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Update on Patentability of Diagnostic Claims: Canada

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This is an update to our 2014 10-part series "The Thorny Problem of Patentable Eligible Subject Matter" regarding new guidance in Canada for examining diagnostic method claims.

Impact of Practice Notice PN2015-02

The ***Canadian Intellectual Property Office (CIPO)*** released Practice Notice PN2015-02 (Practice Note), which instructed examiners to use an application's description and the common general knowledge to identify an unaddressed "problem" and its proposed "solution".

A determination of whether a diagnostic method claim is patent eligible is made based on the essential elements as determined through a purposive construction of the claim. A proper purposive construction is a two-step analysis requiring an Examiner to identify (1) the problem the inventors set out to solve; and (2) the solution disclosed.

For diagnostic methods, only two types of mutually exclusive problems are recognized: data acquisition problems and data analysis problems. "Data acquisition" problems involve, for example, identifying, detecting, measuring, etc., the presence or quantity of analyte X in a sample, while "data analysis" problems involve, for example, analyzing the significance of the acquired data (such as how the presence, increase/decrease in quantity, etc., of analyte X correlates to condition Y).

The Practice Notice indicates that the "essential elements" of a claim are limited to those that work together to solve this restricted problem. Other "non-essential" claim elements are said to "merely define the context or the environment of a specific working embodiment, but do not actually change the nature of the solution to the problem…" These non-essential elements are excluded from later analysis.

The Practice Notice suggests that "data analysis" solutions will generally be viewed as unpatentable, particularly when the identified solution is only provided by an element or set of elements associated with the analysis or significance of acquired data. The CIPO views that the recitation of only data analysis elements that are disembodied (e.g., mental process, lacking physicality, or having no physical application) is insufficient to meet the subject matter eligibility criteria of the Patent Act.

In contrast, the Practice Notice indicates that a claim having a *physical* step of data acquisition as an essential element likely will be found patent eligible. The Practice Notice provides the following examples as to elements expected to be characterized as "data acquisition":

- detecting protein X in a subject sample;
- measuring the concentration of substrate X;
- determining the expression levels of genes A, B and C;
- contacting a urine sample with antibody A and determining the optical density; and
- incubating a sample with a nucleic acid probe consisting of SEQ ID NO: 1 and detecting hybridization between the probe and target sequence A.

The application of these restrictive guidelines had created what some Canadian practitioners see as a hostile situation for diagnostic claims in Canada. Indeed, Access to Information requests from the biotechnology industry reveal significant discord within the biotechnology examining division in CIPO, leading to examination of hundreds of diagnostic patent applications being placed on hold as CIPO works to develop its policy. These developments suggest that CIPO's position may be challenged in court. In the meantime, applicants should argue against objections raised by CIPO under section 2 until clarity is obtained from the courts.

USPTO Subject Matter Eligibility Guidance

In view of the restrictive climate at CIPO, we at the BRIC Wall thought it would be insightful to update our analysis of subject matter eligibility under Canadian patent law for diagnostic method claims based on the USPTO's May 2016 updated Guidance and Life Science examples for evaluating subject matter eligibility under Section 101 (Guidance).

On July 16, 2016, the USPTO issued a memo commenting on recent decisions by the U.S. Supreme Court (Supreme Court) and the U.S. Court of Appeals for the Federal Circuit (Federal Circuit) in two subject matter eligibility cases concerning life sciences method claims: *Sequenom v. Ariosa* and *Rapid Litigation Management v. CellzDirect*, respectively. The memo concludes that neither decision changes the subject matter eligibility framework and that the existing Guidance and training examples are consistent with these cases; however, the memo also notes that the *Rapid Litigation Management* decision further clarifies the inquiry involved in determining whether a claim is directed to a judicial exception. In particular, the Federal Circuit stated that the "directed to" analysis of a process claim requires more than "merely identify[ing] a patent-ineligible concept underlying the claim" and instead requires an analysis of whether "the end result of the process, the essence of the whole, was a patent-ineligible concept."

The May 2016 Update provided more detailed instructions for Examiners regarding the formulation of a rejection under Section 101 and evaluation of an Applicants response thereto. Specifically, Examiner's must identify the exception to patentable subject matter (referred to as a "judicial exception") that is being claimed, explain what is recited in the claim and why it is an exception, and identify any additional elements that define claim features/limitations/steps that are beyond the exception. The Examiner must then explain why the additional elements individually AND in combination do not result in the claim as a whole amounting to "significantly more" than the

exception.

The May 2016 update also provided additional examples for application of the Guidance to specific types of life science claims, which were not well represented in the previous USPTO Guidance.

Analysis of Life Sciences Examples from May 2016 Update to USPTO Guidance

Example 29 – Diagnosing and Treating Julitis

Background: Example 29 of the May 2016 Update relates to a hypothetical situation relating to an autoimmune disease called “Julitis.” An applicant for a patent discovered that Julitis could be diagnosed by detecting the presence of the hypothetical “JUL-1” protein in patients’ plasma, skin, hair and nails. Applicant has disclosed detecting JUL-1 using anti-JUL-1 antibodies that may be naturally occurring (e.g., a human anti-JUL-1 antibody isolated from a patient known to have julitis), or non-naturally occurring (e.g., a porcine anti-JUL-1 antibody created by injecting pigs with JUL-1, or a specific monoclonal antibody named “mAb-D33”).

