Commissioner’s Decision # 1270

Décision du Commissaire # 1270

TOPIC: C00

SUJET: C00

Application No: 577, 176

Demand no: 577,176

COMMISSIONER'S DECISION SUMMARY

C.D. 1270 Application No. 577,176

Lack of Support (C00)

The application related to a partially characterized tumor necrosis factor inhibitory protein and contained claims to recombinant DNA molecules encoding the protein. The application was rejected by the examiner principally on the grounds that the description failed to provide a complete amino acid sequence of the protein and that the isolation or production of a DNA molecule encoding the protein would require undue experimental effort. The Board agreed with the examiner and found that the description merely directed a person of skill in the art to a pathway which might be followed in order to eventually arrive at the desired DNA products.

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 577,176 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 been considered by the Patent Appeal Board and by the Commissioner of Patents. The findings of the Board and the decision of the Commissioner are as follows:

Agent for the Applicant

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This decision deals with a request that the Commissioner of Patents review the Examiner's Final Action on patent application number 577,176 which was filed on 12 September 1988 and is entitled "TUMOR NECROSIS FACTOR (TNF) INHIBITORY PROTEIN AND ITS PURIFICATION".
The Applicant is Yeda Research and Development Company Limited, assignee of inventors David Wallach, Hartmut Engelmann, Dan Aderka and Menachem Rubinstein.

Since the subject patent application was filed before 1 October 1989, all references to the Patent Act in this decision are to the Act as it read immediately before that date.

The Examiner in charge issued a Final Action on 30 June 2000 in which claims 16 to 21 were rejected under Subsection 34(2) of the Patent Act as being indefinite and claims 1 and 28 to 42 were rejected for lack of support in the disclosure.

On 27 December 2000, the Applicant replied to the Final Action and submitted a new set of 28 claims. In a brief to the Patent Appeal Board dated 25 July 2002, the Examiner stated that the new claims overcame all but one of the objections raised in the Final Action. The Examiner was not satisfied that new claims 15 to 25, directed to products and processes defined in terms of a nucleotide sequence encoding TNF inhibitory protein, are supported by the disclosure.

At the Applicant's request, the Patent Appeal Board conducted an oral hearing on 24 March 2004, at which time the Applicant was represented by Dr. David Conn, Ms. Susan Beaubien and Dr. David Barrans all of the firm of Borden Ladner Gervais LLP, and by Mr. Henry Einav. The Patent Office was represented by Dr. Holly Notman who is the Examiner in charge of the application, Dr. Linda Brewer and Dr. Daniel Bégin.

The invention relates to a tumor necrosis factor (TNF) inhibitory protein isolated from human urine. The protein, which is capable of inhibiting the binding of TNF to cells and therefore of inhibiting the cytotoxic effect of TNF, is characterized in terms of molecular weight, isoelectric point and partial amino acid sequence.

The only issue before the Board is whether there is support in the application for claims directed to a DNA molecule coding for TNF inhibitory protein, replicable expression vehicles and transformed host cells comprising this DNA molecule, and a process which makes use of these products to produce the protein. Although the Examiner did not cite a section of the Patent Act or Patent Rules when rejecting claims for lack of support in the disclosure, the Board has assumed that the rejection was meant to be made under Subsection 174(2) of the Rules.

Claims 15, 21, 23 and 25 are representative of the claims which stand rejected and read as follows:

15. A recombinant DNA molecule comprising the nucleotide sequence coding for a naturally occurring soluble TNF inhibitory protein which comprises the amino acid sequence: Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser, wherein X is an unidentified amino acid residue, and which has the ability to interact with TNF in such a manner as to:
(a) inhibit the binding of TNF to a TNF receptor; and
(b) inhibit the cytotoxic effect of TNF.

21. A replicable expression vehicle comprising the DNA molecule of any one of claims 15 to 19 and capable, in a transformant host cell, of expressing said soluble protein.

23. A host cell transformed with the replicable expression vehicle of claim 21 or 22.

25. A process for producing a soluble TNF inhibitory protein, having the ability to interact with TNF in such a manner as to:
(a) inhibit the binding of TNF to a TNF receptor; and
(b) inhibit the cytotoxic effect of TNF, comprising the steps of:
culturing a transformant host cell according to claim 23 or 24 in a suitable culture medium; and isolating said protein.

In her Final Action, the Examiner stated, in part:

> Applicant has not isolated or even located the relevant gene producing the inhibitory protein and is thus not entitled to claim genomic DNA. Applicant is not entitled to claim cDNA coding for the protein as applicant has not sequenced the entire protein and is therefore unable to specify a nucleotide sequence which would code for the protein. It follows that applicant is also not entitled to claim vectors incorporating a cDNA or cells transformed by said hypothetical cDNA. Without a complete protein sequence, the production of cDNAs, vectors, and transformed cells, or the identification of the genomic sequence, would require undue experimentation, even for the skilled artisan.

The Examiner's Final Action also refers to a Commissioner's Decision (hereinafter "Pasteur") on the application which issued as Canadian patent no. 1,338,323 (see *Re Institut Pasteur Patent Application* 76 C.P.R. (3d) 206). With respect to this decision, the Examiner stated, in part:

> The Commissioner was considering claims to monoclonal antibodies which had not been prepared but which were considered by the applicant to be obtainable by one skilled in the art using traditional techniques. The Commissioner's decision stated that while the methods of making monoclonal antibodies to various antigens were known in the art at the time of filing (1987), applying these methods to a new antigen constituted a new process requiring a new protocol to produce the secreting hybridomas and novel monoclonal antibodies specific to the antigen. The decision went on to state that had any hybridoma 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. However, where no hybridoma or monoclonal antibody was prepared, there was nothing upon which to base a sound prediction. It therefore follows that as no cDNA's vectors, or transformed cells have been prepared in the instant application, and no genes or functionally equivalent proteins have been identified, such products cannot be claimed.

