" principle. In this case there is no consideration given by the disclosure to any monoclonal antibody so that there is nothing upon which to base a sound prediction". The claims to hybridomas and monoclonal antibodies in the application were rejected by the Commissioner.
>
> The instant application can be distinguished from the application resulting in the Monsanto

decision (Monsanto Co. v. Commissioner of Patents [1979] 42 C.P.R. [2d] 161) wherein all of the claimed subject matter was disclosed and what was predicted was that all of the disclosed subject matter would have utility based on structural similarities between those compounds disclosed but not made and those disclosed, made, and tested. The Supreme Court in the Monsanto decision did not rule that products which were not disclosed and thus could not be described were patentable.

. . .

> While every claim in a patent application need not be fully exemplified, there must be full disclosure of the claimed subject matter. Applicant has not taught the steps required to successfully produce nucleic acids, vectors, transformed cells, or antibodies. Applicant is claiming hoped-for compounds which he has failed to demonstrate can be successfully produced or used. The compounds covered by claims 19 to 34 are not described "distinctly and in explicit terms" as required by Subsection 34(2) of the Patent Act as it read immediately before 1 October 1989 and therefore are not allowable.

(b) The Applicant=s Response and Submissions

[14] The Applicant=s arguments in favour of the patentability of the claimed subject matter consist of the following:

(i) a written response to the Final Action accompanied by copies of two court decisions from the United States, a copy of one page of claims from a corresponding United States patent application, a copy of a scientific article and a copy of certain pages from a laboratory textbook;
(ii) oral submissions presented at the hearing;
(iii) written submissions submitted at the hearing; and
(iv) affidavits from two scientific experts.

(i) The Response to the Final Action

[15] In the response to the Final Action, the Applicant put forth, in part, the following argument with respect to the Examiner=s rejection of the claims:

> This case can be reduced to the issue of sufficiency or otherwise of disclosure in respect of claims relating (A) to antibodies; and (B) to nucleic acid sequences.
>
> (A) The Antibody Claims 25 to 28
>
> The Goding reference referred to at page 10 is a very widely known detailed description of the manner in which monoclonal and indeed polyclonal antibodies may be produced. The title page and contents pages are forwarded herewith and we believe the Examiner can see that based on the teaching in the specification, a person skilled in the art would have clearly been able to produce both monoclonal and polyclonal antibodies according to the teachings of the specification as of the date of filing of the application.
>
> Insofar as specific examples of antibody production are described we refer the Examiner to page 18 lines 10 through 21 which describe the production of a polyclonal antiserum raised against 100 µg of purified ALS. This antiserum was successfully used in radioimmunoassay experiments, for example as described at page 18.
>
> The example on page 18 provides clear evidence of antibody production and a demonstration of utility by the invention date.
>
> Applicant respectfully submits that the state of the art as of the Canadian filing date was such that a person skilled in this art without use of the inventive faculty could have prepared not just polyclonal antibodies (as exemplified on page 18 (see above)), but also could have prepared monoclonal antibodies capable of binding to acid labile subunit (ALS) of insulin-like growth factor (IGF). The description clearly shows the preparation of ALS and the Examiner, in

deeming claim 1 allowable, appears to accept this. The question that arises then is whether or not there is support for claims to monoclonal antibodies based upon the preparation of ALS and based upon such statements as those found in the description on page 9, line 33 to page 10, line 19 highlighted above.

The Examiner relies upon Commissioner's Decision 1206 in rejecting claims 25 to 28. Applicant respectfully submits that for several reasons the Commissioner's decision is flawed.

. . .

The Goding reference referred to on page 10 concedes on page 59 in the chapter entitled "Production of Monoclonal Antibodies" that "the technology of hybridoma production is now firmly established". This statement supports Applicant's contention that the description is indeed sufficient for a person skilled in the art to go on to produce monoclonal antibodies without use of the inventive faculty.

. . .

The error in the scientific reasoning of the Commissioner [in the *Pasteur* decision] is manifest. A person skilled in this art knows there is a reasonable expectation that a monoclonal antibody can be produced to a particular antigen, but there is no reasonable expectation that a monoclonal antibody will produce a "cure". Many different monoclonal antibodies can be produced against antigen. Whether or not one or more such antibodies can then be used as a "cure" requires a further step, the end-product of which is not being claimed in any of claims 25 to 28.

A further error in the scientific reasoning of the Commissioner in Decision 1206 is the Commissioner's conclusion that the description of "monoclonal antibodies as neutralizing or binding with antigens is not considered a specific description". By definition each antibody is highly specific. Antibodies are commonly defined in terms of their antigen specificities.

. . .

With this understanding, the Examiner's admission quoted in the Commissioner's decision that "once an antigen is available, a hybridoma and a monoclonal antibody can be prepared using well established techniques" should be dispositive that monoclonal antibodies and hybridomas are for making and purifying the antigen.

. . .

(B) Claims to Nucleic Acids and Vectors and Host Cells Containing them (Claims 19 to 24 and 29 to 34)

Concerning the Examiner's objection to the remaining claims directed to recombinant nucleic

> acids, expression vectors and host cells containing the same and nucleic acid isolates (claims 19 to 23, 29 to 34) it is the Applicant's position that the specification provides a person with skill in the art with all that is necessary to practice the invention as claimed, given the state of knowledge in the field at the priority date of the application.
>
> It is the Applicant's position that the specification taught for the first time the isolation of the ALS peptide and provided amino acid sequence information of this polypeptide.
>
> Recombinant techniques were well known at the time the application was filed, and are generally outlined in the specification at pages 11-13. Given the ALS peptide and the present disclosure, the skilled artisan could readily obtain the claimed nucleic acids. This is demonstrated by the enclosed Exhibit A, Leong et al, which confirms that obtaining the claimed cDNA, vectors and transformed host cells is routine after protein isolation.

Exhibit A [a copy of Leong *et al.*, *Molec. Endocrinol.*, 1992, volume 6, pp. 870-876] shows the complete sequence of a vector used to express ALS. Exhibit A is meant only to confirm that the expression of ALS was in fact performed, after filing of the present application. Exhibit A is in no way an attempt to add information to the specification. It is the Applicant=s position that the vector can be constructed on the basis of the guidance provided in the specification.Exhibit A confirms the assertions in the application that a vector can be constructed to produce ALS. Applicant points out that no evidence has been presented which would cause doubt on the assertions in the application. On the other hand, Applicant has confirmed the assertions in the application with enclosed Exhibit A

As mentioned above, the specification teaches, for the first time, the isolation of the ALS peptide and provides amino acid sequence information of this polypeptide in Example 3 on page 26. On page 26, lines 19 to 21, Applicant states:

AThis amino acid sequence shows no obvious homology to other IGF proteins or receptors@.

A person skilled in this art armed with the specification is given ALS, in pure form, methods of purification of ALS in the Examples and methods for determining utility of ALS as well as the first 18 amino acid residues of ALS. It does not require use of the inventive faculty or undue experimentation to obtain (a) the complete amino acid sequence and then by reverse coding alternative nucleotide sequences all of which code for ALS, or (b) complementary DNA to messenger RNA coding for ALS given description pages 11-13. The inventor has provided clear directions in the specification as to how a person skilled in the art such as a technical assistant can practise the invention and this is all that is required.

(ii) The Written Submissions

[16] At the oral hearing the applicant present the Board with a brief outlining additional reasons why, in the Applicant=s opinion, the claims were compliant with the Act and the Rules. Those submissions read, in part, as follows:

> Applicant points out that *Institut Pasteur*, a decision by the Commissioner of Patents, does not alter the established law concerning sufficiency of description as established by the Supreme Court of Canada interpreting Section 34(1). This section, in essence, asks the inventor "What is your invention? How does it work?" [citing *Consolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd.*, [1981] S.C.R. 504. at 520]. A disclosure that does not enable any person skilled in the art to practice the invention is invalid for "insufficiency" [citing *Pioneer Hi-Bred Ltd. v. Canada (Commissioner of Patents)*, [1989] 1 S.C.R. 1623 & 29]
> . . .
> Applicant submits that, in setting forth the requirements for sufficiency of the specification, the

> Supreme Court was clear that the patent specification must **describe** the invention. The Supreme Court did not say that an invention must have been physically constructed before it can be patented. This is not a requirement for compliance with Section 34(1) of the *Patent Act* and Applicant submits that any interpretation of *Institut Pasteur* to this effect is simply incorrect.
> . . .
> Applicant draws the Commissioner's attention to the review of the Canadian case law regarding sufficiency of the patent description recited above and respectfully points out that the examiner erred by applying an incorrect test. In particular, the examiner took the position that nucleic acids, vectors and host cells could not be claimed for the reason they had not been prepared at the time of the application. As Applicant has pointed out above, the correct test, as affirmed by the Supreme Court of Canada, for sufficiency of a patent specification is whether the specification **describes** the invention, not whether the invention has been constructed. Accordingly, the examiner failed to consider whether the invention had been adequately described, but rather refused the claims for the reason that the embodiments had not been constructed.
> . . .
> Applicant respectfully submits that, as of July 15, 1988, the earliest priority date of the instant application, those skilled in the art, given the information in the patent specification, the state of the art and the widely available Maniatis manual, could have readily obtained a nucleotide sequence encoding an ALS polypeptide comprising the N-terminal amino acid sequence as set forth in claim 20. Furthermore, given the widely available technology as of the priority date, no undue experimentation would have been required to obtain this nucleotide sequence.
> . . .
> As discussed above, the patent application at issue in *Institut Pasteur* related to the discovery of a new class of HIV retrovirus, HIV 2. The inventors did not describe purifying or sequencing the proteins of HIV 2 nor did they provide any guidance as to how they would carry out such procedures. Furthermore, the inventors did not produce antibodies (either polyclonal or monoclonal) to proteins from HIV 2 nor did they include any information on the protocols that would be necessary to do so.
> . . .
> Applicant acknowledges that, in *Institut Pasteur*, it was open to the Commissioner of Patents to conclude that producing monoclonal antibodies to protein antigens from the HIV 2 virus was not sufficiently enabled by the description of the patent application before him. It was a factual determination that the Commissioner made based on the contents of the patent specification and the evidence before him at the time. However, Applicant respectfully submits that the inventors of the present application have provided a sufficient disclosure to enable one of skill in the art to produce antibody reagents to ALS. In particular, Applicant points out that the patent specification describes a well characterized antigen, which includes the amino acid sequence of the N-terminus. Furthermore, the inventors have described producing a polyclonal antibody to ALS, which is itself an antibody reagent and, as well, an important precursor to a monoclonal antibody. [emphasis in original]

[17] Certain other parts of the Applicant=s written submissions are quoted below.

