Association of University Technology Managers®
Advancing Discoveries for a Better World®

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George Elliott
Deputy Administrator for Policy & External Affairs
United States Patent and Trademark Office

Dear Mr. Elliott,

Thank you for providing AUTM the opportunity to speak at the January 10, 2013 Roundtable on Genetic Diagnostic Testing. We appreciate the preparation which went into the event, the diversity of views presented and the presence and attentive listening of three senior USPTO representatives including yourself, Deputy Under Secretary of Commerce for Intellectual Property Teresa Stanek Rea, and Patent Reform Coordinator Janet Gongola.

AUTM's has more than 3,200 members who work in universities, research institutions, teaching hospitals, government agencies and companies across the globe. Our members manage and license innovations with the primary objective of making them available to the public. Often, but not always, AUTM members elect to file U.S. patents on these inventions to facilitate technology transfer and public access to these discoveries.

AUTM members are skilled at working with a diverse group of stakeholders, - from academic inventors to entrepreneurs, from start-ups to large companies, from government funding agencies to nonprofit organizations and foundations. Our members often have interdisciplinary backgrounds. Many have advanced degrees in the scientific discipline associated with the inventions that they manage plus business development and contract negotiation experience. Others have a law degree and subsequently acquired technology sector specific expertise over the course of their careers. AUTM members are skilled at negotiating license agreements which align interests among diverse groups of stakeholders. As such, we are uniquely qualified to respond to the four questions in section 27 of the America Invents Act (AIA).

General Statement

AUTM members want first opinion, better opinion and different opinion diagnostic tests, available to as many people as soon as possible. We believe skilled licensing aligns interests and fulfills the promise of personalized medicine. AUTM's view on this matter is described in detail in Point 2 of the Association's Nine Points to Consider in Licensing University Technology[i]. These objectives are all possible now under the Bayh-Dole Act which provides universities needed flexibility to license technologies on terms that encourage prompt commercialization making federally funded inventions available to protect public health and welfare. Rushing to enact additional legislation can do

more harm than good, particularly if it is designed to solve a poorly defined problem. It would also be a serious mistake to pressure agencies to invoke march in rights provisions against companies who have fully complied with the terms of their licenses. Such changing the rules at the end of the game would undermine industry confidence in universities and federal laboratories as reliable research partners. The resulting damage to our economy would far outweigh any short term benefits.

Approach

This letter, per the request in your letter dated January 22, more fully explains our January 10 remarks, citing selected examples from the AUTM Better World Report "BWR" publications, data from our AUTM Surveys, and other references and public information.

Definitions: What is a "genetic diagnostic test"?

Before focusing on possible legislative remedies, we should focus on and better define the issue at hand, -patient benefit from access to diagnostic tests, -"genetic" or otherwise. We don't think the term "genetic diagnostic test" is clear or useful. Even if there were a clearly defined "genetic diagnostic test", AUTM believes that patients should benefit from access to all diagnostic tests.

Looking over recent examples of diagnostic products in AUTM Better World Reports, listed in an Appendix to this letter, more than half the products described use protein analytes to find protein biomarkers. These are diagnostic tests, but are they "genetic diagnostic tests"? Here is a description from the Argonne National Laboratory 2010 Better World Report[ii]: "Each serves as a miniature laboratory with a unique protein, antibody or nucleic acid that will attach to a particular DNA sequence or antigen to identify infectious diseases, such as …". Is that a "genetic diagnostic test"?

Using public patent databases, it is possible to find patents by inventors named in the Better World Reports, and peruse the patent claims. In many cases the claims cover biomarkers which are not nucleic acids. Sometimes the claims do reference nucleic acids. Sometimes a single patent has claims which reference both proteins and nucleic acids. These observations are consistent with the BNA[iii] findings, and support our remarks January 10, 2013. Patents do not map to well to types of products or to types of diagnostic tests. Sometimes, the same patents are relevant to both therapeutics and diagnostics.

Evolving science: What is "genetic"?

Scientific discoveries published as recently as September 2012 continue to change our understanding of the word "gene". Some DNA sequences code for protein, -but other sequences determine whether or not the protein is made at all. [iv] Using an imperfect but still helpful cooking analogy, if a "gene" (recipe) is the instructions for protein manufacture, are the instructions the i) the ingredients list only (the protein coding region), or ii) the ingredients list plus mixing and cooking instructions (epigenetic modifications)?
See "The Epigenetics Revolution: How Modern Biology is Rewriting Our Understanding of Genetics, Disease, and Inheritance"[v] , for a compelling and accessible discussion of the many types of "cooking instructions", -from methyl groups on nucleotides, to acetyl groups on histones, to ncRNA's (non coding RNA). All this new science, only 11 years after the publication of the human genome, raises the issue of definition and stability of the definition of "gene". What is a "gene", what is "genetic", and what is a "genetic diagnostic" test? What will we think a "genetic diagnostic test" is in five years?

