WHEREAS one might think ideally medicine should one day be able to diagnose everything, not only an existing illness but also a risk of developing a disease in the future, this has not been achieved yet, although... The pharmaceutical and diagnosis industries endeavour to provide ever more accurate and more reliable tests to ascertain the presence of a disease, to try and prevent its onset or to follow its progression in the view of optimising a treatment.

Innovations benefitting patients include the ever deeper understanding of molecular and cellular mechanisms and thus of those populations now known not to respond to some treatments (and that would not be usefully treated with said treatments) and knowing that others (having «the» correct mutation or expressing «the» correct gene) will be good candidates for some other treatments.

But innovation implies patent protection. In the patent world, a diagnostic method is a method practised on the human or animal body constitutive for deciding on a treatment or for selecting the appropriate treatment.

This is a little bit more complicated when the possibility to obtain patent protection for a diagnostic method is not the same from one country to the next and its scope defined by national laws differs. Additionally, the enforcement of these laws does not seem to be fully controlled in some countries and confusion was created during the spring by a decision issued by the Supreme Court of the United States (see below), one of the few countries allowing patentability for diagnostic methods.

Considering the market of diagnostics as it is, i.e. a global market, patent systems all round the world should be reviewed as to the protection of diagnostic methods.
In Europe, the European Patent Convention (EPC) has always excluded diagnostic methods from patentability. The first version of the EPC («EPC 1973»), which came into force in October 1977, used a legal fiction, the lack of industrial applicability, to bar these methods from being patentable inventions (Article 52(4) EPC 1973). Debates reflected then a clear willingness not to encroach on medical and veterinary practitioners’ activities, while these should not be hindered by the existence of any monopoly. As early as in this first version of the EPC, it has been specified that the concerned diagnostic methods are those practised on the human or animal body.

About 30 years later, the second version of the EPC («EPC 2000» which came into force in December 2007), reconsidered in some way the legal grounds of this exclusion by substantiating it more by public health reasons, in agreement with the contents of the debates in the 70s.

In this new version of the EPC, diagnostic methods have thus become part of the «Exceptions to patentability», together with inventions contrary to public order or morality, plant varieties and animal races, for which a patent shall not be granted (Article 53 EPC 2000). However this “article change” was meant not to alter the legal status of diagnostic methods in Europe...

It should in fact be emphasized that in the interval (December 2005), the Enlarged Board of Appeal (EBA) of the European Patent Office (EPO), following two conflicting decisions given by the technical boards of appeal, issued a decision (G1/04) specifying the reasoning for excluding a diagnostic method from patentability.

The EBA thus stated that for a diagnostic method to be excluded from patentability, it must comprise several steps, i.e. technical steps interacting with the human or animal body involving collecting data (examination phase, e.g. taking the pulse or testing the pupils in a patient), comparing them with standard values (comparison phase), recording any significant deviation between them, and an intellectual step of establishing a diagnostic (deductive decision phase) which involves allocating a clinical picture to the deviations observed between the collected data and the standard values commonly used.

The EBA specified that the type or intensity of interaction with the human or animal body is not really relevant, and whether the diagnostic method is excluded or not from patentability depends neither on the involvement of medical or veterinary staff, nor on the involvement of the patient himself or herself or any automated system, to perform the method.

So, whereas ex vivo diagnostic methods (performed from biological fluids sampled from the body and then returned to said body) are also excluded from patentability, diagnostic methods carried out in vitro (i.e. outside the human or animal body) are fully patentable in Europe. So are reactants and materials used for implementing diagnostic methods such as probes and primers, labelling or contrast agents, biomarkers, etc... This applies likewise to methods relating to the collection of «intermediate» data which if considered alone cannot lead to a diagnostic (such as certain data obtained by imaging). Finally, medical devices are of course patentable in Europe.