(iii) The Affidavits from The Scientific Experts

[18] The first affiant for the Applicant was Dr. Charles Roberts, an expert in the field of biochemistry and molecular biology. The most pertinent excerpts from his affidavit are presented and discussed below in the Analysis section.

[19] The second affiant for the Applicant was Dr. James W. Goding, an expert in immunology and the author of *Monoclonal Antibodies: Principles and Practice* (Second edition, 1986, Academic Press)[*Goding*], one of the textbooks cited in *Re Institut Pasteur Patent Application* (1995), 76 C.P.R. 3d 206, Commissioner=s Decision No. 1206 [*Pasteur*]. The most pertinent

excerpts from his affidavit are also presented and discussed below in the Analysis section.

IV. LEGAL FRAMEWORK

(a) Statutory Provisions

[20] 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 as well as by the Section 38.1 of the Act as it now reads. Accordingly, unless otherwise indicated, references to the *Patent Act* in this document refer to the Act as it read immediately prior to October 1, 1989.

[21] Contrary to the Applicant=s statement in his written submissions to the Board, the present application is also clearly governed by Subsection 174(2) of the *Patent Rules* as they read on the date of the Final Action since that Subsection falls within Part V of the *Rules* under the heading AApplications Filed Before October 1, 1989.@

[22] 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.@

[23] Since a regulation is a subordinate form of legislation which cannot operate outside its enabling statute, Subsection 174(2) of the Rules should be read in conjunction with 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.

[24] A separate and distinct companion to Subsection 34(1) of the Act is Subsection 34(2) which reads as follows:

> (2) The specification referred to in Subsection (1) shall end with a claim or claims stating distinctly and in explicit terms the things or combinations that the applicant regards as new and which he claims an exclusive property or privilege.

[25] Since the present application deals with biological material, Section 38.1 of the Act as it now reads may come into play. That section is applicable by virtue of Section 78.1 of the *Patent Act* and reads as follows:

> (1) Where a specification refers to a deposit of biological material and the deposit is in accordance with the regulations, the deposit shall be considered part of the specification and, to

> the extent that Subsection 27(3) [formerly Subsection 34(1)] cannot otherwise reasonably be complied with, the deposit shall be taken into consideration in determining whether the specification complies with that Subsection.
>
> Deposit not required
>
> (2) For greater certainty, a reference to a deposit of biological material in a specification does not create a presumption that the deposit is required for the purpose of complying with Subsection 27(3).

[26] The date by which a biological deposit must be made is on or before the filing date: Section 184 of the *Patent Rules*.

(b) Case Law

(i) Subsection 174(2) of the Rules

[27] The courts have provided little judicial interpretation of Subsection 174(2) of the *Rules* or any its equivalents; *e.g.*, Section 25 of the *Rules* as they read before October 1, 1989, Subsection 138(2) of the *Rules* in respect of applications in the period beginning on October 1, 1989 and ending on September 30, 1996, or Section 84 of the *Rules* in respect of applications filed on or after October 1, 1996. However in *Re Application of CIBA* (1974), Commissioner's Decision No. 208, the Board, after noting that it may be possible for a single sentence in the disclosure to provide sufficient support to warrant claims to some inventions, stated 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 & 28, 27 C.P.R. 1), and the Board went on to consider whether the invention had been sufficiently described as required by the statute [then Section 35 of the *Patent Act*; Subsection 34(1) for today=s purposes] and as expressed by the case law. This approach was also taken by the Board in *Pasteur* when it considered whether there was Asupport@ for claims to monoclonal antibodies and hybridomas.

(ii) Subsection 34(1) of the Act

[28] The equivalent of Subsection 34(1) has been interpreted in *Minerals Separation North American Corp. v. Noranda Mines Ltd.*, [1947] Ex.C.R. 306 at 316-317 [*Minerals Separation*] to demand the following:

> Two things must be described in the disclosures of a specification, one being the invention, and the other the operation or use of the invention as contemplated by the inventor, and with respect to each the description must be correct and full. The purpose underlying this requirement is that when the period of monopoly has expired the public will be able, having only the specification, to make the same successful use of the invention as the inventor could at the time of his application. The description must be correct; this means that it must be both clear and accurate. It

> must be free from avoidable obscurity or ambiguity and be as simple and distinct as the difficulty of description permits. It must not contain erroneous or misleading statements calculated to deceive or mislead the persons to whom the specification is addressed and render it difficult for them without trial and experiment to comprehend in what manner the invention is to be performed. It must not, for example, direct the use of alternative methods of putting it into effect if only one is practicable, even if persons skilled in the art would be likely to choose the practicable method. The description of the invention must also be full; this means that its ambit must be defined, for nothing that has not been described may be validly claimed. The description must also give all information that is necessary for successful operation or use of the invention, without leaving such result to the chance of successful experiment, and if warnings are required in order to avert failure such warnings must be given. Moreover, the inventor must act *uberrima fide* and give all information known to him that will enable the invention to be carried out to its best effect as contemplated by him. [emphasis added]

[29] Affirming these comments are those of the Supreme Court in *Consolboard Inc. v. MacMillan Bloedel (Sask.) Ltd.*, [1981] S.C.R. 504 & 27, 6 C.P.R. (2d) 146 [*Consolboard*]:

> Section [34(1)] seeks an answer to the questions: "What is your invention?" How does it work?" With respect to each question the description must be correct and full in order that, as Thorson P. said in *Minerals Separation North American Corporation v. Noranda Mines, Limited* . . . [emphasis added]

[30] It was also stated in *Consolboard* at paragraphs 22 - 23 that:

> Section 36 of the Patent Act lies at the heart of the whole patent system. The description of the invention therein provided for is the *quid pro quo* for which the inventor is given a monopoly for a limited term of years on the invention. As Fox points out in Canadian Patent Law and Practice (4th ed.), p. 163, the grant of a patent is in the nature of a bargain between the inventor on the one hand and the Crown, representing the public, on the other hand. The consideration for the grant is twofold: "first, there must be a new and useful invention, and secondly, the inventor must, in return for the grant of a patent, give to the public an adequate description of the invention with sufficiently complete and accurate details as will enable a workman, skilled in the art to which the invention relates, to construct or use that invention when the period of the monopoly has expired". The "description" to which Fox refers is that required by s. 36 of the Patent Act.
>
> It cannot be said that s. 36 of the Act is happily phrased. It gives the impression of a mélange of ideas gathered at random rather than an attempt to enunciate, clearly and concisely, a governing principle or principles. This is perhaps understandable in that the section is the product of amendment over a period of many years. The language simply does not lend itself to a tight, literal interpretation. It is, and should be treated as, a parliamentary pronouncement, in general terms, of that which must be set forth by the applicant to the world before being qualified to receive the grant of monopoly under a patent.

[31] In a decision that touched biological subject matter the Supreme Court commented favourably on both *Consolboard* and *Minerals Separation* adding in *Pioneer Hi-Bred Ltd. v. Commissioner of Patents*, [1989] 1 S.C.R. 1623 & 27, 25 C.P.R. (3d) 257 [*Pioneer Hi-Bred*] that:

> Disclosure also has an important part to play in identifying the steps followed and distinguishing between the discovery of a theoretical principle or a product occurring in nature and an invention which requires human activity for its development . . . The specification will thus facilitate the work of the Examiner and the Commissioner of Patents as well as the task of appellate Courts.

[32] *Pioneer Hi-Bred* (& 31-32) is also authority for the proposition that methods outlined in a patent specification for obtaining a biological product -- in that case a plant variety developed through plant breeding -- must allow a person of skill in the art to arrive at the invention claimed without other instructions and that the invention must not be a Adiscovery by chance@. The facts in that case indicated that the inventor had employed Aunique controlled plant breeding techniques@ and that a person skilled in the art could only discover the steps involved by empirical means.

[33] From *Minerals Separation*, *Consolboard* and *Pioneer Hi-Bred* we gather that, fundamentally, compliance with Subsection 34(1) requires that the specification provide two fundamental things: (i) a written description of the claimed invention, and (ii) an enabling description of how of the invention, actually was, or at least can be put into practice. In respect of each requirement it is understood that there must be a correct and full compliance; AThe onus of disclosure that [Subsection 34(1)] places on an inventor is a heavy and exacting one@: *Radio Corporation of America v. Raytheon Manufacturing Co.* (*supra*). There must be a level of assurance that the inventor has fulfilled his end of the bargain and has paid for his monopoly in Ahard coinage@: *Apotex Inc. v. Wellcome Foundation Ltd.*, 2002 SCC 77 & 37, [2002] 4 S.C.R. 153, 21 C.P.R. (4th) 499. A correct and full specification also facilitates the work of the Examiner and Commissioner.

[34] Concerning the requirements of Subsection 34(1), the court in *Ernest Scragg & Sons Ltd. v. Leesona Corp.*, [1964] Ex. C.R. 649 & 209 stated the following:

> It is settled law that a patent specification is not insufficient by reason of the fact that a competent workman of ordinary skill in the art to which the invention relates may have to make trials or experiments in order to accomplish the result of the invention, if such trials or experiments are not themselves inventions and the competent workman can accomplish the desired result by following the teaching of the specification. The specification is sufficient if it enables him to put the invention into practice and sufficient directions are given to him to enable him to know what trials or experiments he may have to make and how to make them.