Thus, rules and policies directed at a poorly defined term "genetic diagnostic test" will be blunt, confusing, costly and ineffective. Appendix 2 of the SACGHS report[vi] and the March 2012 BNA[vii] study show that the field of use of the license, a result of a conversation which takes place at the time the patent is being licensed, is a far superior predictor of the type of product a patent will cover than is the patent itself.

License Exclusivity

As explained in the Nine Points[viii], particularly Point 2 and paragraph 2.1 in the Appendix of the Nine Points, and elsewhere[ix, x], exclusivity is a matter of degree. A few examples from the AUTM 2010 BWR illustrate field specific exclusivity:

Argonne National Laboratory; Rapid, Cost-Effective Diagnostic System based on Innovative Nano Biosensors Helps Identify and Slow Spread of Major Diseases. pp 1-3. Page 2.

The Argonne National Laboratory biochip point-of-care diagnostic portfolio contains 29 issued U.S. patents with six pending applications, and the Argonne TDC [Technology Development and Commercialization organization] has granted *three exclusive licenses with defined fields of use* [emphasis added] to:

- Safeguard Biosystems-focusing on veterinary diagnostics
- Aurora Photonics-developing biochip imager for research and diagnostics
- Akonni Biosystems-developing human diagnostics.

University of Chicago: Minichromosomes Carry the Key to Improved Crops, Better Yields. pp 60-62. Page 62

And, it [Chromatin, Inc.] receives revenues from its licensing contracts with agricultural companies. These include a 2007 collaborative agreement with agricultural giant Monsanto Co. allowing that organization to adapt Chromatin technology for its research crops. Also in 2007, Chromatin granted Syngenta Biology Inc. a nonexclusive license to use the technology for corn and soybeans.

Other agreements have followed — with Dow AgroSciences for research on combining Chromatin minichromosomes with Dow technology and with Bayer Crop- Science for its use in cotton plants. An *exclusive* [emphasis added] agreement with Syngenta lets that company pursue minichromosome technology in sugarcane.

Start-ups and Small Companies

Start-ups and small companies play an important role in making diagnostic tests available. For example, referring to a preeclampsia diagnostic arising from biomarkers studied at Beth Israel Deaconess Medical Center (BIDMC) and Massachusetts General Hospital (MGH)[xi], Mark Chalek, director of the BIDMC technology transfer office said:

"We spent the better part of one year trying to find a big pharmaceutical company to license the technology. Most large pharmaceutical companies were concerned that the clinical trials would be too risky and that the preeclampsia market would be too small to justify an investment".

The BWR goes on to recount that the technology was first licensed to Nephromics, a start-up, which furthered the commercial development before sublicensing a test kit to larger companies. Additional remarks on the role of entrepreneurs and start-ups are found in a BWR on PhyloChip[xii]:

"Virginia de la Puente, senior licensing associate in Technology Transfer and Intellectual Property Management at LBNL [Lawrence Berkeley National Laboratory], is the first to admit that the licensing history of PhyloChip technology is unusual: 'This technology was the overall third-place winner for the Wall street Journal's 2008 Technology Innovation Awards. You might think that would pretty much guarantee a licensing deal, but it was not to be. We had three or four companies interested, but none of them came back with a proposal'. She adds, 'There is a certain amount of tension in tech transfer. Big companies want a certain level of development, and small companies generally don't have a lot of money. You have to find the company that's the right fit for the technology.'"

Not surprisingly, the “right fit” turned out to be a start-up.

Start-ups played a role in almost all the examples in Appendix A, Psynova Neurotech, Diagnostics for the Real World, ContraVac, Akonni, TessArae, Chromatin, Nephromics, Banyan Biomarkers, PhyloChip, and BioArray.

Start-ups and exclusivity

The table below shows exclusivity by type of company from the 2004, 2005 and 2006 AUTM surveys, -the most recent years for which exclusivity data by company type were gathered. Note that the AUTM Survey lumps “exclusive, all field of use” with “exclusive, by field of use”.

AUTM Survey Respondents: % "Excl" (includes Exclusive, All Fields of Use, and Exclusive by Field of Use) by Fiscal Year	to Start-ups	to small companies	to large companies
2004	91%	42%	35%
2005	92%	39%	32%
2006	91%	44%	34%

Data on DNA Patents (patents, which by definition, reference nucleic acids in their claims)[xiii], which were gathered with a category for “exclusive, by field of use” again shows the role of exclusivity for start-ups and small companies. Per figure 5 : Of the 44 licenses to DNA Patents which were granted to start-ups, only 1 was characterized as nonexclusive, 13 as “exclusive, by field of use”, and 29 as “exclusive, all fields of use”.
Thus, AUTM believes that it is important to retain the option of granting licenses with exclusivity to assure continued development of diagnostics in the public interest.

Technology diffusion after granting a license with exclusivity

Licensed technologies can become available by direct sale to consumers[xiv], and also by subsequent sublicenses and strategic partnerships. The preeclampsia BWR[xv] and the minichromosome BWR[xvi] illustrate diffusion via sublicensing. Note that the right to grant sublicenses is essentially only included in licenses with a degree of exclusivity.

