COMMENTARY

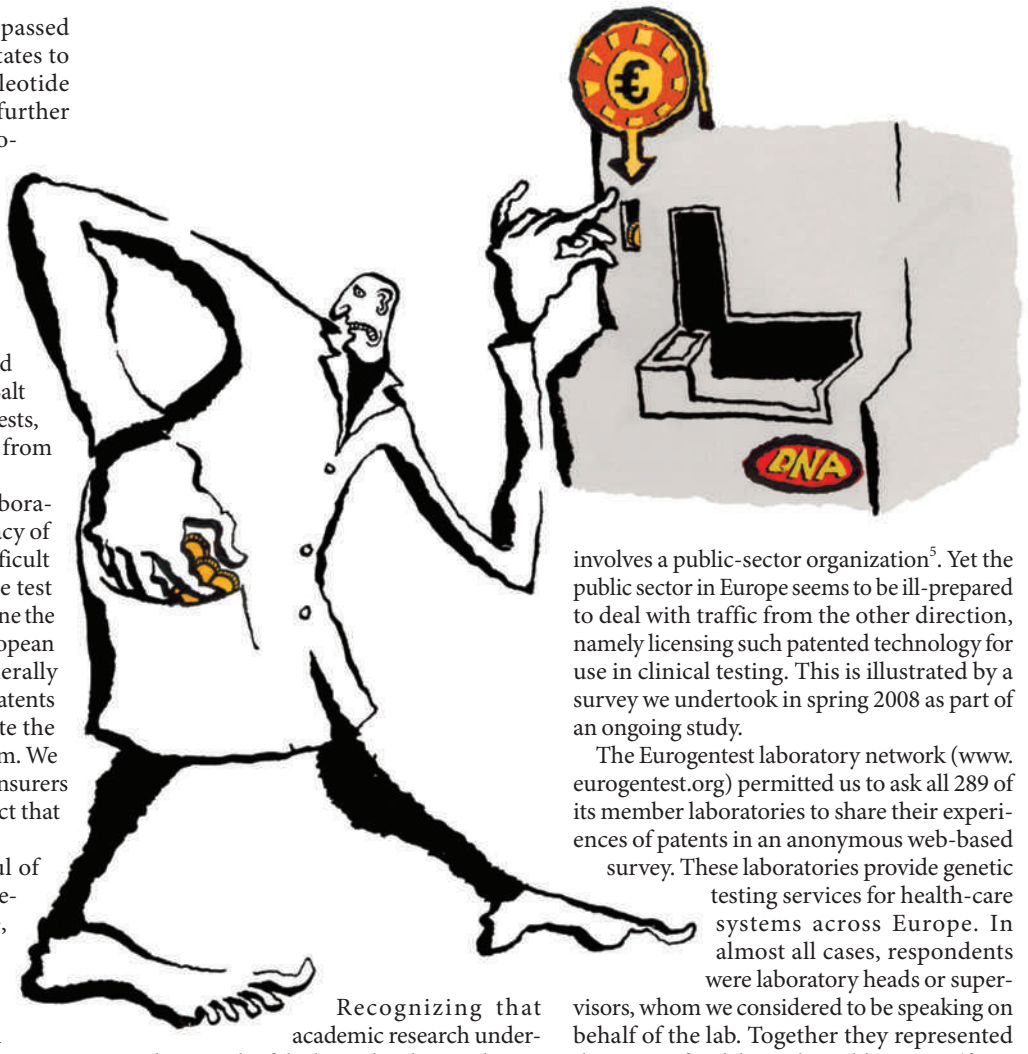
The phantom menace of gene patents

In this, the second of two Commentaries, **Sibylle Gaisser**, **Michael M. Hopkins** and colleagues discuss a survey demonstrating that European health-care systems are ill prepared for the commercial reality of gene patents.

