Canadian diagnostic claims – where do we stand?

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Revised Chapter 17 of the Manuel of Patent Office Practice (MOPOP) released on November 10, 2017 includes a number of new sections including commentary on “Kits and packages” “Medical diagnostic methods”, and “Antibodies - Utility”. All are interesting in their own right. The present article focuses on the Medical diagnostic methods section and the four Examples provided therein.

Most interesting is Example 4 but more on that later.

The “new” “Medical diagnostic methods” section is largely a rehash of the previous Guidance document on Medical diagnostic methods and incorporates the previous approach for assessing whether diagnostic methods are patentable subject matter. As before, the world of diagnostic applications is split into two camps: the “data acquisition” camp and the “data analysis” camp. Using a problem solution approach, the Examiner determines which camp a claim fits. If a claim fits into the first camp, your claim is likely patentable subject matter. If however the Examiner determines your claim falls squarely in the second camp, your claim will be found non-statutory.

The four Examples provide important insight regarding what types of diagnostic claims the patent office may find patentable and the approach that is applied in determining compliance with the requirements for patentability.

Example 1 is directed claims for diagnosing whether a subject is at risk of thyroid cancer related to the presence of a new mutation. It includes the steps: a) providing a biological sample from the subject; b) analysing the sample of step a) to determine the identity of the nucleotide at position 123 of gene XYZ, c) wherein the subject is at risk for thyroid cancer if the identity of the nucleotide at position 123 of gene 123 is nucleotide A. The mutation identified was not common general knowledge (CGK) or disclosed in any prior art. The problem was identified to include a data acquisition problem since a mutation at position 123 of gene XYZ was not CGK and therefore methods of detecting and specifically acquiring data about the nucleotide at position 123 were also not CGK. The solution is provided by a method when practiced provides means for detecting the identity of the nucleotide within a biological sample and specifically acquires data about the identity of the nucleotide and the essential elements are steps a) and b). The claim is found statutory, novel and non-obvious.

In the modified Example 1b, an article, D1, is cited as identifying the mutation as a mutational hotspot in cancers but not thyroid cancers. The mutation at position 123 has been detected but the mutation is not CGK. The article does not change the Section 2 analysis but renders the invention anticipated even though the mutation was not known in thyroid cancers since D1 discloses and enables all the essential elements of claim 1 according the problem identified. Correlating to thyroid cancer risk is not considered an essential element of the claim. It may be possible to amend the claim to specify the sample is thyroid biopsy which arguably would render the claim non obvious in light of the prior art cited. Unfortunately, the Example does not consider such claim modification.

In modified Example 1c, articles D2-D8 are alleged to disclose testing human subjects for *prostate* cancer by determining the identity of the nucleotide at position 123 in XYZ. In this scenario the claim is not patentable subject matter *even though the claim is novel and non-obvious*. The problem to be solved is reassessed in light of the CGK - the problem is no longer how to determine the nucleotide at position 123 of gene XYZ but rather becomes the “need to correlate a particular genotype in a human subject with a risk of developing thyroid cancer”.

What can be gleaned from this example? As the wherein clause is not assessed in the scenario identifying a data acquisition problem, it may be possible to dispense with the wherein clause entirely and claim the method broadly. The first

to discover a mutation could be rewarded with quite broad claims whereas personalized medicine advances where the mutation is known in an unrelated disease will not be protectable according to the examples provided.

Example 2 is directed to an improved diagnostic method of diagnosing disease P in a subject, the method comprising providing a dried blood sample, measuring the activity of enzyme E by mass spectrometry and diagnosing the patient with disease P when the activity is lower than in a control sample. The method which involves measuring enzyme E activity in dried blood is less invasive and faster than the prior art methods which measured enzyme E in cultured skin samples. In this Example, although it was novel to measure enzyme E in dried blood, an article is identified as using mass spectrometry to measure *other* enzyme activity in *other* lysosomal storage diseases. The claim was found to be patentable subject matter but obvious, although the obviousness of the method would seem arguable.