Alternative to patents

We note that the sole alternative to patents is not “open source”, it is also proprietary, forever, databases, unrelated to patents. Some companies, such as the crowd funded µBiome and bioinformatic 23andMe collect tissue samples and other personal information and create proprietary *forever* biomarker databases, -forever in that there is *no* requirement for the company to share the collected information. In contrast, patents incentivize disclosure by granting *time limited* monopolies to innovators who describe and enable their inventions, -and the written description and enablement requirements are substantial in biology.

Evolving patent law.

Concern for patient access has been motivated in part by the case studies in the SACGHS report, which were subsequently published in a special issue of Genetics in Medicine[xvii]. As shown in the BNA paper[xviii], only 10 of 99 of the patents numbers referenced in the case studies and Genetics in Medicine articles have priority dates after the 2001 publication of the human genome. Only 3 of the 99 have priority dates after the September 7, 2005 the in re Fisher decision on specific utility, which of course post dates the 2004 Rochester v. Searle decision on written description and enablement. Thus, the scope of claimable subject matter has been substantially circumscribed relative to the examples often cited to support the proposition that there is a problem with patient access to “genetic diagnostic tests”.

Patents and licenses are incentives

Robust application of the written description and enablement requirements serve the public interest via a requirement to disclose and describe the invention. Licenses also can incentivize disclosure in the public interest. License diligence can include a contractual requirement to publish data or to permit confirmatory laboratory testing by a provider other than the licensee. This type of diligence requirement however is typically present only in licenses with exclusivity.

Insurance

On the whole, getting regulatory approval for a therapeutic is harder than for a diagnostic, and on the whole, getting insurance reimbursement coverage is harder for diagnostic than for a therapeutic. At a workshop at the AUTM 2010 annual meeting: "Incentives in the Diagnostic Marketplace",- during which health economics and insurance reimbursement figured prominently, one speaker showed a slide with sales of OncotypeDx over time, and then insurance reimbursement decisions at points in time, which suggested that sales growth depended on favorable insurance reimbursement decisions.

Favorable reimbursement decisions in turn depend on a consensus assessment of the value provided by the test, by and among patients, physicians, and insurance companies, -a diverse group of stakeholders. Thus, it is as important to maintain the option to create and manage patent and license incentives in diagnostics as it is in other areas of medicine.

Summary

The accumulated evidence on the incentives and benefits created by skilled licensing, -including the flexibility to negotiate exclusivity and diligence, of patented and expiring proprietary rights, supports broad patent eligibility, skillful patent examination and skillful patent licensing as the best means of advancing patient access to diagnostic tests and personalized medicine.

Sincerely,

Todd T. Sherer, Ph. D., CLP
President

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[i] http://www.autm.net/Nine_Points_to_Consider1.htm
[ii] Argonne National Laboratory; Rapid, Cost-Effective Diagnostic System based on Innovative Nano Biosensors Helps Identify and Slow Spread of Major Diseases. 2010 BWR pp 1-3
[iii] Lori Pressman, "DNA Patent Licensing Under Two Policy Frameworks: Implications for Patient Access to Clinical Diagnostic Genomic Tests and Licensing Practice in the Not-for-Profit Sector", BNA Life Sciences Law and Industry Report, March 23, 2012
[iv] Elizabeth Pennisi, ENCODE Project Writes Eulogy for Junk DNA, Science, News & Analysis 7 September 2012: , Vol. 337 no. 6099 pp. 1159-1161
[v] Nessa Carey © 2012, Columbia University Press
[vi] Appendix 2 of the SACGHS Report
[vii] See supra fn 3
[viii] See supra fn 1

[ix] Pressman, L., Burgess, R., Cook-Deegan, R.M., McCormack, S.J., Nami-Wolk, I., Soucy, M., and Walters, L "The licensing of DNA patents by U.S. academic institutions: an empirical survey". *Nat Biotechnol*. 24**:** 31-9., 2006. See figures 4 and 5 in particular
[x] See supra fn 3
[xi] Beth Israel Deaconess Medical Center: Test Warns Mothers Before Preeclampsia Strikes. 2010 BWR pp 4-6
[xii] Lawrence Berkeley National Laboratory, Berkeley, Calif.: DNA Microarray Rapidly Profiles Microbial Populations. 2011 BWR. pp 50-52.
[xiii] See supra fn 9, figure 5 in particular.
[xiv] University of Virginia Patent Foundation: Home Test Confirms Post-Vasectomy Sterilization. 2009 BWR pp 59-61
[xv] See supra fn 11
[xvi] University of Chicago: Minichromosomes Carry the Key to Improved Crops, Better Yields. 2010 BWR pp 60-62
[xvii] Genetics in Medicine Vol. 12, No. 4, April 2010 Supplement.
[xviii] See supra fn 3