Commissioner’s Decision # 1393

Décision de la Commissaire # 1393

TOPIC: GOO (Utility); B20 (Excessive width); C00 (Adequacy of Description); B00 (Lack of clarity); F00 (Novelty); O00 (Obviousness)

SUJET: GOO (Utilité); B20 (Portée excessive); C00 (Inadéquat de la description; B00 (Caractère ambigu); F00 (Nouveaté); O00 (Évidence)

Application No.: 2,544,223

Demande n°.: 2,544,223

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,544,223 having been rejected under subsection 30(3) of the *Patent Rules*, has subsequently been reviewed in accordance with paragraph 30(6)(*c*) of the *Patent Rules*. The recommendation of the Board and the decision of the Commissioner is that the Applicant be informed, in accordance with subsection 30 (6.3) of the *Patent Rules*, that amendments to the claims are necessary for compliance with the *Patent Act* and *Patent Rules*.

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INTRODUCTION

[1] Patent application number 2,544,223 is owned by the Dana-Farber Cancer Institute, Inc., and the President and Fellows of Harvard College. It is entitled "Stabilized alpha helical peptides and uses thereof" and stands rejected after the issuance of a Final Action dated April 10, 2013 for multiple reasons. The Applicant's response to the Final Action did not overcome the rejection, and a review of the rejected application has therefore been conducted in accordance with paragraph 30(6)(*c*) of the *Patent Rules* by the Patent Appeal Board.

BACKGROUND

[2] The subject application was filed in Canada on November 5, 2004. A series of examination reports culminated with the issuance of a Final Action on April 10, 2013 at which time a number of defects were identified in the application, including: lack of utility under section 2 of the *Patent Act*, lack of support under section 84 of the *Patent Rules*, insufficient disclosure under subsection 27(3) of the Act, and indefiniteness under subsection 27(4) of the Act.

[3] In response to the Final Action, the Applicant submitted on October 10, 2013 the claims presently on file and argued in favour of their patentability. These claims were considered defective and new defects in respect of certain claims were identified: lack of novelty under subsection 28.2(1(*b*) of the Act and obviousness under section 28.3 of the Act. A Summary of Reasons (SOR) was therefore prepared and the application was referred to the Patent Appeal Board for review. The present Panel was then established to review the rejected application.

[4] Upon being informed that the application was pending for review, the Applicant responded by submitting a first set of proposed claims on July 10, 2014 that incorporated a feature found in a dependent claim and which is indicated in the Final Action and the SOR to be required for patentability. The Applicant also declined a hearing before the Panel.

[5] Following the Panel's initial review of the application, the Applicant was informed on February 26, 2015 that it was our provisional view that the claims on file are defective and that the first set of proposed claims may be considered patentable if two issues are addressed. The Applicant replied on April 24, 2015 with a second set of proposed claims.

ISSUES

[6] In view of the reasons for rejection set out in the Final Action and SOR, there are a number of issues in respect of the claims, including utility, sufficiency of disclosure, obviousness, anticipation, and claim definiteness:

1) Utility: Do claims 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, and 74-90 contravene section 2 of the Act because they encompass subject-matter for which utility is not soundly predicted? In addition to an objection under section 2 of the Act in respect of the utility issue, the Final Action and the SOR identified section 84 of the Rules as a statutory provision relevant to the question of sound prediction because these claims were considered to be not fully supported. The underlying reasoning for both defects is the same. For the purposes of this review, the utility issue will therefore be dealt with solely as one concerning section 2 of the Act.

2) Sufficiency of disclosure: Do claims 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, and 74-90 contravene subsection 27(3) of the Act because the specification does not correctly and fully describe the claimed invention and does not enable the skilled person to make it?

3) Obviousness: Do claims 31-36, 38-42, 45-47 and 81-90 contravene section 28.3(*a*) of the Act because they are obvious?

4) Anticipation: Are claims 31-36, 38-42, 45-47 and 81-90 anticipated, contrary to subsection 28.2(1)(*a*) of the Act?

5) Claim indefiniteness:

a) Do claims 1, 16, 31, and 81 contravene subsection 27(4) of the Act because the expression "each Xaa is independently an alpha amino acid and is the same amino acid as in an α-helix containing pro-apoptotic polypeptide" does not define the subject-matter of the invention in distinct and explicit terms?

b) Do claims 51, 69, and 84 contravene subsection 27(4) of the Act because the expression "comprising a plurality of the polypeptide defined by" does not define the subject-matter of the invention in distinct and explicit terms?

c) Do claims 82 and 83 contravene subsection 27(4) of the Act because the feature "Xaa" does not define the subject-matter of the invention in distinct and explicit terms?

