

Imprecise Protection? Differing Attitudes of Global Patent Offices to Precision Medicine

While precision medicine is streaking ahead in its development and governments are willing to embrace the new treatment options it offers, patent offices are still lagging behind in the protection they can offer. Fran Salisbury, Partner at Mewburn Ellis, examines the differing attitudes of global patent offices to precision medicine and considers what companies must be aware of in seeking to protect their IP.

Modern medicine increasingly focusses on the needs of individual patients, moving away from the traditional one-size-fits-all approach. This “precision” medicine approach involves analysis and determination of biomarkers; measurable indicators of biological processes such as nucleic acid or protein sequences, mutations or levels in the body or a cell. There might be just one, or a “signature” of lots of different biomarkers, building up a detailed picture of disease in an individual, enabling accurate diagnosis and allowing treatments to be customised to the individual patient.

Many therapeutic agents commonly in use today (such as certain chemotherapeutics) are largely blunt instruments that indiscriminately kill cells, and it can seem like a lottery as to whether the treatment will work or not. Precision medicine is a route to increasing the odds of a successful treatment outcome, as well as avoiding or minimising side-effects and monitoring treatment efficacy to allow the treating physician to respond rapidly should resistance to treatment arise.

Precision medicine has been particularly enabled by recent advances in next-generation sequencing technology, which allows very rapid and sensitive screening of DNA on an unprecedented scale. Whilst the first attempt to sequence a human genome took a global team

of scientists a decade, modern sequencing techniques and equipment allows a patient’s complete genome sequence to be determined in a matter of days. Precision medicine not only looks at the genome of the patient, but advances in analysis of cell-free nucleic acid, proteomics and epigenetic analysis increasingly allow construction of a detailed picture of a disease within an individual patient.

Government Advocacy

Governments around the world are generally supportive of precision medicine, due to the potential for improved outcomes for patients and reduction in healthcare costs, ever a concern in the face of an aging population. In the UK, the government has made funds available to innovators in the precision medicine space, such as through the investment accelerator funding competition. The NHS has established 13 Genomic Medicine Centres as part of its personalised medicine strategy, and supports a number of clinical trials in its hospitals. This support is also apparent in Genomics England – set up and owned by the UK Department of Health and formerly known as the 100,000 genomes project – which collects DNA sequences of individuals with rare diseases, and their close family members, allowing these patients to be diagnosed more quickly. For some patients, this genetic analysis will provide a key that opens the door to curing their disease, rather than just management of their symptoms.

Ethical Considerations

Despite being a potential panacea, precision medicine is not without concerns. A large volume of personal data about individual patients is generated, revealing both the health and prospective health of an individual. The significant role that private companies are playing in developing this technology inevitably leads to questions about whether

the data is adequately protected, and what additional purposes it may be being used for. A concern, particularly in the US, is the potential for this sensitive personal data to be acquired by health insurance companies who might seek to raise premiums, or deny coverage, on the back of it.

Precision medicine also raises questions about the psychological effects that this additional information may have on individuals. While the information may be extremely helpful in treating or preventing diseases, it remains unclear whether or not it is good to know that one has an increased risk of (but no certainty of ever developing) a particular disorder. Having knowledge of this information and the potential – or even theoretical – associated risks an individual may face could lead to modified behaviours, mental health issues, or even new and unrelated health problems such as stress-related illnesses. Whether this risk is proportionate to the medical risks of not knowing is yet to be determined. The flip-side, of course, is whether an individual can be denied this knowledge, if a risk is identified.

Patents Lagging

While governments continue to demonstrate enthusiasm for the greater adoption of precision medicine, including supporting the private sector in discovering new biomarkers and developing precision medicine technologies still further, this degree of eagerness and support is not always reflected in the various patent systems around the globe. These differences can lead to an allegation that the patent systems are not adequately incentivising private companies to develop these exciting and beneficial technologies, or to publicise their findings and innovations. However, with forethought, insight and experience, innovators can obtain granted patents that are useful in the event of a copycat.

Europe

The European Patent Office (EPO) is one of the more applicant-friendly patent offices for this field of technology. At first glance, the law excludes methods of diagnosis from patentability. However, this exclusion is interpreted narrowly, and excludes only methods practiced on the human or animal body. Accordingly, methods practised on samples previously obtained from the body, including blood and tissue samples, can be protected by a patent. European patent examiners can be willing to grant broad claims around new biomarker-disease correlations, but will also grant patents around more subtle developments, such as the identification of new patient subgroups for treatment, or correlation with responsiveness to a particular treatment. Examiners look more favourably on applications where experimental data plausibly shows the correlation for which patent protection is sought. Such data should ideally be included in the application on filing, although supplemental evidence may be supplied during examination of the application.

