COLLEGE of AMERICAN PATHOLOGISTS

September 7, 2021

Department of Commerce
U.S. Patent and Trademark Office
Alexandria, VA 22314

Response to Request for Information: PTO–P–2021–0032

The College of American Pathologists (CAP) appreciates the opportunity to submit comments in response to the U.S. Patent and Trademark Office's request for information on the current state of patent eligibility jurisprudence in the U.S. and how the current jurisprudence has impacted investment and innovation, particularly precision medicine, and diagnostic methods. The CAP is the world's largest organization of board-certified pathologists and a leading provider of laboratory accreditation and proficiency testing programs, serving patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. Clinical genetic/genomic testing is standard-practice and required for the provision of care in an innumerable number of medical conditions. Clinical need for this testing has driven an extremely rapid expansion of genetic testing in clinical laboratory test-menus. Being responsible for diagnostic laboratory testing, pathologists have a vested interest in ensuring that patent reform does not restrict the ability of physicians to provide quality diagnostic services to the patients they serve. Unfortunately, the debate about these issues has largely ignored the impact on physicians and their patients. As such, the thrust of the CAP's responses reflects that narrative.

Response to Questions:

Section I—Observations and Experiences

Please explain what impacts, if any, you have experienced as a result of the current state of patent eligibility jurisprudence in the United States. Please include impacts on as many of the following areas as you can, identifying concrete examples and supporting facts when possible:

Clinical laboratory genomics is a well-established field that has seen extremely rapid growth over the last 2-3 decades with numerous critical implications for patient care. Patents over genes and gene sequences pose a serious threat to patient care, medical advancement, and medical education. Allowing commercial entities to patent genes will impede the provision of genetic-based clinical testing and patient care through exclusive license agreements, excessive licensing fees, and restrictive licensing conditions.

These negative consequences are not conjecture. For example, prior to the Supreme Court's Myriad decision, a woman could find out if she carried a mutated BRCA1 or BRCA2 gene only from a test provided by Myriad at a cost of more than $3,000. The Court's 2013 decision created academic and

College of American Pathologists
1001 G Street, NW, Suite 425W
Washington, DC 20001
202-354-7100

commercial freedom for other companies and researchers to perform novel tests and rapidly create better and more competitive test offerings on the previously patented genes. Now there are tests for BRCA1, BRCA2, and a litany of other pathologically significant genes for as little as $249. It was also previously impossible for patients to obtain an independent second opinion on test-results for genes protected by a gene patent, like BRCA1 and BRCA1. Laboratories would not be able to develop such confirmatory tests, and many clinical labs had previously been served with cease-and-desist letters.

In another example, Sequenome filed for patent-infringement against other companies on its claim that it alone had 504 patent rights over cell free fetal DNA circulating in maternal blood when, in fact, methods to isolate and utilize this material for diagnosis were well known. In litigation, the 504 patent was invalidated because it claimed a natural phenomenon. The use of cell-free fetal DNA represents a substantial testing area in clinical prenatal genetics. If the Sequenome patent-ineligible claims were reverted, the price of non-invasive prenatal testing (for chromosomal abnormalities like Downs syndrome) would spike, and the other commercial and academic labs who had developed tests would probably have difficulties performing their tests. The result would be a significant cost to medical research and development as well as patient care.

Finally, as ‘products of natural phenomena’, gene sequence data is fundamental to the understanding of numerous diseases and should remain exempt from patent eligibility. No commercial entity should have ‘exclusive ownership of a disease’ through license agreements on gene-based tests. This practice has previously been used to prevent physicians and clinical laboratories from performing genetic tests as diagnostic medical procedures. In addition to BRCA, prior examples where testing has been halted due to patent enforcement include Alzheimer disease, Canavan disease, and Charcot-Marie-Tooth disease.

The advancement of personalized precision medicine is a widely embraced humanitarian effort with extensive private and public investment, such as the 21 Century Cures Act. Restricting access to gene sequences, a fundamental and extremely basic part of the biologic sciences, would represent an extreme impediment to academic and commercial innovation/discovery. The angst and outrage related to BRCA1/2 serves as a recent example. At a more granular level, restricting an individual patient’s ability to evaluate and understand their own genetic makeup would be extremely contrary to those goals, the ultimate depersonalization of medicine.

Precision medicine

A patent system should enhance social growth and welfare by encouraging innovation, disseminating useful technical information, and commercialization of new technologies. Eliminating the exceptions created by the Supreme Court would allow commercial interests monopoly rights over naturally occurring phenomena and would significantly obstruct scientific innovation and harm healthcare delivery.

College of American Pathologists
1001 G Street, NW, Suite 425W
Washington, DC 20001
202-354-7100

Reference intervals are important, as they allow healthcare providers to correlate clinical test results against an appropriate population. Pathologists are responsible to ensure that reference ranges are established or verified to be applicable to their patient population for every applicable analyte and specimen source proffered in the laboratory test menu. Multiple methods can be used to ascertain a physiologically meaningful reference interval, but this skill is an essential part of a pathologist's training and duty to patient-care. The court's unanimous ruling in Mayo vs. Prometheus (2012) frees clinical pathologists to practice their medical specialty. In addition, the ruling clarified that ascertainment of a reference range simply describes the relationship between an analyte and a physical condition – "setting forth a natural law". This distinction helps to ensure that no entity could monopolize these natural correlations of the human body, and thus impede improvement in medical knowledge and treatment.