[35] However, in *Di Fiore v. Tardi* (1952), 16 C.P.R. 18 (Ex. Ct.) it was stated that:

> If a specification by itself will not enable a person skilled in the art to which it relates to put the invention to the same successful use as the inventor himself could do, without leaving the result to the chance of successful experiment, the specification is insufficient to comply with the requirements of s. 35(1) of the Act [now Subsection 27(3)] and the patent falls. [emphasis added]

[36] Accordingly, there is balance to be struck between acknowledging the skills carried by a competent workman and acknowledging any shortcomings of a patent specification.

[37] A particular case on point is *Pasteur* (*supra*) which related to the issue of lack of specific support for specific claims to anti-HIV-2 monoclonal antibodies and hybridoma cells producing them. In that case the specification provided neither a full description of the claimed monoclonal antibodies nor the method by which they could be produced. The Board stated, in part, the following:

> The questions before the Board are whether or not the specification describes correctly and fully the preparation and the properties of the hybridoma and the monoclonal antibodies claimed in claims 84 and 85, **and** whether or not such description is set out in such clear concise terms as to enable a person skilled in the art to make and use the invention as required by Subsection 34.(1) of the Patent Act which reads as follows . . .
>
> The Board cannot find any description of the hybridoma of claim 85 or any description of a method of preparing it provided in the above cited statements or in the entire description. No specific description of the monoclonal antibodies in claim 84 or a process for their preparation is disclosed. The only guidance as to the description of the monoclonal antibodies and the process by which they may be prepared is that they can be prepared by "traditional techniques." The sole specific technical teaching provided is the identity of the antigens. Describing and identifying the antigens does not provide support for the hybridoma or the monoclonal antibodies **nor** does it provide sufficient instruction on how to make the antibodies. [emphasis added]

[38] The Board concluded as follows:

> The Board concludes that the hybridomas and the monoclonal antibodies embraced by the claims 84 and 85 are not described or enabled by the present disclosure as required under Subsection 34(1) of the Patent Act. [emphasis added]

[39] From this we conclude that the specification in *Pasteur* was viewed by the Board to be defective in respect of both the written description requirement and the enablement requirement. In the end the applicant was granted a patent with generic claims to an antibody which specifically recognized an HIV-2 antigen.

[40] A more recent case on point is *Re Application of Alonso* (2006), Commissioner=s Decision No. 1269 [*Alonso*], which related to the issue of support for broad claims that encompassed many different types of anti-tumour monoclonal antibodies. In that case the examiner contended that the claims should be limited to the singular monoclonal antibody which had been actually deposited. The Board concluded as follows:

> Section 38.1 of the Act provides for a deposit of biological material to be considered as part of the specification and taken into consideration in determining if Subsection 34(1) of the Act has been complied with. A deposit can therefore be used to supplement the written description of the invention where the requirements of Subsection 34(1) of the Act cannot be complied with by words alone.
>
> In the instant application, the Applicant has disclosed an allegedly novel method for preparing human-human hybridomas secreting monoclonal antibodies. Fifty-six examples are provided where hybridomas were prepared according to the method. Each hybridoma is

> described in terms of the tumour and spleen cells which were mixed together, a fusion line, and class of monoclonal antibody secreted. Each example states that the antibody reacts with an idiotypic surface antigen. Each type of tumor cell listed in claim 7 is used in at least one of the examples.
>
> The Board is satisfied that the Applicant has described its hybridomas and their method of preparation in sufficient detail that one of skill in the art could practice the invention without a reference to a biological deposit. The Board does not agree that claims 10 and 11 are broader in scope than the teachings of the description and must be restricted to [a particular deposited hybridoma]. [emphasis added]

[41] Accordingly, provided there is full support, there is no strict requirement that the claims be limited to only those monoclonal antibody producing hybridomas which had been deposited or that the claims be limited to particular monoclonal antibodies. Importantly, the decision affirms the notion that a deposit may be taken into consideration where words alone may not completely and fully describe a claimed invention. However, reference to a deposit is not intended to replace a written description of an invention but rather to supplement it.

[42] In *Re Application of Yeda Research & Development Co.* (2007), 59 C.P.R. (4th) 464, Commissioner's Decision No. 1273 [*Yeda R & D*], we see a similar scenario played out in respect of a claim to a tumour necrosis factor binding protein prepared by recombinant means as well as a claim to a DNA molecule encoding the protein. In that case the application described the isolated protein and characterized it in terms of partial structure. The application further described techniques -- which themselves were known -- that could conceivably be used to isolate and then characterize a DNA molecule encoding the protein. The Board concluded as follows:

> In the instant application, the Board is satisfied that the Applicant, or one of skill in the art, would have been able to use the amino acid sequence encoding a fragment of TBP-II as a tool to eventually obtain a nucleotide sequence encoding TBP-II and thereafter the products defined by claims 21 to 23, to be used in the process of claim 24. However, the application does not disclose the nucleotide sequence which forms the basis of the claims. Rather, the application describes only a pathway or process to be followed to obtain such a sequence and essentially invites others to follow the pathway to isolate the sequence. In this respect, the application is similar to the APasteur@ application. The Board is not satisfied that there has been Aproper disclosure@ in respect of a TBP-II-encoding nucleotide sequence and hence there is no support for the products and processes defined by claims 21 to 24. The *quid pro quo* of the patent system is that one must disclose one=s invention in exchange for the rights conferred by a patent. [emphasis in original]

[43] From this decision we conclude that the specification in this application was viewed by the Board as principally defective in respect of the written description requirement; the Board having no apparent disagreement with the fact that the specification provided a description of how a person of skill in the art could go about obtaining the desired DNA product.

(iii) The Relevant Date for Assessing Compliance with Subsection 34(1) of the Act

[44] As indicated below in the Analysis section, we do not see the issue of the relevant date for assessing compliance with Subsection 34(1) in respect of the enablement requirement as critical to our findings in the present case. However, in respect of the written description requirement of Subsection 34(1) we are unable to accept the position of the Applicant.

[45] At the hearing and in their corresponding written submissions the Applicant placed considerable emphasis on the proposition that the relevant date for assessing compliance with Subsection 34(1) of the Act is the date the patent is eventually granted. The Applicant submitted the following:

> Nevertheless, it is very important to note that, for a Canadian patent application filed before October 1, 1989, the date at which compliance with section 34(1) of the *Patent Act* is required is the date that the patent is **granted**. See *AlliedSignal Inc. v. Du Pont Canada Inc.* (1995), 61 C.P.R. (3d) 417 (FCA).
>
> This issue was recently discussed in detail in *Aventis Pharma Inc. v. Apotex Inc.* (2005), 43 C.P.R. (4th) 161, affirmed (2006), 46 CP.R. (4th) 401, as follows:
>
> > [262] In *AlliedSignal Inc. v. Du Pont Canada Inc.*, [1995] F.C.J. No. 744 (QL), 61 C.P.R. (3d) 417, &23, the Federal Court of Appeal was called upon to determine the appropriate date for the purposes of assessing the sufficiency of the disclosure. The trial judge had used the priority date - that is the filing date of the corresponding U.S. patent - rather than the date on which the Canadian patent was issued. In concluding that the trial judge had erred in this regard, the Federal Court of Appeal held that it is the date of issue that should be used for assessing the sufficiency of disclosure rather than the priority date.
> >
> > [267] I recognize that using the date of issue for the purposes of assessing the sufficiency of the disclosure in the '206 patent in these circumstances has the effect of allowing Schering to provide deficient consideration for the grant of monopoly rights, and to then benefit from advances in the state of public knowledge and understanding while the application is pending.
> >
> > [268] Nevertheless, AlliedSignal appears to represent the current state of the Canadian law on this point. As a consequence, given that the alleged invention contained in the '206 patent could be put into effect, based upon the general knowledge that would be possessed by a skilled person in 2001, Apotex has not succeeded in persuading me that the '206 patent is invalid for failure to comply with the requirements of Subsection 34(1) of the old Patent Act.
>
> The law is clear that, in the present application, filed before October 1, 1989, the specification need only comply with section 34(1) of the *Patent Act*, **as of the date that the application issues to patent**. Applicant submits that there is no doubt that, as of **today's date**, the preparation of nucleic acids encoding a partially sequenced protein, expression vectors comprising the nucleic acids, cells transformed with the vectors, and polyclonal and monoclonal antibodies to an antigen of interest are all routine matters within the abilities of a person of ordinary skill in the art. [emphasis in original]

[46] In response to this we note that the *AlliedSignal* decision did not expressly overrule earlier cases which point to the filing date as the relevant date. These other cases include *De Forest Phonofilm of Canada Ltd. v. Famous Players Canadian Corp.*, [1931] Ex. C.R. 27 & 19; and *American Cyanamid Co. v. Charles E. Frosst & Co.*, [1965] 2 Ex. C.R. 355 & 228, 47 C.P.R. 215. Decisions from other jurisdictions subsequent to *AlliedSignal* which more closely align with the facts of the present case also indicate that the filing date is the relevant date: see *Biogen Inc. v. Medeva PLC* (1996), [1997] R.P.C. 1 at 54 (H.L.); and *Chiron Corp. v. Genentech Inc.* (2004), 70 U.S.P.Q.2d 1321 at 1325-1326 (Fed. Cir.), 363 F.3d 1247.

[47] In view of the foregoing we are not convinced that the matter is well settled in respect of the enablement requirement of Subsection 34(1).

[48] We also note that the *AlliedSignal* decision did not expressly rule on the relevant date for assessing compliance with the written description requirement of Subsection 34(1). In this respect we do not accept *AlliedSignal* as authority for the proposition that a deficiency in written description can be remedied based on what is known today. To say that the relevant date for assessing compliance with the written description requirement is the day the patent actually issues to patent defies the whole scheme of the *Patent Act.* If the relevant date for providing a written description of an invention was the date of issue, the public would get nothing of substance in exchange for suffering a monopoly.

[49] In addition we note that there are also several indications in the *Patent Act* which suggest that the relevant date for assessing compliance with Subsection 27(3) [formerly Subsection 34(1)] is the filing date.