The exclusion of the diagnostic methods from the patentability being strictly construed, in case of any doubt and sometimes, an appropriate wording of the claims should allow to avoid said exclusion.
In the US, patents on biomarker diagnostics are not prohibited *per se*. But the current state of US law on patenting diagnostics remains unclear following the recent Supreme Court decision in Prometheus, which held that a particular biomarker claim impermissibly claimed a law of nature. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (U.S. 2012). Prometheus provides uncommon facts under which a diagnostic claim is unpatentable, and provides general statements that are not easily interpreted for more common situations.

Prometheus emphasized that one cannot patent a law of nature; instead, one must claim an application of the law of nature to obtain a patent. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (U.S. 2012).

The claims at issue in Prometheus recited two active steps (“administering” a prodrug and thereafter “determining” the level of biomarker in the patient) followed by “wherein” clauses describing what the results of the determining step would mean.

The Supreme Court in Prometheus declined to consider the USPTO’s argument as amicus that the claims could be invalidated as anticipated, because the administering and determining steps were old, and the “wherein” clauses were non-active steps that merely described the significance of the results of the determining step. Prometheus, 132 S. Ct. at 1304.

Instead, the Supreme Court held the claims were invalid under Section 101 as covering a law of nature, but without clear guidance on what claim language would avoid such an outcome.

Entirely mental processes are not patentable according to the Supreme Court. *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972) (“Phenomena of nature, ... mental processes, and abstract intellectual concepts are not patentable.”) Nevertheless, Prometheus did not address the Federal Circuit’s decision in *Metabolite* that a claim may contain a mental step within an otherwise tangible process (*Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1364 (Fed. Cir. 2004) (holding that physicians reviewing the results of a first step of “assaying” total homocysteine necessarily carry out the second “correlating” step, because failure to do so would be malpractice).

The USPTO has issued preliminary guidelines to examiners regarding Prometheus (see http://www.uspto.gov/patents/law/exam/mayo_prelim_guidance.pdf). Unfortunately, these preliminary guidelines are somewhat vague in repeating language from the Prometheus decision, while instructing examiners to ask the applicant to “explain why the claim is not drawn solely to the exception and point to limitations in the claim that apply the law of nature, natural phenomena or abstract idea”.

We await the Federal Circuit’s upcoming renewed decision in *Myriad*. The Supreme Court vacated the Federal Circuit’s original decision for reconsideration in view of Prometheus. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 1794 (U.S. 2012). We may not see clarification for diagnostic claims, because the Federal Circuit’s original Prometheus decision involved claims to “isolated DNA”, diagnostic assay claims that the Federal Circuit had held invalid as an exclusively mental process, and claims to a process of monitoring cell growth rates to screen cancer therapeutics. A decision on such claims may not be relevant to diagnostic claims.

Are patents and diagnostic methods compatible?

Frédérique FAIVRE PETIT - June 2012
It is possible to protect diagnostic methods in Canada. However, the patentability of diagnostic methods in Canada is presently uncertain in view of the decision of the Federal Court of Appeal of Canada in Attorney General of Canada et al. v Amazon.com Inc., 2011 FCA 328, rendered on November 24, 2011.

The Amazon decision dealt with patentability of business methods in Canada and unavoidably with patentable subject matter at large. Pursuant to this decision, the Canadian Intellectual Property Office (CIPO) issued, on April 2, 2012, practice guidelines entitled “Office Practice Respecting Claims to Diagnostic Methods and Medical Uses”, followed by a 30-day public consultation.

These guidelines have been strongly criticized by several IP practitioners and IP professional associations, the CIPO targeted stakeholders. More particularly, CIPO has indicated that in order to be patentable, a diagnostic method must have an inventive concept that is statutory by providing a solution to a technical problem and either have physical existence or manifest a discernible effect or change.

The CIPO guidelines rely heavily on an inventive concept approach. Several IP practitioners have alleged that such guidelines are inconsistent with Canadian Law since failing to acknowledge the leading Supreme Court of Canada case in this area (Shell Oil Co. v. Commissioner of Patents, [1982] 2 SCR 536) and having an unfounded focus on “inventive concept” rather than using a purposive construction of the claims.

