Protecting diagnostic innovation: patent drafting tips and pitfalls

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Diagnostic innovation is part of a global biotechnology industrial phenomenon fuelled by high consumer demand, relatively low cost of component manufacture and the increasing role of diagnostics in sophisticated health care systems. The use of diagnostic assays has become an integral part of routine health care, especially with the move towards personalised medicine. Furthermore, there is an ability to rapidly develop and produce new diagnostic assays to meet unexpected threats to communities such as in the case of swine flu, avian flu and even bio-terrorism. Hence, diagnostic innovation is a vital tool in monitoring personal and community wellbeing. Notwithstanding the important innovative contribution that diagnostic assays provide, protecting this technology faces a number of challenges on a jurisdictional basis.

Diagnostic assays employ a range of biomarkers to measure genomic, transcriptomic, proteomic and metabolomic activity as an indicator of a disease condition or its absence and to monitor disease progression during treatment. For example, the ability to determine minimal residual disease in cancer patients is an important component in the decision process for ongoing therapy. Remission is generally determined by histology, which can potentially detect one malignant cell per 100 cells (frequency of $10^{-2}$). With the development of molecular biological techniques and biomarkers, frequencies of $10^{-8}$ are potentially obtainable. A clinician can then decide with greater confidence whether further therapy is required.

Protecting and commercialising diagnostic innovation faces a number of hurdles including patentability, enforcement and regulatory issues.

Common pitfalls in drafting diagnostic patent specifications

At the technology level, diagnostic patent specifications need to be drafted with care. For example, some diagnostic assays are based on the detection of a polymorphism in an allele of a gene or on a particular methylation pattern. The allele, however, may be non-randomly associated with another allele (linkage disequilibrium). Hence, a narrow claim to one polymorphism or epigenetic pattern could potentially be avoided by screening for another marker in linkage disequilibrium with the first mentioned marker, thereby allowing competitors to potentially avoid infringement. Furthermore, there is a tendency for Patent Offices to require Examiners to raise lack of unity issues when multiple biomarkers are claimed. This is particularly the case, for example, in patents which cover micro arrays of nucleic acids, proteins or antigens. The difficulty is that frequently it is not an individual molecule on the array that is important or even instructive but rather the array itself.
Enforceability considerations

A patent specification defining a diagnostic assay needs to be drafted to take into account the nuances of what constitutes patentable and enforceable subject matter in various jurisdictions. For example, in the United States, if a diagnostic assay requires the step of taking a body fluid sample and then screening for the presence or level of a biomarker, then there is arguably no infringement if one of these steps is performed outside this jurisdiction. In this scenario, a sample may be drawn in the United States but screened for a biomarker in a different jurisdiction. This raises an interesting argument as to whether such a practice goes against the provisions of the International Trade Commission which cover importation of products made by a process which is the subject of a United States patent. The question comes down, in part, to whether the "results" of the diagnostic assay represent a "product". In jurisdictions such as Australia there is also unlikely to be a finding of infringement unless the action could be argued to fall within the provisions governing contributory infringement.

Variable patentability in different jurisdictions

The ability to protect diagnostic innovation varies substantially on a jurisdictional basis. For example, some countries such as Europe and New Zealand do not allow a claim to a diagnostic assay if there is a step which involves performing a function on a human subject. In these countries, claims need to be limited to in vitro assays. In China, methods of diagnosis per se are not patentable, and so, the in vitro limitation is generally not applicable. By way of contrast, Australia, has no such restriction.

Until recently, diagnostic assays were regarded as patentable subject matter in the United States. However, in light of a 2008 Federal Circuit decision, this situation has become uncertain. In re Bilski 545 F.3d 943 (Fed. Circuit, 2008) stated that for a process to be a patentable invention it needs to: (1) be tied to a particular machine or apparatus; and/or (2) transform a particular article into a different state. This case is now currently on Appeal at the Supreme Court. However, it was applied in Cassen Immunotherapeutics, Inc v Biogen Idea where the Federal Circuit invalidated US Patent No. 5,723,283 on the basis that the process claims satisfied neither criterion. It has also been applied in Prometheus Lab, Inc. v Mayo Col. Services Wh 878910 (S.D. Cal, 2008) on the basis that the assay outcome was merely a natural phenomenon or mental step.

Lessons and drafting tips for innovators

Hence, a patent specification directed to a diagnostic assay needs to be drafted to take into account different patentability requirements and an interpretational judicial system. In China, it is best to draft claims in a "use" format, specifying, for example, the particular biomarker targeted by a diagnostic agent and the proposed diagnostic outcome. Kit claims should also be pursued if there is a novel component. In the United States, diagnostic claims need to meet the transformation test of In re Bilski by reciting, for example, the generation of a positive outcome. The recommendation is to avoid "wherein" and "whereby" clauses and to provide actual method steps. The in vitro approach appears to satisfy the patentability provisions in Europe and New Zealand.

Diagnostic innovation is an important tool in promoting health and wellbeing in the global community. The patent system has the ability to contribute to the achievement of this outcome. Therefore, defining the innovation needs to be done keeping in mind patentability and enforcement requirements in each of the intended jurisdictions. Consequently, a multi-faceted approach is required when preparing patents to protect this field of technology.
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