The EPO is also amenable to granting patents to new bioinformatics methods. Again, whilst software can be excluded from patentability, patent protection can be obtained, provided that the method has a technical purpose and amounts to more than a mathematical method.

New biomarkers may themselves be entitled to an additional layer of protection in a “composition of matter” patent, as the EU-wide “Biotech Directive”, which was implemented by the European Patent Office, enshrined the patentability of isolated nucleic acid sequences.

USA

At present, the US patent office (USPTO) is a more challenging office for innovators in this area. The US Supreme Court’s 2013 *Prometheus* and *Myriad* decisions considered the patentability exclusions around natural laws and products. These decisions have resulted in a dramatic shift in the USPTOs approach, prohibiting protection for innovations that were previously patentable. The USPTO



approach is somewhat at odds with the \$215 million Precision Medicine Initiative announced by Barack Obama in 2015.

Diagnostic methods are often excluded from patentability, as the USPTO interprets these as an attempt to claim a natural law, without adding “significantly more”. The USPTO guidance explains that measuring such correlations in an innovative or unusual way, such as by using new antibodies, can make the method patentable, but the protection offered by such patents can be unsatisfactory for applicants, where the correlation could be measured using another means, such as by using a different antibody, and this would not be protected under the patent. The strategy for obtaining patent protection in the US must therefore be considered from the outset, with careful consideration of what the acceptable patent fall-back positions are for this important market.

Another consideration in the USA is the way in which multi-party infringements are considered. Methods of diagnosis are commonly performed by more than one person, with different actors performing the sample analysis and data analysis steps, and with the final determination of a diagnosis falling to the attending physician. In such cases, claims that define the entire diagnostic method can be difficult to enforce, because no single party performs all the steps, and to prove divided infringement a collusion between the parties, or a controlling party must be identified. The situation is even harder for patent holders where some of these activities are performed outside the USA. Care must therefore be taken to mitigate this situation.

A further issue for innovators in this space is that isolated biomarker nucleic acids and proteins may be excluded from “composition of matter” protection under the nature-based product exclusions. However, whilst some examiners have taken a very strict line on this exclusion, the Supreme Court considered that cDNA corresponding to a biomarker was patent-eligible, even though the isolated mRNA or genomic DNA was excluded. Useful patent protection is therefore available in this space, provided that the claimed product has “markedly different characteristics” to that which occurs in nature.

China

In China, diagnostic methods are excluded from patentability, even if they use an *in vitro* sample and are not practised on the patient. As such, China is one of the most reticent patent offices to grant patents in this space, despite precision medicine forming part of the Chinese government’s 2016 five-year plan.

Instruments, substances and materials useful in diagnostic methods can be patentable. However, where the invention relates to the discovery of a new biomarker correlation, it may be difficult to obtain a patent with claims that are actually useful to the applicant.

With an aging population and growing middle class, China currently offers a significant growth market in healthcare, and so will remain an important jurisdiction for patent protection. It will be interesting to see whether patent law in this area evolves in coming years, as the significant number of Chinese companies innovating in this area seek to protect and enforce their IP.

Japan and Korea

Although “methods of diagnosis” are excluded from patent protection in Japan and South Korea, methods relating to the acquisition of data, such as information useful in the diagnosis of disease, can be patented. With careful drafting, applicants can therefore obtain reasonable patent protection in these countries. However, patent examiners in these countries are often reluctant to grant patent claims that they consider unduly speculative, following careful analysis of the data in the patent application. As with Europe, the experimental evidence provided in the patent application therefore has a decisive effect on the success of patent applications in Japan and Korea.

Conclusions

Although different countries hold differing perspectives on patenting precision medicine inventions, the common theme is that data is key. The level of data required is somewhat less than would be required for journal

publication, and is certainly short of a clinical trial. Patent examiners need to be convinced that there is a plausible link between biomarker and disease, and as such animal, human patient, and *in vitro* data, as well as statistical/informatics analysis can all be useful additions to a patent application.

Flexibility is also an important component of patent strategy in this area, and the different approaches of the various patent offices, and potential development of the technology need to be considered at an early stage, to ensure that fall-back positions are drafted into application at the beginning. Innovators must also be mindful about inadvertently creating prior art against themselves, as all disclosures of the technology made before a patent application is filed (including an applicant’s own earlier application) can be detrimental to the requirement for inventions to be new and not obvious for a patent to be granted.

Those organisations currently working to drive the technology forward still further need to be acutely aware of the complex and overlapping nature of the global IP framework vis-à-vis precision medicine. It will be interesting to see whether government support for these technologies is reflected in an evolution in the approach adopted by the patent offices, to provide further incentive for innovators in this space.



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