The reference to a “technical problem” that was criticized in the Amazon decision has also been criticized by the IP practitioners. It will thus be interesting to see how CIPO will react and if the guidelines will be modified accordingly.

In Brazil, diagnostic methods, for use on the human or animal body are not considered to be inventions according to Article 10 (VIII) of the Brazilian Industrial Property Law, Law no. 9.279/96. Furthermore, the Brazilian Patent Office Guidelines for the Examination of Biotechnology and Pharmaceutical Patent Applications defines that methods of diagnosis are those that directly conclude about the state of health of a patient as a result of the technique used and, as such, may not be regarded as patentable subject matter in light of the dispositions of the Brazilian Industrial Property Law.

Nonetheless, according to the relevant literature, diagnostic methods consist of three distinct stages, namely, (1) examining the patient by observing, feeling and listening to various parts of the body thereof (2) subjecting the patient to clinical tests, and (3) comparing the results obtained in said tests with normal values, and attributing the deviations from the norm to a particular medical condition - the medical deductive phase.

Therefore, in cases where this last phase is not present, such methods should not be regarded as a diagnostic method, since they do not refer directly to a method of assessing the health state of the patient, but rather to a method of data collection that may be subsequently used in a diagnostic method.

Accordingly, in general, methods of obtaining information from the human or animal body are regarded as patentable in Brazil, since the collected data represents only an intermediate result that alone is not
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sufficient for a decision regarding the appropriate treatment. Examples of such patentable methods include methods of measuring of blood pressure, X-rays, blood tests, methods of detecting the presence and/or quantifying a molecule such as a protein, a DNA, an antibody or a metabolite in a biological sample, among others.

On the other hand, methods for the determination of allergic conditions, where the outcome is observed in the body of the patient, are methods that are not regarded as patentable subject matter because they constitute diagnostic methods (conclusive as whether there is an allergic state or not) used in the human or animal body.

In summary, Brazil tends to be conservative when granting patents for diagnostic methods. However, it is often feasible to obtain protection for such methods using cleverly written claims that do not directly encompass a method of assessing the health state of the patient, but rather address the methods used to obtain the relevant information necessary for subsequent analysis of the health state of the patient and possible treatments and prophylaxis to be used.

India adopted the exemption of Article 27(3) (a) and (b) of TRIPS and under section 3(i) of the Patent Act, 1970 excluded inventions related to any process for the medicinal, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment of human beings or any process for a similar treatment of animals to render them free of disease or to increase their economic value or that of their products from patentability.

However, there is no clarity on diagnostic method per se. This paper examines the following questions. What constitutes a diagnostic method according to section 3(i) of the Act? Does it exclude all diagnostic methods such as in-vitro, in-vivo, and ex-vivo method or only in-vivo method such as angiography and angioplasty?

It is often seen that the Examiners at the Indian Patent office invariably object to claims pertaining to a diagnostic method that comprises even one step performed on human or an animal body and reject the same under Section 3(i).

Manual of Patent Office Practice and Procedure (March 22, 2011) (MPPP), a practical guide for effective prosecution of patent applications in India does not provide any clarity of the nature of methods of diagnosis which are excluded under section 3(i).

It states that diagnosis is the identification of the nature of a medical illness, usually by investigating its history and symptoms and by applying tests. It further states that determination of the general physical state of an individual (e.g. a fitness test) is considered to be diagnostic.

The wordings of the statement are too broad and encompass all diagnostic methods i.e in-vitro, in-vivo, and ex-vivo. This would mean that an in-vitro method of diagnosis performed by a diagnostic lab, and not necessarily, by itself rendering a human free of a disease, is also not patentable under section 3(i), because an in-vitro method also identifies nature of medical illness and comprises various steps.