In 1998, the European Parliament passed a law that requires EU Member States to recognize isolated genes and nucleotide sequences as patentable inventions, further reiterating obligations under the European Patent Convention. Patents can also be granted for methods of genetic testing without claiming genes themselves, as illustrated by recent rulings of the European Patent Office Board of Appeal. These rulings upheld patents granted to the biotechnology firm Myriad Genetics and the University of Utah, both based in Salt Lake City, for *BRCA1*-related cancer tests, in the face of considerable opposition from European scientists.

Some European clinical-genetics laboratories refuse to recognize the legitimacy of such patents, arguing that they are difficult to invent around, excessively increase test prices and hinder innovation[1].To examine the extent of such effects we surveyed European labs and found that, in fact, they generally had little experience of dealing with patents and require more support to negotiate the changing patent landscape around them. We suggest that public and private health insurers will have to come to terms with the fact that costs could rise.

Although we found only a handful of cases in which there was patent enforcement against testing labs in Europe, the financial stakes are rising. More companies are investing in genetic diagnostics, and private market analyses have projected high annual growth in the next 5 years[2].



B. MELLOR

Fair and reasonable

As the market matures, so too must the views of those offering or buying genetic tests. For example, there are different perceptions of what constitutes 'fair' or 'reasonable' licensing fees between non-commercial clinical scientists and biotechnology investors[1]. Such problems are compounded by the licensing strategies of some patent holders, who could deny laboratories the choice to offer a test[3].

Health-care systems must respond to the possibility that the tests they rely on may be patented by organizations seeking a return on their investments high enough to compensate for the risk of commercial failure.

Recognizing that academic research underpins the growth of the biotechnology industry, European countries have strongly promoted patenting in the public sector[4]. This had been spurred on by the lucrative profits of some universities and by the 1980 Bayh–Dole Act in the United States, which permitted patenting of research supported by federal funding. Similarly, the European Parliament's 1998 law (Directive 98/44/EC) that encouraged gene patents is itself a policy response to the perceived economic value of biotechnology patents.

As a result of such stimuli, one in three patent applications on human genetic material involves a public-sector organization[5]. Yet the public sector in Europe seems to be ill-prepared to deal with traffic from the other direction, namely licensing such patented technology for use in clinical testing. This is illustrated by a survey we undertook in spring 2008 as part of an ongoing study.

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The Eurogentest laboratory network (www.eurogentest.org) permitted us to ask all 289 of its member laboratories to share their experiences of patents in an anonymous web-based survey. These laboratories provide genetic testing services for health-care systems across Europe. In almost all cases, respondents were laboratory heads or supervisors, whom we considered to be speaking on behalf of the lab. Together they represented the views of 77 labs in the public sector (from hospitals, universities and government labs).

The response rate is lower than that of a similar survey in the United States[6], perhaps indicating that the issue of patenting is seen as less important in European labs. Indeed, in telephone calls to non-responders, lack of time was the only reason given for not participating. We detected no response bias in nationality or laboratory size. Because of low response numbers per country, we report on the experiences of European labs overall rather than drawing national-level inferences.

Our findings highlight poor aware-

ness of patent licensing conditions in the European Union. Only 22% of responding labs (17) thought they performed tests on patented genes, while 55% (42) said they did not and 23% (18) did not know. Notably, of the 17 labs testing patented genes, just one lab paid royalties directly, another lab had negotiated with a licenser, but did not pay. Two further labs were aware that royalty fees were included in test-kit prices. There is little evidence of labs being put off patented tests by licensing costs. Only four labs reported costs to be prohibitive, whereas 60% (46) said they did not know enough about licensing costs to comment.

This lack of awareness may be because labs sometimes buy kits for which a patent licence is bundled in the purchase price. In other cases, labs simply develop in-house tests with little concern for patent infringement[3]. These 'home brews' vary in quality but are often less expensive than buying commercial kits[7]. Nevertheless, their use could prompt legal action by patent holders. We did not explicitly ask lab supervisors to state if they infringed patents as this may have discouraged some from responding to the survey. Furthermore, such a question would assume the act of infringement is clear cut. Often labs fail to check for patents, and in other circumstances may be able to work around a patent or challenge its validity.