LEGISLATIVE PROVISIONS AND LEGAL PRINCIPLES

Claim construction

[7] In accordance with *Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust*] essential elements are identified through a purposive construction of the claims done by considering the whole of the disclosure, including the specification and drawings (see also *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at paras. 49(f) and (g) and 52). In accordance with the *Manual of Patent Office Practice* §13.05 [revised June 2015; MOPOP], the first step of purposive claim construction is to identify the person skilled in the art and their relevant common general knowledge ("CGK"). The next step is to identify the problem addressed by the inventors and the solution disclosed in the application. Essential elements can then be identified as those elements of the claims that are required to achieve the disclosed solution.

[8] In the present case, it is noteworthy that if an element essential to the operation of the solution has not been defined in the claim, the claim may be defective for overbreadth and/or for lack of utility (MOPOP, §13.05.02c).

Utility

[9] Section 2 of the Act requires than an invention be useful. As of the filing date of the application, there must be either a demonstration or a "sound prediction" of the utility of the subject-matter that falls within the scope of a claim: *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 ("*AZT*"). In the present case, the Applicant must rely on a sound prediction to establish utility.

[10] According to *AZT* (para. 70), the doctrine of sound prediction has three components :

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

[11] A factual basis can rely on information disclosed in the specification as well as information forming part of the common general knowledge of the skilled person, the latter of which need not be explicitly disclosed in the specification (see *Bell Helicopter Textron Canada Limitée v Eurocopter*, 2013 FCA 219 at paras. 153-155).

[12] Predictions are measured taking into account any explicit "promises" made in the specification; however, "if there is no explicit promise of a specific result, then a mere scintilla of utility will do" (see *Sanofi-Aventis v Apotex Inc*, 2013 FCA 186 at para. 50). Where a promise is clearly and unequivocally expressed by the inventor in the claims, then that expression can be viewed as the promise of the patent (see *Fournier Pharma Inc v Canada (Health)*, 2012 FC 741 at para. 126).

Sufficiency of disclosure

[13] The portions of the Act relevant to the question of sufficiency of disclosure are paragraphs 27(3)(*a*) and (*b*). They read as follows:

> The specification of an invention must:

> (*a*) correctly and fully describe the invention and its operation or use as contemplated by the inventor;
>
> (*b*) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;

[14] The courts have indicated that sufficiency of disclosure relates to two questions that are relevant for the purpose of paragraphs 27(3)(*a*) and 27(3)(*b*) of the *Patent Act*: What is the invention? How does it work? (see *Consolboard v MacMillan Bloedel*, [1981] 1 SCR 504 at 526, 56 CPR (2d) 145 at 157). With respect to each question the description must be correct and complete in order that when the period of the monopoly has expired the public, having only the specification, the skilled person will be able to make the same successful use of the invention as the inventor could at the time of his application, without having to display inventive ingenuity or undertake undue experimentation.

[15] Issues of sufficiency of disclosure under section 27(3) of the Act and issues of sound prediction under section 2 of the Act can both concern the scope of the claims in relation to what has been disclosed. However, the case law indicates that the two issues are "separate and distinct" (see *Eli Lilly v Novopharm*, 2010 FCA 197 at para. 120; "*Lilly v Novopharm*") and can be approached from different perspectives.

Obviousness

[16] The question of obviousness was raised in view of a prior art document co-authored by one of the inventors – indicating that subsection 28.3(*a*) of the Act is the relevant statutory provision. That subsection provides that the subject-matter of a claim must not have been obvious to persons skilled in the art or science on the relevant date:

> The subject matter defined by a claim in an application for a patent in Canada must be subject matter that would not have been obvious on the

> claim date to a person skilled in the art or science to which it pertains, having regard to
>
> (a) information disclosed more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere;

[17] In *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para. 67 ("*Sanofi*") the Supreme Court indicated that it is useful in an obviousness inquiry to follow a four-step approach:

> (1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

Anticipation

[18] The question of anticipation was raised based on the alleged prior disclosure of the subject-matter of the claims in a prior art document co-authored by one of the inventors. Subsection 28.2(1)(*a*) of the Act provides the relevant statutory basis for the rejection:

> The subject-matter defined by a claim in an application for a patent in Canada (the "pending application") must not have been disclosed
>
> (a) more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the

> applicant, in such a manner that the subject-matter became available to the public in Canada or elsewhere;

[19] In *Sanofi*, the Supreme Court endorsed a two-pronged approach to the question of anticipation in which "prior disclosure" and "enablement" are considered separately (*Sanofi* at para. 28). There is anticipation if a single prior art publication discloses all of the essential elements of a claimed invention in an enabling manner: *Free World Trust* at para. 25.

Claim definiteness

[20] Subsection 27(4) of the Act requires that the specification "end with a claim or claims defining distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed."

[21] In *Minerals Separation North American Corp v Noranda Mines Ltd*, [1947] Ex CR 306 at 352 (cited with approval by the Supreme Court in *Free World Trust*, *supra*, at para. 14), the court indicated that the scope of the claims should be clear, precise and free from avoidable ambiguity or obscurity:

> 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.

Proposed claim amendments considered necessary under Rule 30(6.3) for compliance

[22] In the present case, the Applicant has proposed claims after expiration of the time limit to respond to the Final Action. However, at this time the Applicant cannot, as a matter of right, amend their application after the time limit to respond to a Final Action has expired. In circumstances where the Commissioner first determines that the application does not comply with the Act or Rules, the Commissioner shall inform an applicant that specific amendments are necessary for compliance. A

review of the claims on file therefore precedes a consideration of proposed claims. Subsection 30 (6.3) of the Rules provides:

> If, after review of a rejected application, the Commissioner determines that the application does not comply with the Act or these Rules, but that specific amendments are necessary, the Commissioner shall notify the applicant that the specific amendments have to be made within three months after the date of the notice. If the applicant complies with that notice, the Commissioner shall notify the applicant that the application has been found allowable and shall requisition the payment of the applicable final fee set out in paragraph 6(*a*) or (*b*) of Schedule II within the six-month period after the date of the notice of allowance.

CLAIM CONSTRUCTION

Background context

[23] Polypeptides and proteins are made up of unique strings of amino acids – something akin to beads on a necklace. A particular sequence of amino acids defines the "primary" structure of a polypeptide or protein. Strings of amino acids can also adopt three dimensional "secondary" structures, one of which is an alpha helical shape that resembles a coil. Secondary structures play a critical role in protein-protein interactions and can consequently affect the overall activity of a given protein or polypeptide.

[24] The present application concerns certain polypeptides that have alpha helical secondary structures stabilized through a cross-link. The polypeptides are derived from members of the "Bcl-2" family of proteins that modulate "apoptosis", a phenomenon also known as "programmed cell death" which is involved in the spread of cancerous cells in the body. Apoptosis modulation by a Bcl-2 protein can either be pro-apoptotic or anti-apoptotic in nature, and can change depending on cellular conditions.

[25] Of particular interest to the inventors are sub-regions of Bcl-2 proteins that define alpha helical secondary structures known as "BH" domains. These domains interact with other proteins and are critical for apoptosis-modulating activity.

The person of skill in the art and the common general knowledge

[26] The Applicant was informed of the definition of the skilled person and of the common general knowledge in our letter of February 26, 2015. The Applicant did not provide arguments or submissions to the contrary.

[27] Based on the Background of the invention mentioned in the description, we consider the person of skill in the art to be a protein chemist/biochemist familiar with the proteins involved in apoptotic pathways.

[28] The common general knowledge possessed by the skilled person would include: knowledge of the physical aspects of the secondary structures of proteins, polypeptides, and peptides; including knowledge of alpha helices; knowledge of methods of chemical synthesis typically employed in peptide synthesis; knowledge of proteolytic cleavage assays, methods of determining physical interactions amongst peptides and/or polypeptides; and, knowledge of proteins involved in apoptotic pathways. It includes the skilled person's knowledge – which was not contested by the Applicant – that protein function is directly dependent upon protein structure (including secondary structures, such as alpha helices), as pointed out on page 3 of the Final Action (citing page 34 of *Advanced Biology*, by Michael Kent, Oxford University Press, 2000.