[50] Section 38.1 of the Act indicates that biological deposits may be taken into consideration when assessing biotechnological inventions for compliance with Subsection 27(3) but sections 104, 160, and 184 of the *Patent Rules* indicate that deposits *must* be made on or before the *filing date* otherwise they cannot be considered. Therefore, in the case of an invention which relies on a biological deposit in order to satisfy the written description and/or enablement requirements of Subsection 27(3) it is clear by statutory definition that the relevant date is the filing date.

[51] Subsection 38.2(2) of the Act indicates that the specification cannot be amended to add matter not reasonably to be inferred from the specification or drawings *as originally filed*; *i.e.*, no new written description may be added, including descriptions of critical structural information, such as a complete amino acid sequence, discovered after filing.

[52] Remembering that Subsection 34(1) lies at the whole heart of the patent system, we therefore reject the notion that an applicant can monopolize something he cannot describe at the time of filing by pointing to a description of the invention only provided to the public later.

(iv) Foreign Authorities Relevant to Subsection 34(1)

[53] Both the Examiner and the Applicant have referred to various authorities from the United States in support of their position.

[54] For example, in the Final Action the Examiner referred to *Fiers v. Sugano* (1993), 25 U.S.P.Q.2d 1601B1607 (Fed. Cir.) as authority for the proposition that a claim to a chemical molecule (in that case, a nucleic acid encoding human fibroblast beta-interferon) requires more than a conception of the molecule; what is required is a precise written description of the molecule, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed molecule.

[55] In the written submissions the Applicant referred to *Noelle v. Lederman* (2004), 69 U.S.P.Q.2d 1508 (Fed. Cir.) as authority for the proposition that as long as an applicant can fully describe an antigen, either by structure, chemical name, or physical properties, or by depositing the antigen in a public depository, then the applicant can then claim an antibody, including a monoclonal antibody, by its binding affinity to that described antigen.

[56] While United States decisions are not binding in Canada, we do understand that they can be of some guidance, especially in view of the fact that the wording of Subsection 34(1) was

originally borrowed from the equivalent section of the United States statute. However, we have comfortably reached only two conclusions after having considered United States practice. Firstly, we note that United States practice, based on numerous decisions, recognizes that under 35 U.S.C. 112 first paragraph there is a written description requirement and a separate enablement requirement: United States Patent and Trademark Office *Manual of Patent Examination Procedure*, Section 2161. Secondly, it is apparent that under United States practice, a specification can be considered enabling without describing the invention and visa-versa.

[57] Apart from the law in the United States, we also note that Lord Hoffman in *Synthon BV v. SmithKline Beecham plc*, [2005] UKHL 59 commented at paragraph 28 as follows:

> It is very important to keep in mind that disclosure and enablement are distinct concepts, each of which has to be satisfied and each of which has its own rules.

[58] Thus, this decision from the United Kingdom also affirms the existence of the same two distinct legal concepts, disclosure [written description] and enablement, each of which must be examined for the purpose of assessing sufficiency.

(v) Subsection 34(2) of the Act

[59] Turning now to guidance on Subsection 34(2) of the Act, we note that the following was stated in *Minerals Separation* (at 352):

> By his claims the inventor puts fences around the fields of his monopoly and warns the public against trespassing on his property. His fences must be clearly placed in order to give the necessary warning and he must not fence in any property that is not his own. The terms of a claim must be free from avoidable ambiguity or obscurity and must not be flexible; they must be clear and precise so that the public will be able to know not only where it must not trespass but also where it may safely go.

[60] In *Yeda R & D* the Board, citing *Minerals Separation* as authority, also considered a rejection to a claim based on Subsection 27(4) (formerly Subsection 34(2)) of the Act) in respect of a claim to the tumour necrosis factor binding protein which was defined in terms of its partial structure and function. In that case the Board took no issue with the language of the claim and found that A[i]t is clear to the Board what the Applicant seeks to protect@; thus acknowledging that the Apublic notice function@ of the claims had been accomplished: *Whirlpool Corp. v. Camco Inc.*, [2000] 2 S.C.R. 1067 & 42, (2001) 9 C.P.R. (4th) 129.

V. ANALYSIS AND FINDINGS

[61] Although claims 19 to 34 appear to have been rejected for the same reasons, the claims relate to two types of technical subject matter: nucleic acid molecules (claims 19 to 24 and 29 to 34) and antibodies (claims 25 to 28). Since each type of subject matter presents their own technical issues we will deal with each claim grouping separately.

[62] Accordingly, there are a number of particular issues related to the nucleic acid claims that must be addressed: whether the nucleic acid claims comply with Subsection 34(2); whether the nucleic acid claims comply with the enablement requirement of Subsection 34(1); and, whether the nucleic acid claims comply with the written description requirement of Subsection 34(1). These same particular issues will also be addressed in order in respect of the antibody claims.

[63] Since the Applicant indicated at the hearing that claim 19 will be deleted, we will proceed on the understanding that this claim is not in dispute and that it will be deleted. No consideration will be given to this claim.

(a) Compliance of the Nucleic Acid Claims with Subsection 34(2) of the Act

[64] The last sentence of the Final Action states that Athe compounds covered by claims 19 to 34 are not described >distinctly and in explicit terms= as required by Subsection 34(2) of the Patent Act as it read immediately before 1 October 1989 and therefore are not allowable.@ Although only mentioned in passing in the Final Action and assumed by the Applicant B based on the Examiner=s other comments B to be intended to be a Subsection 34(1) defect, we will nonetheless address any issue with Subsection 34(2) before proceeding to the more substantive issue of compliance with Subsection 174(2) of the Rules and Subsection 34(1) of the Act. The same will hold true for our analysis of the antibody claims.

[65] Claims 20, 29 and 30 are representative of the nucleic acid claims which were rejected in the Final Action and which are still contested. These claims read as follows:

> 20. A recombinant nucleic acid sequence according to claim 19, wherein said acid- labile subunit (ALS) has the following partial N-terminal amino acid sequence:
> Gly
> Asp Pro Gly Thr Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys
> Ala
>
> wherein said first amino acid may be Gly or Ala.
>
> 29. A nucleic acid isolate comprising nucleic acid encoding the sequence:
> Gly
> Asp Pro Gly Thr Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys
> Ala
>
> wherein said first amino acid may be Gly or Ala.
>
> 30. A nucleic acid isolate comprising nucleic acid encoding residues 1-5, 2-7, 5-9, 7-11, 8-14,11-15,13-17,3-9, 2-8, 4-10, 6-12, 8-14, 10-16, 12-18, 1-6, 3-9, 5-11, 7-13, 9-15, 11-17, 4-9, 6-11, 8-13,10-15, or 12-17 of acid-labile subunit (ALS), wherein the amino acid residues of acid-labile subunits (ALS) are numbered from the N-terminus of the amino acid sequence as defined in claim 1.

[66] Starting first with claim 20, we note that the claim refers to a Arecombinant nucleic acid sequence@ which encodes the Aacid-labile subunit (ALS) of insulin-like growth factor (IGF)@ which is characterized by the partial N-terminal amino acid sequence(s) indicated in the claim.

[67] The field of the invention indicates that the Ainvention relates to a previously unknown and uncharacterized polypeptide, hereinafter referred to as the acid-labile sub-unit (ALS) of insulin like growth factor (IGF) binding protein complex.@ The term AALS@ is used numerous times in the description, for example starting on page 5, line 12 to page 7, line 26:

> - AThe present invention relates to ALS, a polypeptide which binds to, and stabilizes in-vivo, a complex between IGF and its acid-stable binding protein BP-53" (page 5, lines

12-15);
- AALS preferably has the following partial N-terminal amino acid sequence . . .@ (page 6, lines 28-29) ;
- AALS is functionally defined as an acid-labile polypeptide which is capable of binding to or associating with complexes formed when IGF is bound or associated with the acid stable binding protein BP-53 defined above@ (page 7, lines 4-7); and
- AALS may be characterized in that it:
(i) is acid-labile, that is, it is unstable at a pH less than 4,
(ii) binds to an acid stable IGF binding protein which is occupied by IGF, and
(iii) has an approximate molecular weight between 80 Kd and 115 Kd as determined by SDS-PAGE@ (page 7, lines 16-22). [emphasis added]

[68] From the description we gather that some of these features used to describe the ALS polypeptide are merely preferred, *e.g.* the N-terminal amino acid sequence and its molecular weight. Therefore we understand that the term AALS@ when used alone literally encompasses any polypeptide with the stated functionality.

[69] Importantly, the amino acid sequence referred to in claim 20 serves a critical function in distinguishing the ALS polypeptide of the claims from other types of polypeptides since the N-terminal sequence is said to show Ano obvious homology to other IGF proteins or receptors@ (page 26, lines 20 to 21).

[70] The expression Arecombinant nucleic acid sequence@ would be understood by a person of skill in the art as implying that the nucleic acid sequence of the claim was, or could be, prepared or obtained using techniques commonly used in the art of molecular biology or genetic engineering such as those outlined in *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbour Laboratory, New York, 1992, Maniatis et. al. (referred to on page 11, line 5 of the description [*Maniatis*]).

[71] Since the claim uses the term Asequence@ there may be a marginal basis for suggesting that the claim is ambiguous in that it is improperly directed to Asequence information@ as opposed to proper subject matter, *i.e.* a chemical compound. However, we will proceed on the reasonable assumption that the term Asequence@ would be understood by a person of skill in the art to mean Asequence molecule@ or simply Amolecule@. Thus the claim is reliant on the provision of a nucleotide Asequence structure@ of a nucleic acid molecule and not simply a nucleic acid molecule inherently capable of encoding an ALS polypeptide.

[72] In view of the foregoing, a person of skill in the art would understand that the subject matter which the A*applicant regards* as new and which he claims an exclusive property or privilege@ is a family of nucleic acid molecules which may be prepared using recombinant techniques and which encode a polypeptide that binds to, and stabilizes *in vivo*, a complex between IGF and its acid-stable binding protein BP-53, and which minimally comprises the partial N-terminal amino acid sequence(s) recited in claim 20. It is through these Athings or combinations@ that the Applicant states in distinct and explicit terms that which he proposes to monopolize.

