

The impact of human gene patents on genetic testing in the United Kingdom

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Purpose: This article reports the results of an empirical study examining the impact of human gene patents on the development and delivery of genetic tests in the public sector in the United Kingdom. **Methods:** Semi-structured qualitative interviews. **Results:** The study found that, despite the potential for gene patents to have significant negative consequences for genetic testing, in fact, human gene patents have little or no impact on practice for those developing genetic tests in the public sector in the United Kingdom. This is not because patents are managed optimally; rather, gene patents are essentially ignored. This article reports the factors that motivate this behavior. **Conclusions:** At least insofar as there seems to be no apparent problem of lack of patient access, there is no significant public health problem. However, there is divergence between the legal and the practical situation. Complacency about the lack of impact of patents on access to diagnostics is risky, and concerns about patents should be addressed proactively, rather than reactively. *Genet Med* 2011;13(4):320–324.

Key Words: patents, intellectual property rights, genetic tests, human gene patents, UK

Human gene patents give rise to more than usual controversy; significant public, medical, and academic opposition to these patents exists. A certain amount of this opposition stems from principled objections to the patenting of human genetic material; a feeling that this amounts to the patenting of human life or is contrary to human dignity.^{1–4} In addition, many are concerned that patents on human genes will have a negative impact on patient access to medical care and diagnostic services. Thousands of patent applications relating to human DNA have been filed in patent offices around the world in the past 15 years.⁵ Some relate to the gene sequence as a compound per se, and others claim methods of diagnosis.⁶ A significant number of these applications have been granted, and many are still pending.^{5,7} Although many of the initial concerns about the potential negative impact of biotechnology patents have subsequently declined,^{8,9} concerns persist about the impact of gene patents in the field of genetic diagnostics.^{5,10,11} The recent Secretary's Advisory Committee on Genetics, Health and Society Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests again highlighted the difficulties of patents in the area of genetic testing and made controversial recommendations.¹² Recent and pending patent law de-

isions in the United States and Europe may also have important implications for gene patents and their application to genetic testing.^{13–17} All these decisions and reports evidence the controversy and uncertain state of the law in this area.

The existence of gene patents gives rise to certain key potential difficulties for those conducting diagnostic testing. There is the possibility that “patent thickets” may arise in genetic testing. A patent thicket arises where a multitude of patents required for a particular innovative product or process is held by a multitude of owners and may be horizontal or vertical.^{18,19} Vertical thickets arise where narrower and more specific gene patents, for example, for individual causative mutations are granted. Horizontal thickets may increase as genetic tests for more complex genetic disorders are developed, in which many different mutations in many different genes will need to be tested. A related problem that arises from patent thickets is “royalty stacking.” If many patents need to be licensed and each requires the payment of a royalty, then the resulting test may become very expensive.²⁰ Finally, the transaction costs of investigating freedom to operate, including identifying relevant patents, determining whether the test falls within the scope of the claims, and then negotiating necessary licenses, or defending infringement proceedings, are high, even for individual patents. When multiple patents are held by multiple owners, the costs are likely to increase accordingly.²¹ In the public sector, or smaller companies, there tends to be little infrastructure support for investigating freedom to operate.²² In the United Kingdom, the existence of an experimental use defense to infringement means that research to develop new genetic tests is unlikely to constitute patent infringement, but the limits of the defense have not been fully tested. At the very least, it seems clear that tests that have clinical relevance to individual patients will not fall within the scope of the defense and, thus, could constitute patent infringement. A significant proportion of the genetic tests conducted in genetics laboratories around the world are likely to fall within the scope of existing gene patents, especially if no attempt is made to invent around any existing patents.⁶

These are significant potential problems that could have a considerable impact on the delivery of genetic tests to patients. Despite the fact that little empirical evidence of impact actually exists, some commentators continue to contend that gene patents impede patient access to genetic diagnostic testing.²³ Other commentators conclude that lack of empirical evidence correlates to lack of negative impact on patients.²⁴ In the United Kingdom, however, with the notable exception of Myriad Genetics and breast cancer genetic testing, there have been few controversies about access to genetic testing. As gene patent disputes have resulted in very few legal cases,²⁵ the traditional means of legal analysis of case law will not provide illumination of the way in which gene patents influence practice. Other methods of investigation, most usefully empirical research into practice, are required.

This article reports the results of an empirical study examining the impact of human gene patents on the development and delivery of genetic tests in the public sector in the United Kingdom. Although there are some important differences between patent law in different jurisdictions and there are also

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differences in the health care context within which gene tests are delivered, lessons can be learned from the way in which different jurisdictions address the common challenges that patents pose for genetic testing.

