US NIH draft guidelines threaten diagnostics sector

The US National Institutes of Health (NIH; Bethesda, MD, USA) introduced draft guidelines on March 5 that suggest that patents covering diagnostics should be licensed on a nonexclusive basis and that universities should not patent genomic technologies if significant research and development is unnecessary to get a product to market. Many in both academia and industry worry that the draft will become policy and eventually diminish the number of biotech products that reach the market.

Genomic inventions include technologies and materials such as cDNAs, expressed sequence tags, siRNAs, genes and their expression products, and methods and instrumentation for sequencing genomes and other genetic modifications, according to the draft. The draft claims that, based on anecdotal data, academic and nonprofit institutions exclusively licensing genomic technologies that are considered diagnostics could have "detrimental" effects on the quantity and quality of healthcare products and services (see **Box 1**). "Without a choice of tests, patients, physicians and hospitals must use and buy from the sole supplier," reads the draft. "Society suffers if the test isn't as good or as available as it could be were there competitors."

But diagnostics command a considerable investment of time, both in development and in seeking and obtaining regulatory approval, says Adda Gogoris, a principal in the intellectual property law firm Darby & Darby (New York). "Diagnostics are notoriously low-profit-margin products," she says. "If the right to develop a diagnostic were to be shared by more than one company, the economic incentive to develop it is likely to evaporate. Who would go through the development and approval process only [to compete] with another company for a low-profit market?"

Some genomic inventions can be used as a research tool, a drug development aid, a diagnostic and a therapeutic, says Gogoris. Depending on the degree of commercial interest in the material, a technology transfer officer may have no choice but to license it exclusively if only one company expresses interest; otherwise, the technology might never be licensed and turned into a product, she says.

> Nonexclusive licensing can be good for universities and biotech companies

Michael Lytton, a general partner with the venture capital firm Oxford Bioscience Partners (Cambridge, MA, USA), says exclusive licenses should be granted case by case. "It all depends on the technology involved," he says. "My concern would be tarring with too broad a brush all tool technologies." For example, it would make sense to nonexclusively license a single biomarker, he says, but if it was a collection of biomarkers that together could function as a diagnostic test, the guideline could be harmful because it could prevent a university from realizing the value of the collection.

Another concern among the university community is that researchers will need to follow these guidelines in order to receive NIH funding—which is what happened with the NIH Research Tools guidelines that were introduced in 1999 (*Nat. Biotechnol.* **17**, 819–820, 1999). One part of those guidelines says that research tools such as cell lines, monoclonal antibodies, animal models, growth factors and cloning tools would be prohibited from being exclusively licensed. Although most in the tech transfer community say good things about the NIH's research tools guidelines, they don't like that the policy denies funding to those who don't follow it.

Thomas Ittelson, director of the Intellectual Property office at the Whitehead Institute for Biomedical Research (Boston, MA, USA), believes the NIH should back up the premise of the guidelines with data, not just anecdotal evidence that says diagnostic companies abuse their powers. And the NIH and Department of Energy (Washington, DC, USA) are currently conducting a survey that will provide such data, the results of which are expected to be published within the next six months. Preliminary data from the survey—which analyzes almost 3,000 DNA-based patents held by 18 top universities—shows that about 30% of the patents have never been licensed, 45% have been licensed once and about 1-2% have been licensed ten or more times. But without further analysis, no one knows whether the university community is giving out 'bad' licenses; if they are not, then there isn't really a problem and the new NIH guidelines are unnecessary, says Ittelson.

But NIH officials say that all the concerns are much ado about nothing, because the draft guidelines are a still work in progress and there is no reason for academics to think that following the guidelines will become conditions for grants. The agency has been following the guidelines internally for the past ten years, and makes a distinction between diagnostic and therapeutic uses of DNA and gene patents, says Claire Driscoll, director of the technology transfer office at the National Human Genome Research Institute. Within the NIH, licensing of diagnostic inventions is usually done nonexclusively, whereas therapeutic inventions are done exclusively, says Driscoll.

Nonexclusive licensing can be good for universities and biotech companies, says Driscoll. For example, the Cohen-Boyer gene-splicing patent held by the University of California at San Francisco (San Francisco, CA, USA) and Stanford University (Stanford, CA, USA) was nonexclusively licensed, and it earned more than $255 million in royalties between 1980 and 1999.

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Box 1 Myriad's 'bad behavior'

One of the anecdotes that the draft guidelines refer to is Myriad Genetics' (Salt Lake City, UT, USA) exclusive license of the breast cancer susceptibility genes *BRCA1* and *BRCA2* from the University of Utah. The Institut Curie (Paris) has led opposition hearings against the *BRCA1* patent at the European Patent Office (EPO; Munich), in part because Myriad has not licensed out diagnostic tests and asks researchers to send diagnostic samples to its US headquarters for testing. "This is the case that is considered to be the most egregious example of 'bad' licensing and 'bad' licensee behavior," says Driscoll. Although Myriad maintains that its test is the best available for mutation detection in the *BRCA1* and *BRCA2* genes, opponents say that other tests are less expensive and more accurate (*Nat. Biotechnol.* **20**, 1175–1176, 2002).

In February, the EPO granted Cancer Research UK (CRUK; London) a broad patent covering any activity concerning the identification of mutations in *BRCA2*, which means that Myriad and other companies will have to obtain a license from CRUK before they can market *BRCA2* testing in Europe. In addition, CRUK will allow European laboratories to test for *BRCA2* without paying fees. The EPO plans to decide on the Institut Curie case in May (*Nat. Biotechnol.* **22**, 373, 2004). *AS*