Diagnostic claims comprising combinations of markers as shown in Example 3 will typically be patentable subject matter although based on the art may be obvious if prior art exists for each of the markers.

Now back to Example 4. It is a curious example for a couple of reasons. Most notably claim 2 of the Example is identified in the commentary as *patentable, novel and non-obvious*. However in the claim summary, claim 2 is identified as patentable *but anticipated and obvious*. A further sentence suggests claim 2 does not meet all the requirements of patentability. Which is correct? This is unclear. It does seem however that the Patent Office may have had some internal strife in deciding how to assess this claim.

In this Example, measuring levels of 5 genes associated with a disease using a microarray with a multitude of probes may aid in rendering a claim patentable. The specification discloses that the expression level of 5 genes was consistently upregulated in patients that had both diabetes and high industrial exposure to persistent organic pollutants (POPs). The art also discloses a commercial DNA microarray which we are told was used by the inventors. In addition the link between POPs and diabetes is CGK.

Claim 1 is directed to a method for determining risk of developing POP associated diabetes comprising a) using a microarray to measure the expression levels of genes T, O, X, I, C in a blood sample obtained from a patient, wherein the microarray comprises oligonucleotide capture probes that are complementary to nucleic acids corresponding to T, O, X, I and C and wherein each probe is attached to a solid support at a discrete position and b) wherein the patient is at risk of developing diabetes if the expression levels of genes T, O, X, I and C are increased relative to the expression levels of the genes in a control sample representative of normal subjects. Claim 2 is a use claim.

According to the Example, although the probes for the genes T, O, X, I and C were represented in the commercial microarray, it is not CGK to both specifically measure the expression levels of the genes and specifically acquire the data about the expression levels (while disregarding the levels of all other genes). The problem is identified as the determination of the expression levels of only genes T, O, X, I and C in a patient sample. The problem is solved by 1) specifically measuring the expression levels and 2) specifically acquiring data about expression levels of the 5 genes.

It is not readily apparent which features make the claim patentable subject matter. It is unclear if including the microarray in the claims is necessary. Both the patentable subject matter assessment and the novelty assessment stress the importance of specifically acquiring data about the expression levels on only these genes while disregarding the levels of all other genes. This argument would however seem to apply almost regardless of the method used.

Would Example 4 claim 1 be patentable if directed to measuring and acquiring data on the expression level of one gene by microarray? Again the reasoning of acquiring data on the gene expression level while disregarding all other genes would seem to apply.

Comparing Example 4 to the previous examples, it seems the combination of markers and lack of association with disease may be relevant. In Example 4, the 5 genes may be known genes but have not been specifically acquired together. Also there is no information that any of the 5 genes have been associated in any disease. In Example 1, when the123 mutation is not known (or CGK), identifying the single mutation is sufficient for patentability. In modified Example 1c, once the mutation is known (even though in another disease), the claim is identified as non-patentable subject matter.

Although it is not clear whether the use claim in Example 4 is novel and non-obvious, it is patentable subject matter. It is also not clear if the “wherein” clauses are necessary for patentability. What is clear is that identification of what is CGK, the problem and the solution is key to determining whether a diagnostic claim is patentable. This has important implications

when drafting and prosecuting patent applications in Canada. What is also notable is that the determination of the problem and the solution affects more than just the initial patentability determination - it also affects the novelty and obviousness analysis as well. As noted above, broad claims drafted to detect an analyte, mutation or combination of markers would seem patentable subject matter even if using CGK methods to measure or detect if the analyte, mutation or combination of markers is novel or non-CGK.

Update: As we noted, claim 2 of Example 4 was initially identified in the commentary section of the revised MOPOP chapter as *patentable, novel and non-obvious* but in the claim summary, as patentable *but anticipated and obvious*. CIPO has now corrected the Example 4 claim summary section and has confirmed that the claim is indeed *patentable, novel and non-obvious.* The error arose in the English version during the preparations for publication. The French version was correct upon publication.