The problem and solution

[29] The Background portion of the description indicates that the problem faced by the inventors involves generating polypeptides with stabilized alpha helical domains. In particular, page 3 of the description indicates that stabilizing alpha helical BH3 domains from proteins of the Bcl-2 family is key to the proposed solution.

[30] The Summary of the invention indicates that the proposed solution involves using a technique known as "hydrocarbon stapling" to chemically cross-link amino acids in

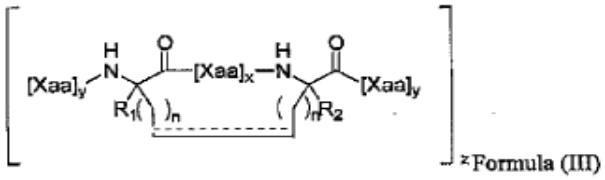
alpha helical domains of polypeptides derived from apoptosis-related proteins. By using a chemical cross-link, or staple, the alpha helical coil is prevented from unravelling. Apoptosis-modulatory activity is thus maintained and the polypeptide is protected from degradative enzymes.

The claims

[31] Claims 1, 16, 31, 48, 49, 50, 51, 66, 67, 68, 69, 81, 82, 8, and 84 are drafted in independent form and encompass two types of polypeptides: apoptosis modulators, and polypeptides that are simply cell membrane penetrators. Each type is defined with reference to a general chemical formula as having an alpha helical portion that is cross-linked with a hydrocarbon stable. None of the independent claims indicate the presence of a structural element, e.g., a BH3 domain, responsible for apoptotic-modulatory activity – an element indicated in the description to be essential to the operation of the solution. However, certain dependent claims do include such a feature and are indicated in the SOR to be patentable.

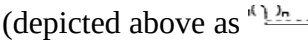
[32] Claim 1, on file, is generally representative of the manner in which the Applicant has claimed apoptosis modulating polypeptides:

1. A pro-apoptotic α-helix containing polypeptide, wherein said polypeptide is of Formula (III):



Formula (III)

wherein;
each R_1 and R_2 is independently H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, arylalkyl, cycloalkylalkyl, heteroarylalkyl, or heterocyclylalkyl;
each n is independently an integer from 1-15;
x is 2, 3 or 6;
each y is independently an integer from 0-100;
z is an integer from 1-10; and
each Xaa is independently an alpha amino acid and is the same amino acid as in an α-helix containing pro-apoptotic polypeptide.

[33] Consistent with the proposed solution, the polypeptides of claim 1 are indicated to have certain essential elements: an alpha helix secondary structure, a hydrocarbon staple (depicted above as ), and an indication of apoptosis modulatory activity. However, what is notably absent from the claim is the presence of a structural element responsible for apoptotic-modulatory activity, e.g., a BH3 domain derived from a Bcl-2 protein. Other independent claims defining this type of polypeptide are claims 16, 48-50 and 66-68.

[34] Independent claims 31, and 81-83 feature polypeptides with the essential element of cell penetration but do not include an indication of apoptosis modulatory activity. Moreover, what is also absent from these claims is, again, a structural element responsible for apoptotic-modulatory activity, e.g., a BH3 domain derived from a Bcl-2 protein.

UTILITY: DO CLAIMS 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, AND 74-90 CONTRAVENE SECTION 2 OF THE ACT BECAUSE THEY ENCOMPASS SUBJECT-MATTER FOR WHICH UTILITY IS NOT SOUNDLY PREDICTED?

The utility

[35] The nature of the utility was disputed in the present case.

[36] According to the Final Action, the claimed polypeptides are apoptosis modulators (i.e., they are "pro-apoptotic" or "anti-apoptotic") and are useful on that basis. Based on that assessment of the claimed polypeptides' utility, the Final Action explains that the absence of a structural element, e.g., a BH3 domain, responsible for apoptotic-modulatory activity is problematic.

[37] By contrast, the Applicant contended that "the actual utility of the claimed polypeptides as a whole is broader from that alleged by the Examiner" (response to Final Action, page 7, first para.). Pointing to page 20, last paragraph of the description, the Applicant suggested that "the novel cross-linked polypeptides are useful, for example, to mimic or study proteins or polypeptides having one or more alpha helical domains" and that they may simply have the ability to penetrate cell

membranes (response to Final Action, page 6). The Applicant further argued that pages 46-48 of the description identify other polypeptides that may be cross-linked.