When it comes to support in dealing with patents, 37% (28 of 75; some did not respond) of public labs reported that they did not have sufficient information or support to deal with patent-related issues. Only 32% (24/75) said they were confident that they did. Furthermore, when asked if the legal advice they needed was available, 26% (19/73) said yes, but for 33% (24/73) legal advice was not available.

"This is the logical consequence of current policy, and the price we pay for the commercialization of science."

No menace in Europe — yet

For all the concern from geneticists about the effect of patents on genetic diagnostics (see 'The fear of patenting'), there is still relatively little evidence of friction in Europe between patent owners and labs. We found that just 4% (3/77) of responding public-sector labs have ever been prevented from offering a testing service because of a patent-related issue. Three out of six private companies that also responded to our survey said they have been similarly prevented. These figures are still low compared with previous surveys in the United States where 25% (30/122) of labs reported not being able to offer a service as a result of patents held by other organizations[6]. This may be due to a delayed effect, either because patents take much longer to grant in the European Union than in the United States, or because patent owners are yet to take action. But, at this time, our data suggest the concerns about patented genetic inventions have been overstated in Europe.

One possible reason for the trans-Atlantic difference is that fewer genetic inventions are patented in Europe. A 2007 study of human nucleotide sequence patents followed more than 15,000 patent applications filed before December 2003 and found that only 750 had been granted in Europe compared with more than 5,000 in the United States by 2005 (ref. 8). In part, this reflects the higher costs of patenting and the historically higher patentability bar in Europe in this field. Thus, many US inventors have not patented in Europe to the same extent that they have domestically, even though they have had the opportunity to do so. Other reasons for differences in observed enforcement may be due to differences in patent law, market size and patterns of service delivery that make litigation by patent owners (anywhere in the world) less attractive in the European Union. In addition, the European Commission monitors closely the implementation of the EU biotechnology directive and its effects[9].

Although gene patents might not be as menacing as some geneticists have suggested[1,10], government and health-care systems can no longer afford to ignore patents on genetic inventions. Their current approach might be perceived as hypocritical. Governments continue to promote patenting as a means to improve the return on investment in scientific research, and hospital labs operate increasingly like businesses by charging for their services.

Furthermore, labs generally offer many types of genetic tests, and a growing number use multiple nucleotide sequences, for example, in DNA 'chips' (microarrays). Thus it is increasingly likely that a test that laboratories wish to offer will be affected by a patent at some point. Accordingly, labs are more likely to be called on to respect valid patents, negotiate licences for expensive technologies and pass costs on to their clients. Equally they must be able to spot invalid patents or workarounds. Governments and health-care systems must ensure patients can access useful tests, provide support to labs facing commercial challenges and pick up the bill. This is the logical consequence of current policy, and the price we pay for the commercialization of science. ■

The fear of patenting

Comments made on our survey reflect the fears, both real and perceived, surrounding gene patents in the European Union:

"Enforcement of intellectual-property right would ruin most of the private laboratories. It's a threat."

"The costs for paying royalties are not covered by the fees paid by health-insurance companies, nobody is aware of these costs."

"The system will collapse, because the patent owners will never get their money, except in the very big labs, or via kits."

Sibylle Gaisser is at the Fraunhofer Institute for Systems and Innovation Research, 48 Breslauer Street, 76139 Karlsruhe, Germany; **Michael M. Hopkins** is at SPRU: Science and Technology Policy Research, at the University of Sussex, Brighton BN1 9QE, UK; **Kathleen Liddell** is at the Centre for Intellectual Property and Information Law, University of Cambridge, Cambridge CB3 9DZ, UK; and **Eleni Zika** and **Dolores Ibarreta** are at the European Commission Joint Research Center, Institute for Prospective Technological Studies, Edificio Expo, Inca Garcilaso, E-41092 Seville, Spain.
e-mail: m.m.hopkins@sussex.ac.uk

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