Thus, as per the plain wordings of the manual, all the diagnostic method are clearly barred from patentability in view of Section 3(i), since the section does not explicitly differentiate between an in-vitro, in-vivo and ex-vivo method of diagnosis.
However, as a matter of fact, Examiners are selectively allowing the claims pertaining to *in-vitro* diagnostic method such as a method of diagnosis performed using ELISA or PCR. Thus, it is possible that in so far as a method pertains to an *in-vitro* method of diagnosis only, the same is often not rejected in India. It may be added that any step of a process, whether *in-vitro* or *in-vivo* (such as angiography) that is directed to the human or animal body is highly likely to be objected by the Examiners.

Since, there is no case law(s) on the patentability of diagnostic method *per se*, the issue is not settled.

Further, Indian Patent Office allows product claims pertaining to diagnostic products such as primer sequences, probes, biomarkers, gene sequences, and DNA chips and diagnostic devices or apparatus.

In China, according to Article 25.1(3) of the Patent Law, methods for diagnosis or for treatment of diseases can not be granted patent rights. That is, the processes of identifying, determining, or eliminating the cause or focus of diseases which are practiced directly on living human or animal bodies are not patentable in Chinese Practice.

Based on 4.3.1.1 of Chapter 1, Part II of the Guideline for the Examination, where a method involving diagnosis of a disease complies with the following two requirements, it is considered as a diagnostic method and cannot be granted a patent right: (1) it is practiced on a living human or animal body; and (2) its immediate purpose is to obtain the diagnostic result of a disease or health condition.

Based on the Guideline for the Examination, by using the words "(2) its immediate purpose is to obtain the diagnostic result of a disease or health condition", it means that the diagnostic result of a disease or health condition can be reached immediately based on the information obtained from the disclosure of the specification and medical knowledge in the prior art, then the method can be regarded as satisfying the above requirement (2).

That is, an applicant claims to protect a method including detection steps but not diagnostic steps. However, if those skilled artisans can conclude from the disclosure of the specification that diagnostic result of a disease or health condition can be obtained from the results of the said method, the method is considered as a method for diagnosis of disease.

However, even if an invention, as viewed from its description, is practiced on samples *in vitro*, but its immediate purpose is to obtain the diagnostic result of a disease or health condition for the same subject, it can not be granted a patent right.

For example, the method for detecting viral infection in blood or sputum samples derived from human or animal body for obtaining the result of disease or health condition is considered as a method for diagnosis of diseases and can not be granted as a patent. In this case, if the specification teaches the method for detecting viral infection in blood, sputum, water, soil and other samples derived from the environment, the applicant may exclude the diagnostic method from the claim and only seek to protect the method for detecting virus in water, soil and other samples derived from the environment.

The following are examples of diagnostic methods not patentable according to Chinese Practice:

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However, instruments, or apparatus for implementing these methods of diagnosis or treatment, or kits or compositions for use in such methods are subject matters for which patent right may be granted.

Therefore the SIPO will have more restrictive than the requirement of EPO for the diagnosis.

Before 1st February 2010, the diagnosis of disease based on sample in vitro from the human body could be patentable.

In Japan, a claim relating to a diagnostic method of human is, in general, not allowed because the claim is regarded as not having industrial applicability.

If a diagnostic method has the technical feature of using a substance for detecting a disease, it would be preferable to use a “product-type” claim instead of a “method-type” claim in order to avoid a possible objection concerning industrial applicability.

For example, if a diagnostic method is characterized by using an antibody for detecting protein X which is associated with disease Y, a claim reciting “a method for diagnosing disease Y, by determining the presence of protein X in a sample derived from a patient, using an antibody against protein X” is not considered to have industrial applicability. On the other hand, a claim reciting “a composition for detecting disease Y, comprising an antibody against protein X” is generally considered to have industrial applicability.

Regarding a method for performing an analysis such as a comparison with a control using a sample or data derived from the human body, the Japan Patent Office (JPO) Examination Guidelines state that as long as the method does not include a step wherein a medical doctor evaluates the conditions or physical conditions of human being, the method DOES NOT correspond to a diagnostic method.