[38] In our view, the indications in the description that certain of the claimed polypeptides can have the property of cell penetration would not be taken by the skilled person to be indications of their underlying utility. While cell penetration would be seen as a beneficial property, it would not be seen as a stand-alone utility common to all the claimed subject-matter. We note that the response to the Final Action asserts that the factual basis for the predicted utility for the claims is found in the description as filed and that "the description as a whole is directed to pro- and anti-apoptotic proteins" (page 2, second paragraph).

[39] While the description states on page 20 that the polypeptides are generally useful as mimics or for study, we do not consider the utility requirement of section 2 of the Act to be satisfied merely by stating that something is useful as an object of study. If that were so, establishing a sound prediction of utility would be reduced to a triviality.

[40] Further, while all may be cross-linked using the same basic technique, the skilled person would not appreciate that the various polypeptides mentioned on pages 46-48 of the description would carry the same underlying utility. It is only "in some instances" that cell penetration is involved (summary of the invention, description page 4, second paragraph).

[41] The broader utility alleged by the Applicant also rests on the argument that "cross-linking a polypeptide by connecting at least two modified amino acids can conformationally bestow the native secondary structure of that polypeptide." Page 10 of the response to the Final Action explains that "many anti-apoptotic and pro-apoptotic polypeptides comprise multiple BH domains, for example BH1, BH2, BH3 and BH4 domains which are known to exhibit partial alpha-helical conformation in solution." Thus, the Applicant argues it would be unfair to insist, as indicated in the Final Action, on limiting the claim to polypeptides which include a BH3 domain.

[42] In our view, this line of argumentation neither clarifies the utility of the claimed polypeptides, nor does it address the concern that the claims make no mention of any structural element that the skilled person might plausibly consider responsible for conferring apoptotic-modulatory activity.

[43] Accordingly, we agree with the assessment indicated in the Final Action that the predicted utility is that all of the claimed polypeptides possess apoptosis modulating activity.

Factual basis

[44] According to the Final Action and SOR, the factual basis includes the disclosure that the polypeptides that were tested and that were demonstrated to have utility are about 18-23 amino acids in length, comprise a BH3 domain, and have a hydrocarbon cross-link. The factual basis includes the observation "that all such polypeptides were members of the Bcl-2 family and contained a BH3 domain" (SOR, page 2).

[45] The factual basis also includes the skilled person's common general knowledge that protein function is directly dependent upon protein structure, especially secondary structures such as alpha helices that are at issue in this case.

Sound line of reasoning

[46] In our view, the inventors did not have, at the filing date of the application, an articulable and sound line of reasoning from which the desired result could be inferred from the factual basis. In considering the CGK and the factual basis, it is not clear to us how the skilled person would expect all of the claimed polypeptides to possess apoptotic-modulatory activity without an explicit indication in the claim of a structural element responsible for that activity. Further, apart from arguing that the utility of the claimed polypeptides is broader than indicated in the Final Action – an argument addressed above – the Applicant did not provide a line of reasoning for our consideration that could lead to a different conclusion.

[47] The record establishes that a given protein function follows from its particular protein structure, which the skilled person would understand to include its primary

and secondary structure. As explained on page 3 of the Final Action, "although a particular relationship may be established between structure and function for one protein, that relationship cannot be reliably predicted for other proteins with no underlying similarity in amino acid sequence." It is also understood by the skilled person that, while a protein or polypeptide may include an alpha helical domain, it does not follow that it is also necessarily able to modulate apoptosis.

[48] In the context of the present invention, in order for a polypeptide to have utility, the skilled person would appreciate that the alpha helical segment of an apoptosis modulating polypeptide must constitute an appropriate structural element that confers apoptotic-modulatory activity.

[49] It follows that because claims 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, and 74-90 are not explicitly limited to apoptotic modulating polypeptides that have a structural element that confers apoptotic-modulatory activity, the utility of all the polypeptides of these claims is not soundly predicted.

Proper disclosure

[50] In this case, the third requirement of proper disclosure under the *AZT* test need not be addressed because the second requirement of the test has not been satisfied.

SUFFICIENCY OF DISCLOSURE: DO CLAIMS 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, AND 74-90 CONTRAVENE SUBSECTION 27(3) OF THE ACT BECAUSE THE SPECIFICATION DOES NOT CORRECTLY AND FULLY DESCRIBE THE CLAIMED INVENTION AND DOES NOT ENABLE THE SKILLED PERSON TO MAKE IT?