[73] In this case we conclude that the meaning of the terms and limitations used in claim 20 with respect to the ALS polypeptide would be understood by a person of skill in the art. There does not appear to be any reason that would suggest a person of skill in the art would not be able to comprehend the meaning of the claim language or its scope. Just as in *Yeda R & D*, we find a

polypeptide defined by partial structure and function. The extension of claim 20 to encompass a recombinant nucleic acid sequence which encodes an ALS polypeptide would also appear to be clearly understood by a person of skill in the art.

[74] Concerning claims 29 and 30, we note that these claims are broader than claim 20. In the case of claim 29, there is no reference to an AALS@ polypeptide. In the case of claim 30, there are references to peptide *fragments* of the N-terminal sequence of ALS. In the case of claim 29, there appears to be a removal of the functional limitation carried by the term AALS@ and, in the case of claim 30, there appears to be a removal of a structural limitation, *i.e.* the requirement for the entire N-terminal amino acid sequence which is recited in claim 20. Nonetheless we are again left to conclude that claims 29 and 30 are definite in respect of the polypeptide and indicate clearly to a person of skill in the art that which the Applicant regards as his invention largely due to the presence in these claims of the same structural features which have been indicated to be distinguishing.

[75] In contrast to claim 20, claims 29 and 30 also refer to a Anucleic acid isolate comprising nucleic acid encoding . . .@ . Based on this terminology, the claims can be reasonably interpreted to mean that they are directed to Aa nucleic acid isolate which includes a part which itself is capable of encoding a polypeptide which minimally includes the peptides referred to in the claim.@ As such, the claims encompass an isolate, such as a clone or plasmid or vector, which is inherently able to encode a complete ALS polypeptide. Unlike claim 20, there is no requirement that the claims include an explicit indication of the structure or nucleotide sequence of the part which codes for a complete ALS polypeptide.

[76] Before leaving the issue of compliance with Subsection 34(2) it is important to understand that, in this case, claims 29 and 30 can be reasonably and broadly interpreted to encompass a genus of nucleic acid molecules, the most desirable member of which is a nucleic acid molecule that is capable of encoding the *entire* amino acid sequence of a full length ALS polypeptide. A full length ALS polypeptide would be approximately 800 to 1100 amino acids long if the Applicant=s estimation of its molecular weight is correct. Similarly, we would say that claim 20 also encompasses a nucleic acid molecule which has a nucleotide sequence encoding a *full length* ALS polypeptide.

(b) Non-Compliance of the Nucleic Acid Claims with Subsection 174(2) of the Rules and Subsection 34(1) of the Act

[77] The principle grounds for rejection of the nucleic acid claims is failure to comply with Subsection 174(2) of the *Patent Rules*, which necessarily implies that the claims are also not compliant with Subsection 34(1) of the Act. Indeed the Final Action and the Applicant=s response and submissions deal almost exclusively with such issues.

[78] It is the question of support for a claim to a nucleic acid molecule encoding a *complete* ALS polypeptide which both the Examiner and the Applicant are most concerned with. Therefore, the principle question before us now, phrased more specifically, is whether or not the disclosure of an ALS polypeptide provides sufficient support for claims to nucleic acid molecules which are able to encode a complete ALS polypeptide.

(i) Non-Compliance of the Nucleic Acid Claims with the Enablement Requirement of Subsection 34(1) of the Act

[79] We glean from the specification the following information concerning ALS:

> (i) ALS is a type of polypeptide functionally defined as an acid-labile polypeptide which is capable of binding to or associating with complexes formed when IGF is bound or associated with the acid stable binding protein BP-53;
> (ii) the description discloses N-terminal sequence information for an ALS polypeptide;
> (iii) the size of an ALS molecule is estimated to be 80 Kd to 115 Kd; and
> (iv) an ALS polypeptide apparently has been purified and (partially) characterized to an extent considered adequate to allow claims to ALS polypeptides *per se*.

[80] Directing the reader to *Maniatis*, the description outlines proposed methods thought to be useful in obtaining a recombinant ALS cDNA molecule (page 11, second paragraph). Briefly stated, these methods refer to techniques commonly used in the art, such as mRNA extraction, cDNA synthesis, subcloning, screening, and other manipulations.

[81] One proposed method in particular describes the insertion of cDNA into an expression vector followed by screening based on reaction of expressed ALS polypeptide with an antibody raised against the purified polypeptide (page 11, lines 25 to 29). Such an antibody is exemplified and described on page 18, lines 10 to 12. Thus there is support in the application for one reagent which could be used by a person of skill in the art to clone or obtain a nucleic acid molecule encoding ALS. Whether the antibody is able to *specifically* react with an ALS expression product in a screening assay remains an unanswered question since the application does not provide any data for the antibody *viz-a-viz* possible cross reactivity with other proteins.

[82] Another proposed method (the Adegenerate probe@ method) described in the application on page 11, lines 19 to 23 relies on Aspecific oligonucleotides based on the aforementioned N-terminal amino acid sequence of ALS@ for screening a cDNA library or a commercially available lambda library. Given an amino acid sequence, a person of skill in the art can easily deduce and describe a nucleic acid sequence which encodes it by simply back-translating the amino acid sequence. Thus an oligonucleotide encoding all or a portion of the N-terminal part of the ALS polypeptide can be easily described and made. Again, there is support in the application for another type of reagent that could be used to attempt to clone or obtain a nucleic acid encoding an ALS polypeptide; *i.e.*, a nucleic acid which encodes the N-terminal portion of the ALS polypeptide. It is less clear, due to sequence degeneracy, whether any given nucleic acid sequence, or oligonucleotide, would bind exclusively to a target nucleic acid when used in a screening assay. However, as understood from reading the whole of the specification and the Applicant=s submission, it is a much larger nucleic acid molecule which encodes a complete ALS polypeptide which is the most sought after type of nucleic acid molecule encompassed by the claims.

[83] With respect to enablement, the Applicant has taken a position which can be summarized by reference to the paragraph bridging pages 7 and 8 of the written submissions presented to the Board at the oral hearing:

> Applicant respectfully submits that, as of July 15, 1988, the earliest priority date of the instant application, those skilled in the art, given the information in the patent specification, the state of the art and the widely available manual, could have readily obtained a nucleotide sequence encoding an ALS polypeptide comprising the N-terminal amino acid sequence as set forth in claim 20. Furthermore, given the widely available technology as of the priority date, no undue

experimentation would have been required to obtain this nucleotide sequence.

[84] In support of this position the Applicant has provided an affidavit from Dr. Charles Roberts, an expert in the field of biochemistry and molecular. We have reviewed the affidavit, in particular paragraphs 10, 15, and 21-23 which state the following:

> 10. As of 1988, two general approaches to probe construction were widely known and in common use by molecular biologists. One method involved synthesis of a mixed set of short oligonucleotides representing various probe sequences which, due to degeneracy, could encode the same amino acid sequence. These collections were referred to as "degenerate probes." The second method involved synthesis of a single, long oligonucleotide probe referred to as a "guessmer" probe which had a greater length but less degeneracy. The guessmer sequence was based on available information regarding which codons were preferentially used for particular amino acids. The rationale for this approach was that, even if a single probe contained some mismatches with the authentic target sequence, this would be ameliorated by the greater length and stability of the probe compared to shorter degenerate probe sets. It was common practice as of July 15, 1988 to use DNA probe(s) based upon either strategy (a "degenerate probes" strategy or a "guessmer" probe strategy) to isolate nucleic acids from genomic DNA and cDNA libraries.
>
> 15. Given the state of the art of molecular biology as of July 15, 1988, one of skill in the art would have had a strong factual basis for predicting that, given a known polypeptide sequence, a genomic DNA or cDNA encoding the polypeptide sequence could be isolated using the technique of DNA hybridization. Furthermore, one of skill in the art would have a strong factual basis for predicting that the DNA isolated could be used in the manufacture of a vector and the transformation of a host cell using techniques which were widely available in well known manuals and textbooks.
>
> 21. The fact that design, synthesis, and use of"guessmer" DNA probes to isolate protein-encoding nucleic acids were techniques that were known and in use well before July 15, 1988 is attested to by at least the following publications, copies of which are provided herewith as Exhibits 2, 3, 10, and 11.
>
> 22. Based on the information provided in the Patent Application, specifically that the N-terminal sequence of the ALS was known, as of 1988, one of skill in the art could have created a probe which would detect an ALS cDNA clone, even in the presence of other related, but not exactly complementary, probe sequences.
>
> 23. In fact, subsequently reported procedures described in the Patent Application would be effective to isolate a cDNA clone of ALS. In a paper published in 1992, (Leong et al., *Molec. Endocrinol.* 6:870) "Leong", a copy of which is attached hereto as exhibit 12, cloning of a cDNA encoding human ALS using the same techniques as set out in the Patent Application is described. Leong describes how four DNA probes were made, each corresponding to a different ALS peptide. Leong did not use degenerate DNA probes. Instead, Leong designed and synthesized <u>one</u> guessmer probe for each of four peptides. Given the fact that Leong reported success with two of four of the DNA probes, one of skill in the art would expect that use of degenerate probes corresponding to, e.g., the N-terminal peptide, would also have been successful.

[85] Thus the affidavit indicates that there were two cloning methods commonly available at the time of filing the application which would have been known to a person of skill in the art; those being the so-called Adegenerate probe@ method and the Aguessmer probe@ method.

[86] As mentioned above at paragraph 82, the degenerate probe method is described in the

application on page 11, lines 19 to 23. The degenerate probe method is also described in *Maniatis*.

[87] The guessmer probe method is not specifically mentioned in the application. However, because our findings, as stated below, do not turn entirely on this omission we do not *necessarily* view the omission, by itself, as a fatal defect. That is not to say that the failure to say anything at all about the guessmer probe method in the specification is of no consequence whatsoever. We view the the guessmer probe method as an alternative to the degenerate probe method; both of which, according to the affiant, were well known to a person of skill in the art even if not expressly stated in the specification. As explained below, it is the direction given in the specification and the choice, by a person of skill in the art, of one over the other and the resultant consequences that is more critical. Similarly, we do not see the issue of the relevant date for assessing the sufficiency of the specification as determinative since both methods were apparently well known, available and accepted methodologies, and understood to be such by a person of skill in the art, even as early as the filing date of the application.