In its response to the Final Action, the Applicant argued as follows:

> Support is to be found in the description on pages 21 to 33 for a number of ways to obtain the claimed DNA as well as cloning an expression vector. It is respectfully submitted that the teaching found in the description along with the state of the art at the time of filing of this application was and is sufficient for a person skilled in this art without use of the inventive facility but desiring success and not failure to obtain the invention without undue experimentation.

The Applicant also stated that in "Pasteur", "the Commissioner erred on some scientific and legal points" and "relied upon U.S. case law that does not reflect the state of the law in the U.S." At the oral hearing, the Applicant argued that "Pasteur" is not relevant to the case before the Board in that 1) the application does not refer one of skill in the art to "traditional techniques" to practice the invention but instead provides instructions for carrying out the invention, and 2) the Applicant's sound prediction is not supported by post-filing work done by others but rather "a post-published scientific paper by scientists in the inventors' laboratory (Nophar et al.) confirm the successful practice of the invention .... using the same directions provided in this application."

The claims that stand rejected are defined, directly or indirectly, in terms of a nucleotide sequence encoding TNF inhibitory protein. However, this sequence is not disclosed in the application. Rather, the application describes processes, known in the art and not invented by the Applicant, that could be carried out to obtain the sequence. The Applicant describes how mRNA could be extracted from cells that produce TNF inhibitory protein and converted to cDNA using reverse transcriptase. The cDNA could then be made double-stranded and inserted into a vector for transforming a suitable host cell. An oligonucleotide probe could then be used to screen for clones containing cDNA encoding the protein and if the desired cDNA is found, it could then be inserted into an expression vector for transforming a host cell which in turn could be cultured to produce the protein. However, there is no evidence in the application, nor was any presented at the hearing, that at the filing date of the application, a cDNA had been isolated and characterized.

At the hearing and in its "Oral Hearing Brief", the Applicant argued that the claims rejected for lack of support meet the test of "sound prediction" as set out by the Supreme Court in *Apotex et al. v. Wellcome Foundation Limited et al.*[2002] 4 S.C.R. 1530 (hereinafter "Apotex") where the "doctrine of sound prediction" was defined in terms of three components: 1) a factual basis for the prediction; 2) an articulable and "sound" line of reasoning from which the desired result can be inferred from the factual basis; 3) proper disclosure. In "Apotex", the patentee was predicting that AZT would be useful in the treatment and prophylaxis of HIV/AIDS in humans and the 3-part test set out by the Court was a test for predicting "utility". The patentee was not predicting, as in the instant application, that a chemical compound (oligonucleotide sequence) which had not been disclosed could be obtained by following a prescribed pathway. Similarly, in an earlier decision of the Supreme Court in *Monsanto Co. v. Commissioner of Patents* [1979] 2 S.C.R. 1108, the "utility" of a group of compounds as rubber vulcanization inhibitors was "soundly predicted". Although only several members of the group had been prepared and tested, all of the compounds were fully disclosed in terms of a chemical structure.

In “Pasteur”, the Commissioner refused to grant a patent with claims to monoclonal antibodies because none had been disclosed and there was nothing upon which to base a sound prediction. The rejection was not, as the applicant has suggested, because the “traditional techniques” referred to were not fully disclosed in the application or because the prediction that monoclonal antibodies could be obtained by following the teachings of the disclosure was verified/supported by post-filing work done by others rather than by someone in the inventor’s laboratory. The “Pasteur” application referred one of skill in the art to techniques which could be used to obtain monoclonal antibodies without actually disclosing the antibodies.

The Board is satisfied that the Applicant, or one of skill in the art, would have been able to use the partial amino acid sequence disclosed in the application, as a tool to eventually obtain a cDNA, and possibly a gene, encoding TNF inhibitory protein. At the hearing, the Applicant described how scientists in the inventors’ laboratory were able to do this. 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 “Pasteur” application. The Board is not satisfied that there has been “proper disclosure” in respect of a TNF inhibitory factor-encoding nucleotide sequence and hence there is no support for the products and processes defined by claims 15 to 25. 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.

In summary, the Board concludes that claims 15 to 25 do not comply with Subsection 174(2) of the Patent Rules and that the Examiner correctly rejected these claims. The Board recommends that the Commissioner:

1) inform the Applicant, in accordance with paragraph 31(c) of the Patent Rules, that the following amendment of the application is necessary for compliance with the Patent Act and Patent Rules: deletion of claims 15 to 25 and the renumbering of claims 26 to 28 as claims 15 to 17, respectively;

2) invite the Applicant to make the above amendment within three (3) months of the date of the Commissioner’s decision; and

3) advise the Applicant that, if the above amendment is not made within the specified time, the Commissioner intends to refuse the application.

M. Gillen	M. Wilson	J. Cavar
Chairman	Member	Member

I concur with the findings and recommendations of the Patent Appeal Board. Accordingly, I invite the Applicant to make the above amendment within three (3) months from the date of this decision, failing which I intend to refuse the application.

David Tobin
Commissioner of Patents

Dated at Gatineau, Quebec,
this 4th day of December , 2006