[51] The issue of sufficiency of disclosure was raised in the Final Action because an "undue burden is placed on the skilled worker to determine which polypeptide structures fall within the scope of the claims and which do not" (Final Action, p. 5). Whereas the description provides structures derived from Bcl-2 proteins, it was reasoned in the Final Action that the claims encompass unrelated structures requiring undue burden of the skilled person to synthesize and test a myriad of possible structures.

[52] It appears that the Applicant addressed the issue in the response to the Final Action as one of utility and argued accordingly. However, whether there is a sound prediction of utility under section 2 of the Act is distinct from one of sufficiency of disclosure under subsection 27(3) of the Act: *Lilly v Novopharm*, *supra*.

[53] The skilled person would appreciate that, armed only with the CGK and the description, an attempt to practise the claimed invention across its breadth would not be possible. Some routine experimentation is permissible to practise the claimed invention. In this case, however, because of the nature of the generic chemical formula recited in the claims and the failure to otherwise limit the scope of the claims, the skilled person would face extensive experimentation and would be required to synthesize and test far too many candidate polypeptides in the hopes of achieving success. In our view, that would amount to an undue burden.

[54] We therefore agree with the Examiner that the specification is insufficient under subsection 27(3) of the Act to support the breadth of claims 1-4, 6-10, 13, 14, 16-19, 21-25, 28, 29, 31-46, 48-54, 56-60, 63, 64, 66-72, and 74-90.

OBVIOUSNESS: DO CLAIMS 31-36, 38-42, 45-47 AND 81-90 CONTRAVENE SECTION 28.3(*a*) OF THE ACT BECAUSE THEY ARE OBVIOUS?

The person of skill in the art and the common general knowledge

[55] Definitions of the person of skill in the art and the common general knowledge have been set out above at paragraphs 27-28.

Identify the inventive concept of the claim in question or if that cannot readily be done, construe it

[56] Claims 31-36, 38-42, 45-47 and 81-90 are indicated in the SOR to be obvious. Of these, claims 31 and 81-83 are drafted in independent form. Although the independent claims vary slightly in their wording, they all encompass cell membrane penetrating polypeptides, are defined with reference to a generic chemical formula, have a hydrocarbon cross-link, and have an alpha helical structure in aqueous

solution. With the exception of dependent claims 32, 33, 47, 85, 86 and 90 the inventive concept of the rejected claims is taken as the combination of these features.

[57] The inventive concept of claims 32, 33, 47, 85, 86 and 90 is altered through their inclusion of the following features:

a) "binds to a BCL-2 family polypeptide" – claims 32 and 85;
b) "activates mitochondrial cell death" – claims 33 and 86; and
c) "comprises a BH3 domain" – claims 47 and 90.

Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed

[58] The prior art document identified in the SOR concerning the question of obviousness is Schafmeister et al., *An All-Hydrocarbon Cross-linking System for Enhancing the Helicity and Metabolic Stability of Peptides, J. Am. Chem. Soc*., 2000, 122: 5891-5892 [*Schafmeister*].

[59] *Schafmeister* discloses peptides from an enzyme known as "RNAse A" that have an alpha helical portion cross-linked with a hydrocarbon staple in order to enhance their helicity and metabolic stability in aqueous solution. The peptides are defined in structural terms such that they appear to be within the scope of claims 31, and 81-83.

[60] The introductory paragraph of the reference indicates that increasing stable helices in a peptide is generally expected to facilitate cell membrane penetration: "the intramolecular hydrogen bonding associated with helix formation reduces the exposure of the polar amide backbone, thereby reducing the barrier to membrane penetration". However, no testing was done on the RNAse A peptides to determine the effect of alpha helix cross-linking on cell membrane penetration.

[61] The difference between the inventive concept of the independent claims and *Schafmeister* is the following: there is no disclosure that the prior art peptides are able to penetrate a cell membrane.

[62] In respect of dependent claims 32, 33, 47, 85, 86, and 90, the differences between the inventive concepts of these claims and *Schafmeister* lies in the features stated above since they are not disclosed, i.e., the reference does not disclose a peptide that "binds to a BCL-2 family polypeptide", "activates mitochondrial cell death" or "comprises a BH3 domain".

Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[63] In our view, the differences between the inventive concept of independent claims 31 and 81-83 constitute steps that would have been obvious to the skilled person. There is no inventive step in ascertaining that a peptide as disclosed by *Schafmeister* can penetrate a cell membrane, given that the reference indicates the expectation that the peptides would have such a property. Apart from claims 32, 33, 47, 85, 86, and 90, this finding extends to claims that depend from claims 31 and 81-83 because we do not believe there are features in the claims that the skilled person would regard as constituting an inventive step.

[64] In the response to the Final Action the Applicant submitted information establishing that the peptides disclosed by *Schafmeister* do not exhibit apoptosis modulating activity. The Applicant has also characterized the statement cited from the introductory paragraph of the reference concerning cell membrane penetration as "merely a forward looking statement" and that "further experimentation is required to characterize the polypeptides of [*Schafmeister*]". However, the independent claims at issue are not restricted to apoptosis modulators.

[65] In respect of dependent claims 32, 33, 47, 85, 86, and 90, we are satisfied that the skilled person would read *Schafmeister* and not take from its disclosure that it is related to polypeptides that bind a BCL-2 family polypeptide, that activate mitochondrial cell death, or that comprise a BH3 domain. These properties are suggestive of some property associated with apoptosis. Although the skilled person carries an awareness of apoptosis, there is no specific suggestion in *Schafmeister*

guiding the skilled person to apply the disclosed cross-linking techniques to apoptosis-related polypeptides.

[66] Claims 31, 34-36, 38-42, 45, 46 and 81-84, and 87-90 therefore contravene section 28.3(*a*) of the Act because they are obvious to the skilled person.

ANTICIPATION: ARE CLAIMS 31-36, 38-42, 45-47 AND 81-90 ANTICIPATED, CONTRARY TO SUBSECTION 28.2(1)(*a*) OF THE ACT?

[67] The first prong of the test for anticipation requires that a single prior art reference disclose all the essential elements of the claimed invention. In this case, it is apparent from the obviousness analysis set out above for the same claims that there is at least one essential element of each claim that is not disclosed in *Schafmeister*: the property of cell membrane penetration. Moreover, the record does not establish that such a property is inherent to a peptide disclosed by *Schafmeister*.

[68] As such, the first prong of the test for anticipation is not satisfied in this case and there is no need to consider the second prong of the test that deals with enablement.

[69] Based on the record, claims 31-36, 38-42, 45-47 and 81-90 are not anticipated and comply with subsection 28.2(1)(*a*) of the Act.

CLAIM INDEFINITENESS: DO CLAIMS 1, 16, 31, AND 81 CONTRAVENE SUBSECTION 27(4) OF THE ACT BECAUSE THE EXPRESSION "EACH Xaa IS INDEPENDENTLY AN ALPHA AMINO ACID AND IS THE SAME AMINO ACID AS IN AN α-HELIX CONTAINING PRO-APOPTOTIC POLYPEPTIDE" DOES NOT DEFINE THE SUBJECT-MATTER OF THE INVENTION IN DISTINCT AND EXPLICIT TERMS?

[70] The Final Action and the SOR suggest that claims 1, 16, 31, and 81 are indefinite, contrary to subsection 27(4) of the Act, because they indicate that a variable alpha amino acid, defined as "Xaa", is "the same amino acid as in an α-helix containing pro-apoptotic polypeptide".

[71] The Final Action (p. 6) indicated that the expression is meaningless because all alpha helical polypeptides contain amino acids and all biologically relevant amino acids are alpha amino acids.

[72] In our view, the skilled person would be aware that amino acids with biological activity of other configurations exist, including, for example, those with beta or gamma configurations. Thus, the skilled person would regard it as a meaningful limitation. We are also of the view, in accordance with the Applicant's argument, that the use of the expression is intended to "capture the various possibilities of different sequences" that make up apoptosis modulating polypeptides (response to the Final Action, p. 15).

[73] Claims 1, 16, 31, and 81 comply with subsection 27(4) of the Act because the expression "each Xaa is independently an alpha amino acid and is the same amino acid as in an α-helix containing pro-apoptotic polypeptide" defines the subject-matter of the invention in distinct and explicit terms.

CLAIM INDEFINITENESS: DO CLAIMS 51, 69, AND 84 CONTRAVENE SUBSECTION 27(4) OF THE ACT BECAUSE THE EXPRESSION "COMPRISING A PLURALITY OF THE POLYPEPTIDE DEFINED BY" DOES NOT DEFINE THE SUBJECT-MATTER OF THE INVENTION IN DISTINCT AND EXPLICIT TERMS?