GENETIC TESTING IN THE UNITED KINGDOM

The framework for provision of genetic tests varies in different countries. In the United Kingdom, the vast majority of all genetic diagnostic testing is carried out by the National Health Service (NHS) and not by private companies. Patients may be referred for genetic testing and genetic counseling by general practitioners or consultants. There are approximately 25 regional genetics laboratories in the United Kingdom that carry out the genetic testing for the NHS.^{26,27} These laboratories provide genetic services for their regional area and also tend to specialize in particular disease areas and offer these specialist services across the United Kingdom. The majority of this testing is commissioned under the NHS payment arrangements, although most laboratories will also conduct a very small percentage of private testing, which is charged directly to the patient in question, often for specialist services for overseas patients.

Tests for a small number of disorders, such as cystic fibrosis, may be conducted with a kit manufactured by a company. Other “home-brew” tests are developed as required by the clinical scientists in the genetics laboratory, by consulting publicly accessible databases and the relevant scientific literature. In the future, it is expected that much more testing will be done using microarray technology, or using full sequence analysis, should this ever become cost-effective. Currently, the genetics laboratories work closely with academic departments in universities to facilitate patient testing for rare genetic disorders where the testing is not yet well characterized. In many cases, consultant clinicians have joint university and hospital posts and divide their time between clinical and research laboratory work. Often, their translational research yields results in the form of better diagnostic tests that can be offered to patients. Frequently, this testing may be done as part of a research project, with the results being fed back in to the project, but later the testing is taken over by the NHS genetics laboratory.

It is relevant to note that much of the testing currently conducted is for very rare disorders, with the volume of even the most common test in a large laboratory being in the order of 500 per year. For other disorders, there may be only one or two tests in any given year.

GENE PATENTS AND GENETIC TESTING IN THE UNITED KINGDOM

Methodology

A series of qualitative interviews were conducted with stakeholders in the translational research process in genetics in the public sector in England and Wales. Participants were recruited from three groups: genetics laboratory management, technology transfer professionals, and researchers and clinicians. Targeted sampling was used to ensure an appropriate spread of interviewees. Seventeen interviews of approximately 1 hour each were conducted. The interviews were conducted as semistructured qualitative interviews and were conducted face-to-face. The issues and phenomena identified and discussed by the interviewees were broadly consistent across all interviews. Where the responses did differ was in matters such as the degree of knowledge of interviewees and the levels of rationalization of

behavior. Interviews were recorded and transcribed, and analyzed using grounded theory methodology, using NVivo7.

Because the majority of genetic testing in the United Kingdom is conducted within the NHS, this study of the role that patents play within these organizations gives a good indication of the role that gene patents play in genetic testing in the United Kingdom more generally.

RESULTS

Despite the potential for gene patents to have significant negative consequences for genetic testing, this study found that, on the whole, human gene patents have little or no impact on practice for those developing genetic tests in the public sector in the United Kingdom. This is not because patents are managed optimally; rather, gene patents are essentially ignored. Genetics centers have not reduced services or failed to conduct testing because of patents. With very few exceptions, those developing and carrying out genetic tests did not conduct freedom to operate searches and did not license patents. They did not experience any negative consequences of this failure to take account of existing intellectual property (IP) rights, they had not been approached by patent holders either informally or formally, and they had not been sued for patent infringement.

What factors motivate noncompliance?

There were many nuanced factors that influenced the non-compliant behavior, but these factors fall under two broad types. First, stakeholders had limited awareness of the legal framework. Second, stakeholders perceived the balance of costs and benefits of compliance and noncompliance with the legal framework to be weighted in favor of noncompliance.

Awareness

Awareness is an important precondition to compliance with a legal framework. If someone is unaware that the law might impose particular obligations or restraints on their conduct, then they will not take action to ensure that their conduct is in compliance with those obligations or restraints. Generally, interviewees did recognize that the rules of IP law, and more specifically patent law, could have relevance for their practice. Most were, however, relatively uninformed as to the specific nature of any obligations that they might have under such law.

The controversy surrounding the breast cancer gene patents held by Myriad Genetics has been extremely influential in informing interviewees about gene patents more generally.¹¹ Myriad Genetics holds patents in many countries around the world for breast cancer genes. These patents were highly controversial in Europe and were challenged in highly publicized opposition proceedings at the European Patent Office. The Myriad case has galvanized awareness in the United Kingdom of some of the controversial issues of gene patenting. Many interviewees had some knowledge of the issues arising from the Myriad case, and their views and beliefs about gene patents had to some extent been shaped by this controversy. Interviewees reported that they knew that breast cancer testing continued in the United Kingdom without negative impact from the Myriad patents, and this fact was also highly influential.