[88] The response to the Final Action and the Roberts affidavit both refer to the Leong paper (Leong *et al.*, *Molec. Endocrinol.*, 1992, volume 6, pp. 870-876) as support for the notion that the specification is sufficient. The following is disclosed in the first paragraph under the AResults and Discussion@ heading:

> Amino-terminal and internal amino acid sequence data (Table 1) were obtained from ALS purified from human serum. Initial clones encoding ALS were isolated from oligo(dT) and random primed cDNA libraries made from human liver mRNA. Four oligonucleotide probes derived the amino acid sequence data were used to screen these libraries under low stringency conditions. The positive clones hybridized with probes from the tryptic fragments T16 and T25, with matches of 14 bases in a row. Probes to the N-terminal sequence and to T64 failed to hybridize because less frequently used codons are found in these regions. [emphasis added]

[89] From the disclosure of the Leong paper we gather the following:

> (i) there is disclosure of additional *internal* amino acid sequence information of the ALS polypeptide which is not disclosed in the patent application;
> (ii) the guessmer probe method was used to isolate a nucleic acid sequence encoding the ALS polypeptide;
> (ii) the internal amino acid sequence information was used to generate three guessmer probes, two of which were then used to successfully clone a nucleic acid sequence encoding the ALS polypeptide;
> (iii) a fourth guessmer probe derived from the same N-terminal amino acid sequence information disclosed in the patent application *was not helpful* in cloning a nucleic acid sequence encoding the ALS polypeptide;
> (v) the Leong paper was submitted for publication in December 1991, long after the filing date of the patent application;
> (vi) the Leong paper was co-authored by the inventor of the instant application; and
> (vii) the paper actually discloses a full length nucleic acid sequence which encodes a complete ALS polypeptide.

[90] In our view, these facts are incongruent with the statements made in the affidavit. Specifically, we do not see how the specification as filed disclosed the Asame techniques@ and

probes as those eventually followed and used by Leong *et al.* nor do we see the equivalent internal ALS amino acid sequence information in the specification. In the application we instead find disclosure of N-terminal amino acid sequence information and a suggestion that it can be used to make a degenerate probe(s) which can then be used to clone a nucleic acid molecule capable of encoding the ALS polypeptide. Alternatively the specification teaches a cloning method based on reaction of expressed ALS polypeptide with an antibody raised against the purified polypeptide.

[91] If it is true that a person of skill in the art would have expected success with the degenerate probe method, as the affidavit states, then it is not clear to the Board why this method was not pursued; after all, the requisite N-terminal amino acid sequence information was already in hand and the need for additional experimental work, in the form of obtaining internal amino acid sequence information, would presumably not have been necessary. We are similarly troubled in respect of cloning based on expression and screening using an anti-ALS antibody. None of the methods explicitly mentioned in the specification were actually successfully followed either at the time of filing or afterwards by Leong *et al.*

[92] Unlike the situation in *Yeda R & D*, the Board is not satisfied that the Applicant, or one of skill in the art, would have been able to use the N-terminal amino acid sequence of the ALS polypeptide as a tool to eventually obtain a nucleotide sequence capable of encoding ALS. Contrary to the law set out in *Minerals Separation*, the specification directs a person of skill in the art towards the use of the degenerate probe method, whereas an alternative method -- which itself was not explicitly mentioned in the specification and which relied on critical sequence information not found in the specification -- was eventually successfully used. Here there is evidence of both success and failure in the form of the Leong paper which indicates: (a) that the specification lacks written description of the internal amino acid sequence information which was eventually used to successfully obtain a nucleic acid molecule capable of encoding an ALS polypeptide, and (b) that a method reliant on the same N-terminal amino acid sequence information found in the specification resulted in failure.

[93] The reasoning set out above holds for both claim 20 and claims 29 and 30 since the first step in obtaining a nucleic acid molecule defined by sequence as in claim 20 is to obtain an isolate or clone as defined in claim 29 or 30 and then sequence the portion coding for the ALS polypeptide.

[94] The cumulative effect of all of this leads us to conclude that the specification would not enable a person of skill to obtain a nucleic acid which is capable of encoding the ALS polypeptide, either today or on the date of filing, and we do not see it as a simply a matter of routine for a person of skill in the art to do so.

(ii) Non-Compliance of the Nucleic Acid Claims with the Written Description Requirement of Subsection 34(1) of the Act

[95] With respect to sufficiency of the specification the Applicant has taken a position, based in a number of authorities, which can be summarized by reference to the last paragraph of page 6 and the first paragraph of page 7 of the written submissions presented to the Board at the oral hearing:

> Applicant submits that, in setting forth the requirements for sufficiency of the specification, the Supreme Court was clear that the patent specification must **describe** the invention. The Supreme Court did not say that an invention must have been physically constructed before it

can be patented. This is not a requirement for compliance with Section 34(1) of the *Patent Act* and Applicant submits that any interpretation of *Institut Pasteur* to this effect is simply incorrect.

Claims relating to Nucleic Acids, Vectors and Host Cells

The examiner made the following statement in the Final Action:

> "Applicant has only isolated and partially purified ALS. Applicant has not prepared nucleic acids, vectors, transformed cell or antibodies and is therefore not entitled to claim these products."

Applicant draws the Commissioner's "attention to the review of the Canadian case law regarding sufficiency of the patent description recited above and respectfully points out that the examiner erred by applying an incorrect test. In particular, the examiner took the position that nucleic acids, vectors and host cells could not be claimed for the reason they had not been prepared at the time of the application. As Applicant has pointed out above, the correct test, as affirmed by the Supreme Court of Canada, for sufficiency of a patent specification is whether the specification **describes** the invention, not whether the invention has been constructed. Accordingly, the examiner failed to consider whether the invention had been adequately described, but rather refused the claims for the reason that the embodiments had not been constructed.

[96] The Applicant thus draws a distinction between actual construction of the invention as opposed to a description of the invention. In rejecting the claims the Applicant says that the Examiner misapplied the law and incorrectly demanded that the specification show physical construction of the invention before it can be patented. On this we agree with the Applicant that compliance with Subsection 34(1) of the Act does not *necessarily* demand physical construction of the invention. As the Applicant has correctly emphasised, the requirement is that the specification describe the claimed invention. However, conception of an invention absent a meaningful description of it does not meet the requirements of the law; despite the provision of methodologies which might possibly be used to construct the invention. AIt is not enough for a man to say that an idea floated through his brain; he must at least have reduced it to a definite and practical shape before he can be said to have invented [the invention]@ : *The Permutit Company v. Borrowman* (1926), 43 R.P.C. 356 (P.C.).

[97] In order to provide more than the idea of a genus of nucleic acid molecules which encode the ALS polypeptide the specification must provide a written description of the complete amino acid sequence of the ALS polypeptide; the complete amino acid sequence effectively representing -- due to the skilled person=s knowledge of the genetic code B a complete description of the family of nucleic acid molecules which are capable of encoding it.

[98] Accordingly, the Board finds the following non-exhaustive list of factual considerations helpful in determining whether the specification provides an adequate written description of a nucleic acid molecule capable of encoding a complete polypeptide:

> (i) whether there is a more than merely a general description of the polypeptide, including a description a complete amino acid sequence of the polypeptide which essentially equates, by virtue of the genetic code, to a description of the entire genus of nucleic acid molecules which are capable of encoding the polypeptide;
> (ii) whether the applicant was in physical possession of a nucleic acid molecule capable of encoding the polypeptide, and if yes, whether the specification provides the sequence of

the nucleic acid molecule;
(iii) whether the specification describes an Aisolated@ nucleic acid molecule (*i.e.* a clone such as plasmid or vector) capable of encoding the polypeptide;
(iv) whether the applicant was in a position to provide a biological deposit of a clone capable of encoding the polypeptide; and
(v) whether a biological deposit of a clone was made before the filing date.

[99] Items (i) and/or (ii) are critical in cases where a claim, such as claim 20, relies on the structure (*i.e.* nucleotide sequence) of a nucleic acid molecule capable of encoding the polypeptide. In the case of a claim, such as claim 29 or 30, which is directed to simply an isolated nucleic acid molecule inherently capable of encoding the polypeptide, any one or all of the items may come into play.

[100] In this case it is apparent that:

(i) the specification does not disclose a complete amino acid sequence of an ALS polypeptide; that being provided by Leong *et al.* for the first time only after the filing date of the application;
(ii) the specification neither indicates that the applicant was in physical possession of a nucleic acid capable of encoding an ALS polypeptide nor does it indicate the nucleotide sequence of any such nucleic acid molecule;
(iii) the specification does not describe an Aisolated@ nucleic acid molecule (*i.e.* a clone) capable of encoding an entire ALS polypeptide;
(iv) the Applicant was not in a position to provide a biological deposit of an isolated nucleic acid molecule (*i.e.* a clone) capable of encoding an entire ALS polypeptide; and
(v) a biological deposit of a clone capable of encoding an ALS polypeptide clone was not made before the filing date.

[101] In light of these facts we conclude that the specification does not provide an adequate written description of the subject matter of claim 20 or claims 29 and 30.

(c) Non-Compliance of the Antibody Claims with Subsection 34(2) of the Act

[102] We turn now to the second group of claims which relate to antibodies and address firstly whether the claims are definite as required under Subsection 34(2). The antibody claims read as follows:

> 25. An antibody reagent capable of binding to acid-labile subunit (ALS) of insulin-like growth factor (IGF) binding protein.
>
> 26. An antibody reagent according to claim 25 which is a monoclonal or polyclonal antibody.
>
> 27. An antibody reagent according to claim 25 or 26 which is labelled with one or more reporter groups.
>
> 28. An antibody reagent according to claim 27, wherein the reporter group is selected from fluorescent groups, enzymes or colloidal groups.