[74] The SOR summarily states that "new claims 51, 69 and 84 comprise the expression 'comprising a plurality of the polypeptide defined by' which lacks clarity. It is not clear what a 'plurality of the polypeptide' encompasses."

[75] Claim 51 is representative and reads as follows: "A protein comprising a plurality of the polypeptide defined by claim 49 or 50."

[76] In our view, the skilled person would not regard the language as imprecise or admitting to ambiguity. The claim refers to a polypeptide of claim 49 or 50, each of which presumably accurately defines a polypeptide. As regards the term "plurality", the Merriam-Webster online dictionary defines it as "the state of being plural" where "plural" means "relating to or made up of more than one person or thing."

[77] The skilled person would therefore understand that the claim encompasses a protein that includes several units of a polypeptide as defined in claim 49 or 50 which together form the whole of the claimed subject-matter.

[78] Claims 51, 69, and 84 therefore comply with subsection 27(4) of the Act because the expression "comprising a plurality of the polypeptide defined by" defines the subject-matter of the invention in distinct and explicit terms.

CLAIM INDEFINITENESS: DO CLAIMS 82 AND 83 CONTRAVENE SUBSECTION 27(4) OF THE ACT BECAUSE THE FEATURE "Xaa" DOES NOT DEFINE THE SUBJECT-MATTER OF THE INVENTION IN DISTINCT AND EXPLICIT TERMS?

[79] Claims 82 and 83 include a general chemical formula with a variable defined as "Xaa". However, the claims do not define in distinct and explicit terms what the variable can be.

[80] The feature "Xaa" does not have an art-accepted definition and the skilled person reading the claims could therefore be left in doubt as to the scope of the claimed subject-matter. Further, ambiguity can be avoided through the provision of a distinct and explicit definition of the feature in the claims.

[81] Claims 82 and 83 therefore contravene subsection 27(4) of the Act because they fail to define the feature "Xaa" in distinct and explicit terms.

ARE THE CLAIMS PROPOSED BY THE APPLICANT ON APRIL 24, 2015 NECESSARY UNDER RULE 30(6.3) FOR COMPLIANCE?

[82] Because there are claims on file that have been found to be non-compliant with the Act, specific amendments can be considered to determine whether they will put the application in a state for allowance.

[83] The latest claims proposed by the Applicant are those submitted April 24, 2015. The proposed claims include a feature from an allowable dependent claim, claim 5, indicated in the Final Action and SOR to be required for patentability. That feature is the presence of a BH3 domain, which, in line with our analyses set out above, is one

which limits the claims to subject-matter for which utility is soundly predicted and sufficiently disclosed.

[84] All claims considered by the Examiner to be obvious and anticipated no longer appear in the proposed claim set. The proposed amendment also addresses the other issues identified in the Final Action and SOR with respect to claim indefiniteness.

[85] Having reviewed the proposed claims, and having considered the Applicant's submissions of April 24, 2015, we do not detect any outstanding issues that would bar the issuance of the application to patent. The amendments to the claims as proposed on April 24, 2015 overcome all defects in the application and put the application in allowable form.

RECOMMENDATION

[86] We recommend that the Applicant be informed, in accordance with subsection 30 (6.3) of the *Patent Rules*, that the amendments to the claims as proposed by the Applicant on April 24, 2015 are necessary for compliance with the Act and Rules. The Applicant may cancel claims 1-90 on file and replace them with proposed claims 1-25 submitted by the Applicant on April 24, 2015.

Ed MacLaurin	Cara Weir	Marcin Kaminski
Member	Member	Member

DECISION

[87] I concur with the findings and the recommendation of the Board. In accordance with subsection 30 (6.3) of the *Patent Rules*, the amendments to the claims as proposed by the Applicant on April 24, 2015 are necessary for compliance with the Act and Rules. The Applicant may cancel claims 1-90 on file and replace them with proposed claims 1-25 submitted by the Applicant on April 24, 2015. If those amendments, and only those amendments, are not made within three months from the date of this decision I intend to refuse the application.

Johanne Bélisle,
Commissioner of Patents
Dated at Gatineau, Quebec,
this 5th day of April, 2016