The data used to develop the home-brew tests, which are the predominant type of genetic test in the United Kingdom, are freely available on the internet to all, and there is, in most cases, nothing to alert those looking at such data to the fact that the gene sequences in question could be the subject of patent rights. Researchers and clinicians in particular seemed to be influenced by the fact that gene sequence information was “open access” in

failing to enquire further or believing that gene patents would not influence their work.

Generally, those developing home-brew tests did not carry out any program of freedom to operate searches. This lack of due diligence was partly due to the fact that such programs can be costly, especially if it must be carried out for a number of genes. However, apart from concerns about the cost, there also seemed to be general ignorance that due diligence was necessary; most respondents did not seem to have considered that due diligence was something that they should do. Apart from due diligence, direct contact from a patent holder may serve to make a laboratory aware of a potentially relevant patent. In the United States, cease and desist letters have been sent to genetic testing laboratories, and many laboratories have reported refraining from offering a test for which there is a patent on the basis of receiving a cease and desist letter.²⁸ This was not mirrored in the NHS laboratories contacted for this research. Very few respondents reported having had any direct contact from patent holders. Some laboratory managers also mentioned that direct contact had been made over the cystic fibrosis patents, although they were very vague over details as this was a considerable number of years previously. Patents had not been enforced against those interviewed. Interviewees reported that patent holders generally had not contacted possible infringers in the NHS, had not made approaches about licensing, and had not sent cease and desist letters.

The attitude of many interviewees to gene patents could perhaps best be characterized as “willful blindness.” They had some degree of awareness that gene patents could, or should, influence their practice. Despite this awareness, they believed that if they refused to acknowledge the realities of gene patents, then they would not become an issue in day-to-day practice. Most saw gene patents as a potential problem, which they would prefer not to address if possible. As a result of this willful blindness, respondents often did not engage in any lengthy consideration of patents and did not conduct due diligence or freedom to operate searches, or undertake licensing negotiations. If asked, most denied that they would knowingly infringe a patent and indicated that they would take steps to comply with the law should they be informed that they were infringing a valid patent. Despite these claims, these people in reality took few or no steps to ensure that they actually complied with the law, which meant that it was possible that they were (perhaps unknowingly) infringing patents.

Balancing of noncompliance against compliance

When considering whether to comply with patent law, interviewees engaged in a balancing of the perceived costs and benefits of compliance against the perceived costs and benefits of noncompliance. What they characterized as being a “cost” or a “benefit” was very broad, and it encompassed not only monetary costs but also time and effort, as well as moral issues. This balancing exercise tended to result in general noncompliance.

It was clear that very little due diligence was carried out. This was partly not only due to ignorance that it was necessary but also due to the fact that it was perceived to be difficult and costly, as well as unnecessary. The fact that due diligence was not conducted in the past, with few negative consequences, was influential in this respect.

Interviewees identified a number of reasons that they believed were responsible for the lack of enforcement of gene patents. They were of the opinion that patent holders would have difficulty identifying infringement of gene patents. As the infringing test can be developed from first principles in a laboratory, infringement may be quite easy and may be difficult

to detect, unlike in the case of inventions that may require large manufacturing plants or rare inputs.

A number of interviewees identified as relevant to their considerations the fact that most genetic tests are conducted for rare disorders with multiple causative mutations, each of which is even rarer. As a result, there may only be a few tests for each mutation carried out each year across the United Kingdom or even the world. They reasoned that there were two relevant consequences arising from this. First, rare mutations are unlikely to be the subject of patents as it is not economically viable to patent such a mutation when it is unlikely to be possible to recoup the legal costs. Second, interviewees reasoned that, even if there are patents, the fact that only a few tests are conducted per year makes it unlikely that it will be worthwhile for patent holders to pursue infringers.

The fact that the vast majority of genetic testing in the United Kingdom is conducted within the NHS was mentioned as relevant to gene patent practices in almost every interview. Generally, interviewees saw this fact as contributing to the low costs of noncompliance, for the following reasons: first, there was a perception that the structure of the NHS made it a difficult target to sue. Second, the NHS was perceived as a politically sensitive target, unlikely to be sued. Third, many respondents considered that the NHS would protect them and that they could carry on until told to stop. Finally, there was a perception that the nonprofit nature of the NHS meant that it would not be sued.