[103] Firstly, it is not entirely clear which Acompound@ was being referenced when it was stated in the Final Action that:

> AThe compounds covered by claims 19 to 34 are not described "distinctly and in explicit terms" as required by Subsection 34(2) of the Patent Act as it read immediately before 1 October 1989 and therefore are not allowable.@

[104] One may wonder: is the allegedly ill-defined compound of claim 25 the antibody or the ALS polypeptide?

[105] Although the applicant is the Amaster of his claims, within the breadth of his invention, and entitled to draft them in words wide enough to secure the protection desired@ (*Riddell v. Patrick Harrison & Co.* (1957), [1956-60] Ex. C.R. 213 & 66, 28 C.P.R. 85) and there is no strict requirement that an applicant define his invention by including a complete chemical structure, there is a strict requirement that the *scope of the claims* be clearly delineated such that A[t]he public will be able to know not only where it must not trespass but also where it may safely go@: *Minerals Separation* (*supra*).

[106] In this case it is arguable that claim 25 is indefinite since it defines the scope of protection sought by referring to two types of molecule -- an antibody and an ALS polypeptide -- each of which has been defined in terms of a function and in terms of a very general structure. The terms Aantibody@ and Apolypeptide@ themselves describe classes of compounds with broadly defined structures. The antibody of claim 25 is further defined in terms of its reactivity with an ALS polypeptide. The term AALS@ is defined in its broadest reasonable meaning to be A[a]n acid-labile polypeptide which is capable of binding to or associating with complexes formed when IGF is bound or associated with the acid stable binding protein BP-53 defined above@ (page 7, lines 4-7 of the description).

[107] The functional language (*i.e.*, Acapable of binding to@) of the claim in respect of the Aantibody@ is necessary since it was impossible to provide structural descriptions for all antibodies found, for example, in a polyclonal mixture and since such language was generally accepted in the biotechnological arts at the time of filing. However, the functional language implicitly used to define the ALS polypeptide is more problematic. That is to say, claim 25 in its current form lacks the N-terminal amino acid sequence structure which is admitted in the description to be a distinguishing feature of the ALS polypeptide (page 26, lines 20 to 21 of the description) and yet, in apparent contradiction, is also indicated to be merely a preferred structural feature (page 6, lines 28-29 of the description). The claim also lacks an explicit reference to other properties of the ALS polypeptide such as molecular weight and instability in acid.

[108] Defining the scope of claim 25 by reference to *two* molecules cannot be said to fairly put the public on notice since the public would face the unreasonable task of, firstly, determining whether a given polypeptide fits within the broad function terminology implicit in the claim, and then, secondly, deciding how the polypeptide interrelates, or not, with a given antibody. In this case, a claim to an antibody reactive with an ALS polypeptide would be definite provided the claim adequately defines of the ALS polypeptide since a person of skill in the art would be able to determine whether an antibody is within the claim by performing a routine binding reaction with the polypeptide. A claim framed in such terms provides fair protection for the patentee and reasonable predictability for the public: *Free World Trust v. Électro Santé Inc.*, 2000 SCC 66 & 41, 9 C.P.R. (4th) 168.

[109] We hasten to add that, apart from the question of indefiniteness of claim 25, the scope of the claim in respect of the ALS polypeptide is much broader than the scope of claim 1 which is directed to an ALS polypeptide *per se.* Since an antibody is very often critically defined, at least in part, in terms of its binding properties to a polypeptide, it is important to ensure that the polypeptide of an antibody claim is commensurate in scope with the same polypeptide found in a claim to the polypeptide *per se.*

[110] Since the substantive issue in this case is the question of support for the antibodies, and since neither the Examiner nor the Applicant dealt fully with the issues of scope and definiteness of the antibody claims in respect of an ALS polypeptide, we therefore propose to resolve these issues by requiring the Applicant, in accordance with Subsection 31(c) of the *Patent Rules*, to define the ALS polypeptide by reference to claim 1; *i.e.*, by concluding claim 25 with the phrase Aas defined in claim 1.@ Such an amendment would not appear to raise any new issues and, as we understand the substantive basis for the rejection, such an amendment would put the claims in a form clear enough to be granted except for the question of support for claims to antibodies which will be dealt with next.

[111] The only remaining comment we have on the clarity of the antibody claims is to note that the Applicant, when questioned on this at the oral hearing, did not indicate that the term Aantibody reagent@ as used in the claims was meant to suggest anything other than simply Aantibody molecule@ or even simply Aantibody@. Therefore, we are satisfied, in this case, that the terminology does not offend Subsection 34(2) of the Act.

(d) Non-Compliance of the Antibody Claims with Subsection 174(2) of the Rules and Subsection 34(1) of the Act

(i) Claims to an Antibody in General and a Polyclonal Antibody

[112] Claim 25 is generic and refers to Aan antibody reagent@ capable of binding to ALS. This claim is in a form similar to the claims that issued in *Pasteur*. The claim is fully supported through the description of conventional methods to generally make Aantibodies@, through the description of an actual anti-ALS antiserum (page 18, lines 10-21), and through an adequate description of an ALS polypeptide.

[113] In fact, the antiserum can be viewed as a generic pool made up of many thousands of particular antibodies of several isotypes (*e.g.* IgG, IgM, IgA) - a kind of Asoup@, or family, of many related antibodies with each member of the family binding to a specific antigenic determinant or epitope carried on the ALS polypeptide. As such, the antiserum is adequately representative of the entire family of antibodies which are capable of binding to an ALS polypeptide.

[114] Further, even absent the description of an actual anti-ALS antiserum, it would be reasonable to expect that the ALS polypeptide is immunogenic and implicitly understood to carry many epitopes. The ALS polypeptide -- having been adequately defined albeit not by a detailed complete primary structure -- therefore represents a collective of any and all possible epitopes but not necessarily any specific one. An adequate written description of the ALS polypeptide, in the general sense, thus provides an adequate written description of its corresponding generic or polyclonal binding partner(s).

[115] We therefore conclude that the generic antibody of claim 25 and the polyclonal antibody of claim 26 are enabled and adequately described.

[116] Claim 26 seems to be the more contentious claim since it specifically refers, in the alternative, to a monoclonal antibody. Claims 27 and 28 have not been discussed by either the Examiner or the Applicant. The issue now becomes one of specific support for an anti-ALS monoclonal antibody.

(ii) Compliance of the Monoclonal Antibody Claims with the Enablement Requirement of Subsection 34(1) of the Act

[117] On the question of enablement both the Examiner and the Applicant have referred to *Pasteur*; the Examiner following it, and the Applicant challenging its precedential value.

[118] Concerning *Pasteur*, the Applicant stated the following, in part, in the written submissions:

> [t]he patent application at issue in *Institut Pasteur* related to the discovery of a new class of HIV retrovirus, HIV 2. The inventors did not describe purifying or sequencing the proteins of HIV 2 nor did they provide any guidance as to how they would carry out such procedures. Furthermore, the inventors did not produce antibodies (either polyclonal or monoclonal) to proteins from HIV 2 nor did they include any information on the protocols that would be necessary to do so.
> . . .
> Applicant acknowledges that, in *Institut Pasteur*, it was open to the Commissioner of Patents to conclude that producing monoclonal antibodies to protein antigens from the HIV 2 virus was not sufficiently enabled by the description of the patent application before him. It was a factual determination that the Commissioner made based on the contents of the patent specification and the evidence before him at the time. However, Applicant respectfully submits that the inventors of the present application have provided a sufficient disclosure to enable one of skill in the art to produce antibody reagents to ALS. In particular, Applicant points out that the patent specification describes a well characterized antigen, which includes the amino acid sequence of the N-terminus. Furthermore, the inventors have described producing a polyclonal antibody to ALS, which is itself an antibody reagent and, as well, an important precursor to a monoclonal antibody.
>
> In support of these submissions, applicant draws the [Board=s] attention to the affidavit of Professor James Goding, filed herewith. Professor Goding is one and the same person as the author who was cited with approval by the Commissioner in *Institut Pasteur*.

[119] This brings us to the compelling evidence of Professor Goding who stated the following, in part, in his affidavit:

> The Commissioner's Decision #1206 fails to capture the meaning of the statements which I made in my article and books. Firstly, the passage it is "not a trivial procedure" to produce a monoclonal antibody is cited. My meaning in writing this sentence was to advise the reader that it takes work in the laboratory to produce monoclonal antibodies, whereas a polyclonal antibody can be produced quite simply in an animal. Nevertheless, it is not correct to say that a knowledgeable person would not anticipate success in producing monoclonal antibodies if the well-established protocols were followed. This is incorrect and indeed, my book and several other publications provide specific details of suitable techniques which can be used to prepare monoclonal antibodies. In circumstances where a well characterized antigen is used, by the time of my book (1986) it would have been expected that a monoclonal antibody to an immunizing antigen could be prepared using well-established techniques.

> Specifically, I do not support the proposition that, given a sufficiently purified protein, one would not expect that monoc1onal antibodies could be produced using the techniques described in the second edition of my textbook described at paragraph 4 above. If my writings are cited in support of this proposition, then they are wrongly cited. [emphasis added]

[120] Professor Goding also commented on the present application and stated that:

> I have reviewed Decision #1206 of the Canadian Patent Commissioner, on which the Examiner relied in support of his refusal to allow a claim to antibodies. I note that Canadian patent 1,338,323, which was the subject of Decision #1206, differs in at least two significant aspects from the Patent Application. Firstly, it does not provide a well-characterized antigen, as does the Patent Application. Furthermore, it does not direct one of skill in the art to any references which would provide details of the "traditional techniques" for producing monoclonal antibodies. My book is not mentioned at all in Canadian patent 1,338,323.
> . . .
> The Patent Application describes a highly purified ALS with a known N-terminal sequence. In 1988, a person working in the field of immunology would have certainly predicted that an antibody reagent, such as a monoclonal antibody, capable of binding to ALS could have been produced using standard laboratory techniques which were widely known and available at the time. As evidenced by my articles and books, the necessary techniques for making such monoclonal antibodies were well documented and in widespread use.