As one example of a patentable claim, the guideline presents “a method for testing susceptibility to hypertension of a subject, by determining a type of nucleotide at position of a nucleotide sequence of gene X from the subject and making a comparison with criteria that if the type of nucleotide is A, a subject is susceptible to hypertension, whereas if the type of nucleotide is G, a subject is not susceptible to hypertension”.

As described above, there is a possibility that the change of a “diagnostic method” claim to an appropriate claim format will result in the grant of a patent application.

In Korea, diagnostic method claims could be patented provided that the method is not practiced on a human body.

Particularly, when a human body is required to practice an invention, the invention is deemed to lack industrial applicability (Korean Patent Act, Article 29 (1)). What bars the patentability of these claims is the idea...
that a “human body” must be used to practice the invention.

That it treats a human subject differently from other animals when determine the patentability of certain categories of inventions, such as method of treatment, diagnosis and surgery, is one of the more distinguishing features of Korean patent system. As such, if a human is explicitly excluded from the subject of a diagnostic claim, the diagnostic method could be patented in Korea.

In the same line, if a diagnostic method is limited to an “in vitro” method, excluding the in vivo case or not returning a treated sample back to a human body, the patent protection of these claims cannot be denied.

Diagnostic methods using or applied on body tissues or fluids that have been removed from the human body are also patentable, as long as they are not returned to the human body.

In conclusion, although there is a limitation in the patent protection of diagnostic claims in Korea, this limitation could be minimized by drafting the diagnostic claims properly.

In Australia, there is no statutory definition of patentable subject matter. Methods of diagnosis are not specifically mentioned in the law so are treated by the patent law like other inventions.

The general test for patentability is that an invention is patentable if it provides something that is industrially useful or provides an artificially state of affairs in a field of economic endeavour. Accordingly, unlike most other jurisdictions, methods of treatment and also methods of diagnosis of humans are patentable subject to the usual requirements of novelty, inventive step, utility etc.

Until recently, business methods were generally regarded as patentable, but recent decisions of the Patent Office have started to restrict the extent to which such methods may be patented. It is not yet clear whether this trend to narrowing the scope of patentable subject matter will extend to diagnostic methods where the invention is primarily the correlation between a biomarker and an indication or medical outcome.

When one of Myriad’s patents on the BRCA genes for diagnosing breast cancer was challenged recently in the Federal Court, only the claims to nucleotide sequences were challenged - the diagnostic claims that linked
the identification of a mutation with an increased risk of breast cancer were not challenged.

There has been substantial political controversy in recent years over the scope of patentable subject matter in Australia and a number of proposals have been made to restrict the scope of claims on biological subject matter, particularly genes.

However, these have not come into force. Recent amendments to Australia’s patent law raise the requirements for novelty, non-obviousness and utility, but do not substantially change the scope of patentable subject matter. As a general rule, mere information, schemes and working directions are not patentable subject matter in Australia.

Diagnostic inventions may also protectable as confidential information or trade secrets in Australia, either by way of:

1. obligations of confidence agreed to in a contract (often called a CDA or NDA); or
2. the common law that protects confidential information even in the absence of a contract where information is conveyed confidentially and maintained confidential.

There is no statute law providing for the protection of confidential information. Confidential information is generally not considered a property right.

Accordingly, for the foreseeable future, we expect patent applications to continue to be filed and granted in Australia in respect of many diagnostic methods.

To conclude, even though the patentability of diagnostic methods per se is seldom allowed, the practice currently developed in each country should lead, in most cases, to a patent procedure providing the patentee with a satisfying protection. Of course, for one and the same invention, the national protection eventually obtained will differ from one country to the next, but the same is already true for any invention...

No doubt diagnostic methods are becoming inventions like any others...


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Are patents and diagnostic methods compatible?

Frédérique FAIVRE PETIT - June 2012