The balancing of the relative costs and benefits of compliance versus noncompliance also took account of some complicated moral considerations. It seems that some interviewees, particularly laboratory managers and researchers and clinicians, consciously or unconsciously, chose not to obey the rules of IP law because they considered them to be unjust, with a negative effect on “their patients.” They prioritized their values; to some extent, interviewees considered that their duty to care for patients conflicted with their perceived duties under patent law, so they chose one duty to trump the other. It is not clear how these interviewees reconciled their duties to their patients with their duties to obey the law or whether they contemplated that patent law has moral value in promoting innovation, in turn improving patient health.

Many interviewees expressed objections to the patenting of human genes. Their objections tended to center on a view that patents on genes do not fulfill the patentability requirement of invention, which is congruent with the substance of oppositions to patents at the European Patent Office, and more recent cases challenging gene patents in the United States and Australia.^{13,29} Although this view was widely held, it was not clear how it actually influenced behavior in relationship to patents.

The primary concern expressed by many interviewees working within the NHS was for “their patients.” Where patents were seen to affect patient access to testing, then the duty to comply with patent law rules was seen as conflicting with the duty to treat patients in the best possible way. For many interviewees, the duty to patients was their primary and most important obligation, and any legal obligation that was seen to conflict with this duty was viewed in very negative terms.

Illustrative quotes

Awareness

Interviewer: Have you looked at IP Rights at all?

Respondent: Well, no, I haven't, and I don't think that's been part of the discussion at all. I mean, the assumption is that the gene sequence is publicly available, that

spotting an oligonucleotide on a chip for a published, publicly available sequence does not infringe anyone's intellectual property. I mean, if that's my ignorance or naivety, but I am not aware that there is an issue.

Willful blindness

I really would be surprised if any of my colleagues have even remotely thought about this, we just say here it is, here's a patient, looks like they may have something wrong with that ... I shall sequence that gene using that publicly available sequence using standard technologies ... I'm not going to think about it.

Noncommercial nature of NHS testing

I think ... within the NHS diagnostic labs [we're] very altruistic so ... I think we just want to make sure that the patients get access to everything as simply as possible and I just think that the patents ... well at the end of the day it's to make money isn't it, and that kind of goes against what we believe in.

Infringement proceedings unlikely

I think no company would want to sue the NHS ... it's bad PR.

You can't have a commercial organization that has a genetic marker that's valuable and then going round and suing tens of thousands of clinicians and academics.

I think probably because it's done on such a small scale ... you'd have to chase every individual laboratory and that would probably cost them more than what they would recoup in revenue by the time they get the legal people chasing each laboratory.

Morality of gene patents

I would never have thought of patenting any genes that we've cloned because that's not, as far I'm concerned, that's not something over which you've got any personal rights whatever. I mean, that's part of the make up of humanity and that's just tough, it's just there, and if you happen to discover it, then good, tell somebody.

CONCLUSION

As the research findings demonstrate, many factors influence the behavior in relationship to patents of stakeholders who are involved in the process of translating a genetic test from basic research into clinical use in the NHS. Awareness of patents and the way in which the perceived and actual costs and benefits of compliance are balanced against the costs and benefits of non-compliance are all influential. However, in many cases, analysis is unsophisticated, and the balancing exercise may be largely unconscious.

Questions may be asked about the wider implications of these findings; are they generalizable to other jurisdictions? Some of the factors that motivated behavior were specific to the United Kingdom, or to Europe, such as the public nature of the provision of health care. However, it seems likely that other factors, such as concerns about the morality of gene patents, or

the impracticality of gene patent enforcement may be just as influential on the behavior of stakeholders in other jurisdictions. The findings of widespread noncompliance in this study are mirrored in other studies in Europe and Australia.^{30,31}

The finding of widespread noncompliance gives rise to questions as to the appropriate response or if, indeed, any response is called for. At least insofar as there seems to be no apparent problem of lack of patient access, there is no significant public health problem. However, there is divergence between the legal and the practical situation. The current state of the law in practice uncovered by this research, where patents are essentially ignored, is highly dependent on the lack of enforcement of patents by patent holders. Although they may not be exercised, legal rights remain, and patents could be enforced. In fact, potentially, even one successful case by a patent holder against the NHS, resulting in the NHS licensing and paying royalties to a patent holder, buying in a kit test, or sending samples to a commercial laboratory, could have widespread implications for NHS genetics laboratories. Complacency about the lack of impact of patents on access to diagnostics is risky, and concerns about patents should, therefore, be addressed proactively, rather than reactively.

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