Two representative claims from this Example are analyzed below.

Claim 1. A method of detecting JUL-1 in a patient, said method comprising:

1. obtaining a plasma sample from a human patient; and

2. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody.

Claim 2. A method of diagnosing julitis in a patient, said method comprising:

1. obtaining a plasma sample from a human patient;

2. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody; and

3. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.

Analysis of claims 1 and 2: Claims 1 and 2 would likely constitute patent eligible subject matter in Canada, although an Examiner may require the recitation of a specific anti-JUL-1 antibody (e.g., by SEQ ID NO). However, one caveat is that the “obtaining” steps in claims 1 and 2 might be considered a medical treatment step thus rendering the claim ineligible on that basis alone. In the event such a rejection were raised, it could be overcome by removing this step or making the step of obtaining the plasma sample inactive (such as by reciting a specific anti-JUL-1 antibody).

In the U.S., claim 1 constitutes patent eligible subject matter, while claim 2 constitutes patent ineligible subject matter, as the May 2016 Update indicates that the claim is directed to a judicial exception (i.e., the correlation between the presence of JUL-1 and the presence of julitis in the patient) and as a whole does not amount to significantly more than the exception itself.

Example 31 – Screening for Gene Alterations

Background: Applicant discovered the "wild-type" sequence of the human BRCA1 gene (i.e., the typical sequence of the gene in humans), and has also discovered naturally occurring alterations from the wild-type sequence that are correlated with an increased likelihood of developing breast or ovarian cancer. Applicant's disclosure provides methods of screening patients for alterations in the BRCA1 gene by comparing a patient's BRCA1 sequence with the wild-type BRCA1 sequence. The compared sequences can be germline (genomic) DNA sequences, RNA sequences, or cDNA sequences.

At the time the invention was made and the application was filed, scientists routinely compared DNA sequences using two-data generating techniques: (1) hybridizing two different DNA molecules (e.g., a probe and DNA isolated from a patient sample), and detecting whether the molecules bind to each other and form a hybridization product and (2) amplifying (making copies of) at least part of a DNA molecule such as DNA isolated from a patient sample, by using a set of primers to produce amplified nucleic acids, and then sequencing the amplified nucleic acids. The probes and primers used in these techniques are short single-stranded DNA molecules that typically have a naturally occurring nucleotide sequence.

In one embodiment, applicant discloses using a computer-implemented micromechanical method known as Scanning Near-field Optical Microscopy (SNOM) to detect hybridization of a single probe to its target. At the time the invention was made and the application was filed, the use of SNOM to study DNA hybridization had been discussed in several articles in widely-read scientific journals. However, scientists were not commonly or routinely using SNOM to study DNA hybridization at the time the invention was made and the application was filed. Instead, scientists at the time typically used autoradiography to detect hybridization products.

In another embodiment, applicant discloses using Cool-Melt polymerase chain reaction (Cool-Melt PCR) to amplify BRCA1 DNA from the patient sample. Cool-Melt PCR uses lower melting and annealing temperatures than conventional PCR, which results in Cool-Melt PCR having a 20-fold higher sensitivity of mutation detection than conventional PCR. At the time the invention was made and the application was filed, Cool-Melt PCR was known and used by a few scientists in the field. Several years after filing the application, Cool-Melt PCR became a standard laboratory technique that appeared in virtually every laboratory manual and was conventionally used by most scientists in the field to amplify mutant nucleic acids.

Three representative claims from this Example are analyzed below.

Claim 1. A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject.

Claim 70. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:

hybridizing a wild-type probe to a BRCA1 gene isolated from said sample; and

detecting the presence of a hybridization product by measuring conformational changes in the

probe that are indicative of hybridization to the BRCA1 gene with scanning near-field optical microscopy.

Claim 80. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:

amplifying by Cool-Melt PCR all or part of a BRCA1 gene from said sample using a set of primers to produce amplified nucleic acids; and

sequencing the amplified nucleic acids.

Analysis of claims 1, 70, and 80: Claim 1 would not constitute patent eligible subject matter in Canada (relates to a “data analysis” problem), while 70 and 80 would constitute patent eligible subject matter in Canada (relate to a “data acquisition” problem). In the U.S., claim 1 constitutes patent ineligible subject matter, as the May 2016 Update indicates that the “comparing” amounts to an abstract idea, which is a judicial exception, and the claim as a whole does not amount to significantly more than the exception itself. In contrast, claims 70 and 80 are patent eligible in the U.S., as each claim recites additional elements that distinguishes the claim from well-understood, routine, or conventional techniques in the field (i.e., SNOM and Cool-Melt PCR, respectively), and, therefore, each of claims 70 and 80 as a whole amounts to significantly more than the exception itself.

In view of the above, it is clear that the current standard for determining patent eligible subject matter in Canada based on CIPO’s Practice Notice is similarly restrictive to the patentability of diagnostic method claims as compared to U.S. patent law.

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