As another natural occurring phenomenon, gene sequences are fundamental to both normal physiology and disease, may potentially change over time, and (in healthcare) are critical to the development of diagnostic and therapeutic tools. Genomics is not a stagnant field. Viruses can undergo rapid adaptive evolution and knowledge of the genetic drivers of neoplastic and non-neoplastic diseases has had recent exponential growth. The results of genomic testing can directly alter a patient's treatment algorithms, clinical trial opportunities, and eligibility for targeted therapies. The state of scientific knowledge does not remain static to when a test is first developed, and this leads to relatively quick technological obsolescence in genetic testing. Involvement by a diversity of pathologists and laboratories ensures the ongoing relevance and accuracy of diagnostic tests. The 'state of the art' would stagnate under the duration of a patent term, and patients would be stuck with outdated/suboptimal medical diagnostics.

If gene sequences and other natural phenomena can be considered intellectual property, a company with monopoly rights over the related disease can significantly hinder critical research, make the healthcare industry less productive and less competitive domestically and globally as well as significantly increase the cost of care for patients and society. It is not in the public's interest for single entity to hold ownership over the means to diagnose certain diseases or serve as the sole gatekeeper for targeted therapeutics. This approach would be bad for the patient care, public health, and the United State's standing as a global leader in the provision and quality of health care.

Diagnostic methods

Confirmatory tests are used for test result verification. Confirmatory testing is important for rare diseases, various conditions with difficult screening/diagnostic algorithms, and for tests that carry significant/life-altering implications (e.g., results would change the choice of chemotherapy). Cancer treatment highlights the vital importance of confirmatory tests; testing results frequently affect chemotherapy selection, may avert potentially devastating short and long-term drug toxicities, and may qualify a patient for life-saving targeted therapies.

If companies could patent genes, gene sequences and/or variations, and diseases, it would be possible for them to become a significant roadblock to patient care. For example, if a condition can only be diagnosed using one proprietary test, and development of newer/better testing for the same disease is blocked, this poses significant harm to patients with the disease that may test negative by the patented test, and significantly stymies scientific advancement in healthcare.

Please explain how, in your experience, the status of patent eligibility jurisprudence in the United States has affected any litigation for patent infringement in the United States in which you have been involved as a party, as legal counsel, or as another participant (e.g., an expert witness). For example, please explain whether this jurisprudence has affected the cost or duration of such litigation, the ability to defend against claims of patent infringement, the certainty/uncertainty of litigation outcomes, or the likelihood of settlement.

Pathologists operate at the junction between benchtop research and clinical medicine and are critical to the translation of genetic/genomic information into practical diagnostic tests for patient care. Genetic/genomic data is essential to understanding the pathophysiology of numerous diseases. Patent holders would essentially have corporate ownership of diseases through exclusive or restrictive license agreements on diagnostic testing. Innovation has been stifled in recent history, with physicians and CAP members being served "cease and desist" notification letters from patent holders or exclusive licensees indicating that continued patient testing would be patent infringement. Lastly, many of our members are on the frontline of the COVID-19 pandemic; responding to the pandemic in a situation where the exchange of critical genetic/genomic information was restricted would be disastrous.

Section II—Impact of Subject Matter Eligibility on the General Marketplace

Please identify how the current state of patent eligibility jurisprudence in the United States affects the public. For example, does the jurisprudence affect, either positively or negatively, the availability, effectiveness, or cost of personalized medicine, diagnostics, pharmaceutical treatments, software, or computer-implemented inventions?

The CAP believes patients should be able to obtain information about their own pathology test results, including second opinions on genetic or other clinical tests and interpretations. Unlike most independent second opinions for more conventional diagnostic testing rendered today, patients would have a difficult time obtaining an independent second opinion on a genetic/genomic test protected by a gene patent. No competing laboratory would be able to develop and perform tests for confirmatory purposes, and valuable second opinion genetic testing would be suppressed.

Further, over 30 million people in the U.S. are without health insurance. People without health insurance are less likely to have access to and may not be able to afford the health care services they need. Access to services like preventive care, cancer screenings, and treatment for chronic illnesses are essential for communities of color and other underserved populations. For example,

people of color who are diagnosed with lung cancer face worse outcomes compared to white Americans because they are less likely to be diagnosed early, less likely to receive surgical treatment, and more likely to not receive any treatment. Allowing genes, gene sequences, naturally occurring substances, and diseases to be patented will result in an anti-competitive diagnostic marketplace that prices patients out of the market, in particularly communities of color and underserved communities, for important life-saving diagnostic tests, and consequently necessary treatments.

The CAP continues to believe that patent reform should not condone the patenting of human genes and naturally occurring associations between genes and disease. Doing so would create barriers to patients' access to lifesaving genetic/genomic tests and eliminate access to confirmatory testing. The cost of testing would also substantially increase resulting in a step backward for the provision of health care. Patients would lose benefits from recent technological advances that have reduced costs and expanded access. Therefore, the CAP strongly believes that patent reform must maintain the judicially created exceptions to patent-eligibility as demarcated by the *Mayo, Myriad,* and *Alice* decisions.

The CAP appreciates the opportunity to submit comments. Please contact Darren Fenwick at dfenwic@cap.org if you have additional questions or comments.

Sincerely,

Patrick Godbey, MD, FCAP
President

College of American Pathologists
1001 G Street, NW, Suite 425W
Washington, DC 20001
202-354-7100