[121] In light of this evidence it appears there are concerns with *Pasteur* in so far as it may be relied upon as authority for the proposition that a patent specification is defective for lack of enablement because monoclonal antibody production was not a well developed methodology or merely because it fails to set out a detailed proposed protocol for the production of a monoclonal antibody to a given antigen. Therefore, the precedential value of *Pasteur* has been diminished in respect of its findings on the enablement requirement of Subsection 34(1). Until now *Pasteur* has provided precedence for the guidance of applicants and patent examiners: *Manual of Patent Office Practice*, subsection 21.07. However, the Commissioner is not bound by past practice (*DBC Marine Safety Systems Ltd. v. The Commissioner of Patents*, 2007 FC 1142 & 43) and, in view of the facts and evidence now before us, *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 methods of making a monoclonal antibody are unpredictable.

[122] The evidence supplied by Professor Goding himself as well the totality of the information provided in his textbook indicate that the core steps themselves for producing a monoclonal antibody were well known and reliable as of the filing date. A person of skill in the art would reasonably expect, based on the clonal selection theory, that an antibody reactive with any given antigen does exist since the antibody, in essence, has already been made. As Professor Goding explains in his textbook (section 2.1, pp. 5-6):

> The clonal selection theory (Burnet, 1957) avoided all these difficulties by postulating that each lymphocyte [an antibody producing cell of the immune system] had a unique receptor specificity, and was thus precommitted to making only one antibody after appropriate stimulation
> . . .
> The clonal selection theory provides the conceptual framework for all that follows in this book. [emphasis added]

[123] Thus, the true technological basis for monoclonal antibody production does not reside providing instructions as to how to make an antibody, it resides in the form of practical methods which could be used to isolate and immortalize specific antibody producing cells. These practical methods may involve Aa great deal of work, and a high level of commitment@(*Goding*, chapter 1, p. 3) from a person of skill in the art but success, according to Professor Goding, does not critically depend on a chance outcome.

[124] To be clear, however, the evidence now before us does not diminish the value of *Pasteur* in respect of the written description requirement of Subsection 34(1) which will be considered separately.

[125] The Board finds the following non-exhaustive list of 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 (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.

[126] In the present case we apprehend the following facts:

> (i) the ALS polypeptide is a large polypeptide which would reasonably be expected to carry many putative epitopes and, in fact, is immunogenic (witness the actual production of high titre anti-ALS antiserum described on page 18, lines 10-21);
> (ii) the proposed amendment under Rule 31(c) to claim 25 will render the scope of the claim appropriate;
> (iii) the ALS polypeptide has been purified and has been described and characterized to an extent sufficient to claim it in a *per se* manner;
> (iv) no monoclonal antibody has been prepared;
> (v) there is no evidence of success or failure;
> (vi) there are no indications of a requirement for undue experimentation; and
> (vii) there are no indications that the proposed method implicitly outlined in the specification would not be reproducible.

[127] Furthermore, contrary to the fact pattern in *Pioneer Hi-Bred*, the facts and evidence before us in the present case do not suggest the need for unique techniques or the need to conduct empirical testing in discover the steps *themselves* which would be required in order to make a monoclonal antibody to an ALS polypeptide. The critical feature is the identification and description of an ALS polypeptide, which in this case has been provided.

[128] The cumulative effect of the facts and the Applicant=s submissions, satisfy us that the enablement requirement of Subsection 34(1) has been met, even as early as the filing date of the application and even though no monoclonal antibody has actually been prepared. Therefore the rejection ought not be upheld solely on the grounds that a person of skill in the art could not use the ALS polypeptide as an antigen in the course of preparing a monoclonal antibody to it. We should not be taken to say that the enablement requirement will necessarily be met in all cases through the description of a polypeptide and the recitation of known methods; each case should be considered on its own merits.

(iii) Non-Compliance of the Monoclonal Antibody Claims with the Written Description Requirement of Subsection 34(1) of the Act

[129] Subsection 34(1) of the Act serves a function distinct from that of Subsection 34(2) of the Act. Accommodating the shortcomings of language in respect of a claim to a monoclonal antibody and permitting the use of functional terminology to help define the scope of the monopoly for the purposes of Subsection 34(2) should not necessarily be taken as an indication that the underlying and substantive requirement of written description under Subsection 34(1) can be ignored.

[130] In reaching our conclusion on written description of the claimed monoclonal antibodies we have taken into account a number of considerations beyond the mere ability of the Applicant to draft a claim that literally describes what he proposes to monopolize since the critical issue is compliance with Subsection 34(1).

[131] Remembering that the issue here is one of specific description, it follows that, apart from a token indication of binding functionality, a precise description of a monoclonal antibody could be accomplished by providing a description of the critical parts of each member of the actual binding pair; *e.g.*, a paratope of a monoclonal antibody and/or its corresponding epitope found on the antigen. Descriptions of specific paratopes and epitopes are thus clearly valid considerations in the same way that a general description of a polypeptide is a valid consideration in respect of a claim to a generic antibody; especially as technologies advance and it becomes easier to provide specific descriptions of paratopes and epitopes.

[132] Having said that, we are also mindful of the fact that a description of one member of a binding pair does not necessarily provide an adequate description of its binding partner. For example, witness the Applicant=s discovery and characterization of an ALS polypeptide and the subsequent submission of the present patent application containing claims to the ALS polypeptide itself despite the existence of its binding partners BP53 and IGF which themselves were previously known and well characterized. The mere realization that BP53 and IGF interact with some other polypeptide did not entitle the Applicant to claim the latter polypeptide unless it had been adequately described in meaningful terms such as by structure and/or physical-chemical properties.

[133] Physical possession of a monoclonal antibody undeniably moves it from the hypothetical world to the real world and, to echo the sentiment expressed in *Pioneer Hi-Bred*, such an indication clearly facilitates the work of the examiner and the Commissioner of Patents. An indication of physical possession thus ensures that the public has clearly been given something more than a hypothetical in return for suffering a monopoly. This is a valid consideration we also see as harmonious with a key passage from *Consolboard* which, to restate it, reads as follows:

> Section 36 of the Patent Act lies at the heart of the whole patent system. The description of the invention therein provided for is the *quid pro quo* for which the inventor is given a monopoly for a limited term of years on the invention.

[134] Therefore, actual physical possession of a hybridoma producing a monoclonal antibody is also a valid consideration especially since the Act specifically contemplates it by virtue of Section 38.1 and since a deposit can be used to supplement, but not entirely replace, the written description of the invention where the requirements of Subsection 34(1) of the Act cannot be complied with by words alone.

[135] To summarize, the Board finds the following non-exhaustive 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:

> (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.

[136] Although the specification provides a detailed description of the N-terminal amino acid sequence of the ALS polypeptide, the specification neither clearly teaches that the N-terminal portion comprises an epitope reactive with a putative monoclonal antibody nor does it specifically claim a monoclonal antibody reactive with an N-terminal epitope.

[137] The proposed amendment under Rule 31(c) to claim 25 will render the scope of the claim appropriate.

[138] In summary, we find the following:

> (i) the specification provides neither a more detailed description of an ALS polypeptide nor explicit descriptions of epitopes;
> (ii) the specification does not provide a specific description of a paratope of a monoclonal antibody;
> (iii) after amendment under Rule 31(c), the scope of claim 25 will be appropriate;
> (iv) the Applicant was not in physical possession of a monoclonal antibody;
> (v) the Applicant was not in a position to provide a biological deposit of a hybridoma producing a monoclonal antibody at the time of filing

[139] It is also important to remember that, on the specific issue of adequate written description of monoclonal antibodies, the Board in *Pasteur* commented as follows:

> The Board cannot find any description of the hybridoma of claim 85 or any description of a method of preparing it provided in the above cited statements or in the entire description. No specific description of the monoclonal antibodies in claim 84 or a process for their preparation is disclosed. The only guidance as to the description of the monoclonal antibodies and the process by which they may be prepared is that they can be prepared by "traditional techniques." The sole specific technical teaching provided is the identity of the antigens. Describing and identifying the antigens does not provide support for the hybridoma or the monoclonal

antibodies nor does it provide sufficient instruction on how to make the antibodies.[emphasis added]

[140] We find nothing in *Pasteur* in respect of the written description requirement of the Act that runs afoul with the facts and evidence before us in this case and therefore we do not see a need to depart from *Pasteur* in this respect.

[141] Putting all this together we therefore see reasonable grounds in the Final Action for concluding that the present application does not comply with the written description requirement of Subsection 34(1) and recommend that the Final Action be upheld on these grounds but only in respect of claim 26 in so far as it claims monoclonal antibodies.

V. CONCLUSIONS

[142] In summary, the Board concludes that:

(1) claims 20-24 and 29-34 comply with Subsection 34(2) of the Act;

(2) claims 20-24 and 29-34 do not comply with Subsection 174(2) of the Rules and Subsection 34(1) of the Act;

(3) claims 25-28 do not, in their current form, comply with Subsection 34(2) of the Act;

(4) claims 25, 27 and 28 comply with Subsection 174(2) of the Rules and Subsection 34(1) of the Act; and

(5) claim 26 does not comply with Subsection 174(2) of the Rules and Subsection 34(1) of the Act since it claims a monoclonal antibody which has not been adequately described.

[143] The Board recommends that the Commissioner:

(1) inform the applicant, in accordance with paragraph 31(c) of the *Patent Rules*, that the following amendments of the application are necessary for compliance with the *Patent Act and Rules*:

(a) deletion of claims 19-24 and 29-34;

(b) amendment of claim 25 to conclude with the phrase Aas defined in claim 1";

(c) deletion of the term Amonoclonal or@ from claim 26; and

(d) adjustment of claim numbering and dependencies accordingly; (2) invite the applicant to make only the above amendments within three months from the date of the Commissioner=s decision; and

(3) advise the applicant that, if the above amendments, and only the above amendments, are not made within the specified time, the Commissioner intends to refuse the application.

Ed MacLaurin Mark Couture Paul Fitzner

Member Member Member

VII. COMMISSIONER=S DECISION

[144] I concur with the findings and recommendations 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 25th day of June, 2008