

Exhibit 4

further pressurizing an over-burdened system. At the same time, the plummeting success rates lead referees and applicants alike to focus on safe, incremental research rather than larger, more ambitious work.

But a ban on researchers — even those whose consistent lack of success disproportionately overburdens the system — is a clumsy way to try to break this cycle. When success rates are so low, the peer-review system cannot reliably identify the worst performers: rankings can vary so much from one reviewer to the next that many solid proposals end up being rejected along with the weak ones, just by the luck of the draw. And even if the system were reliable, the scientists involved have no time to adjust: the policy is being applied retrospectively. Worse still, this temporary ban could easily leave a permanent stain — particularly on the careers of young researchers.

Any benefit an applicant ban might have provided is being outweighed by the bad feeling its abrupt introduction has engendered. Some potential reviewers are talking of boycotts because they don't want to contribute to a system in which their decisions can shut

out colleagues. Researchers also feel that they were not sufficiently consulted on the specifics of such a controversial decision.

Other options were available. Using an expert-committee triage to sift through outline applications before the full peer review, for example, would give instant feedback to researchers on where they are going wrong, speeding up the recovery process. Introducing regular deadlines for submission might help regulate the flow of applications from particularly voluminous applicants.

On its own, the ban is likely to achieve little and provoke much. It might have been more happily accommodated if accompanied by an overarching set of reforms, discussed with the wider community. Maintaining the peer-review system for grant applications depends on the trust and cooperation of its reviewers — the researchers themselves, who do the bulk of the work. The EPSRC seems to be alienating the very scientists its system depends on. ■

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Property rights

The granting of patents on human genes has so far not been the disaster it was predicted to be.

In 1980, the Bayh–Dole Act gave US universities the right to patent discoveries made with government funding. Not long after, universities and companies began the much-criticized practice of patenting genes, laying claim to human DNA sequences for research and diagnostic purposes. Europe and Japan followed suit, legalizing gene patenting in the 1990s.

Researchers and health professionals alike attacked the strategy. They worried that patents would make it harder to develop new genetic diagnostic tests; that corporate monopolies would hamper patients' access to the tests; and that thickets of interlinked intellectual property would scare off those interested in researching and improving the tests. To solve these ills, suggestions have included patent pools in which developers would share buy-in rights for a collection of patents — and even the total abolition of gene patents. But for all the fuss, few, if any, of the initial concerns have been borne out.

In the United States, the longer history with gene patents and the privatized nature of health care have indeed enabled a few companies to secure a monopoly on some tests. But as described in the Commentary on page 405, genetic tests from companies with exclusive licensing rights are no more expensive or harder to access than those offered by various providers under non-exclusive licence.

Nor is there any empirical evidence to suggest that companies are quashing innovation. A survey last year revealed that for more than 40,000 gene patents, only six instances of litigation came up in relation to diagnostic testing (C. M. Holman *Science* **322**, 198–199; 2008). All six were settled or dismissed within a year and a half, suggesting that the scale of litigation is not as high as some suspected. Reports of researchers being blocked from access to patented DNA sequences or being sued for infringement are extremely rare, and workarounds

are not difficult from a legal perspective. Moreover, a study by Loet Leydesdorff at the University of Amsterdam and Martin Meyer of the Catholic University of Leuven in Belgium set to be published in *Scientometrics* later this year, suggests that the trend for patenting genes is waning among universities as they increasingly recognize that the return on investment is not as high as had been predicted.

In Europe, the number of gene-patent applications is rising faster than in the United States — although Europe's later start means that the licensing of intellectual property is still extremely low. Moreover, as noted in a second Commentary on page 407, in publicly run academic and medical genetic testing facilities in Europe, users of diagnostic tests are largely unaware of the patent status of the technologies involved — nor do they seem particularly concerned about the legal implications. In part, this attitude may arise because even if they are infringing a patent — which can be difficult to prove — the facilities are so small and dispersed that it would be hard for patent holders to pursue and secure damages.

But such safety from litigation cannot be relied on — witness the long battle by the University of Utah in Salt Lake City to have its patent on the *BRCA1* breast-cancer gene recognized in Europe. European testing labs, some of whom have stated in the past that they intend to continue *BRCA1* testing in defiance of the patent, will need to tread carefully.

Dire predictions that patents will cripple genetics research should be viewed with scepticism on both sides of the Atlantic. This is not an argument for complacency. Nor is it a defence of the patent system as a whole, which needs major reform to address the scope and purpose of patents. If academics are going to continue to patent intellectual property, they need to recognize that it must be respected and licensed properly. Moreover, patent holders need to accept that patent rights come with a responsibility to honour the spirit in which they are awarded. Patents are meant to encourage and reward innovation, and, although this shouldn't happen at the cost of further innovative development, it is a premise that shouldn't be discarded purely because there is a vague hint that harm might one day occur. ■