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BY ELECTRONIC DELIVERY

Andrew Hirshfeld

Commissioner for Patents, Performing the Functions and Duties of the Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office

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Via electronic submission to Docket PTO–P–2021–0032

Dear Commissioner Hirshfeld:

The Biotechnology Innovation Organization (BIO) appreciates the opportunity to provide information in support of the United States Patent and Trademark Office's Patent Eligibility Jurisprudence Study. *See* 86 Fed. Reg. 36257-60. BIO commends the USPTO's continued engagement with the patent user community in assessing how federal jurisprudence in this critical area of law is affecting innovative companies and the U.S. economy. BIO is hopeful that the USPTO's study will help inform policy makers of the negative impacts judicial decision-making in this area has had on the biotech industry and spur corrective action.

BIO is the principal trade association representing the biotechnology industry domestically and abroad. BIO has nearly 1,000 members which span the for-profit and non-profit sectors and range from small start-up companies and biotechnology centers to research universities and Fortune 500 companies. Approximately 90% of BIO's corporate members are small or mid-size businesses that have annual revenues of under $25 million and who count their patents among their most valuable business assets.

BIO is concerned that more than nine years after the Supreme Court decided *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), there continues to be unabated uncertainty about the patent-eligibility of many biotechnological inventions, with diagnostic and prognostic methods being particularly affected. The unstable state of patent-eligibility jurisprudence affects modern biotechnologies ranging from biomarker-assisted methods of drug treatment to companion diagnostic tests, fermentation products, industrial

enzyme technology, and marker-assisted methods of plant breeding. As inventors, developers, and investors in such technologies, BIO's members have a strong interest in clear and predictable rules of patent-eligibility.

In this submission, BIO focuses on the impact of patent-eligibility jurisprudence on the biotech industry including its ability to attract the capital investment necessary to develop products the help heal, feed, and fuel the world. Accordingly, BIO will limit its submission to the USPTO's questions that are relevant to these issues.

3. Please explain how the current state of patent eligibility jurisprudence in the United States impacts particular technological fields, including investment and innovation in any of the following technological areas:

[…]

c. precision medicine;

d. diagnostic methods;

e. pharmaceutical treatments;

Research and development within the biotechnology industry is time and capital intensive. The likelihood of failure is significantly higher than of success. The typical BIO member company does not have a product on the market yet, nor a source of revenue. The biotechnology industry provides employment to over 1.5 million individuals nationwide, and private and corporate biomedical research spending now approaches $70 billion annually. Virtually all of this investment is through private funding.[1] Developing a single therapy requires an average investment ranging from $1.2 billion to over $2 billion, and the clinical testing period alone consumes more than 8 years on average.[2]

The biotechnology industry's ability to develop and deliver precision medicine, pharmaceutical treatments, and diagnostics to patients has been jeopardized by the uncertainty and doctrinal drift in the area of subject matter eligibility. The past decade has seen an unprecedented expansion of common-law exceptions to patentability. All indications are that these exceptions are still expanding, with courts struggling to identify any outer boundaries in the Supreme Court's caselaw. Businesses must rationally assume that patents that are validly issued today can "become" invalid over time, because new creative applications of judicial exceptions may lurk only an appellate decision or two in the future. Nothing could be worse for investment in innovation than changing the rules of patentability after the fact in this way, after large investments have been made in reliance on properly examined and issued patents. If courts continue their current practice of construing judicial exceptions unmoored from the provisions of the Patent Act, without being able to genuinely explain the doctrinal origins of these exceptions or even clearly articulating the policies that are to be achieved, it is no exaggeration to say that

[1] Moving Research from the Bench to the Bedside: Hearings Before the Subcomm. on Health of the House Comm. on Energy and Commerce, 108th Cong., 1st Sess. 47 (2003) (testimony of Phylliss Gardner, M.D) (http://archives.energycommerce.house.gov/reparchives/108/Hearings/07102003hearing990/Gardner1579.htm) ("The biotechnology industry is the most research and development-intensive and capital-focused industry in the world," noting that 98 percent of research and development investment comes from the private sector).

[2] Joseph A. Di Masi and Henry G. Grabowski, The Cost of Biopharmaceutical R & D: Is Biotech Different? Manage. Decis. Econ. 28: 469-479, 2007)(hereafter: "Di Masi and Grabowski").

investment in biotech innovation will sooner or later be negatively affected. By the time we understand the impact on new tests and treatments that may only become available a decade from now, it will be too late.

The ability of innovators to patent diagnostic claims, for example, has been decimated by judicial developments in the area of patent-eligibility. As Chief Judge Moore of the United States Court of Appeals for the Federal Circuit noted in 2019, "[s]ince *Mayo*, we have held every single diagnostic claim in every case before us ineligible" (citing *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 760 F. App'x 1013 (Fed. Cir. 2019) ("Cleveland Clinic II"); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363 (Fed. Cir. 2018); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017) ("Cleveland Clinic I"); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015); *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755 (Fed. Cir. 2014); *PerkinElmer, Inc. v. Intema Ltd.*, 496 F. App'x 65 (Fed. Cir. 2012)).

Given that a diagnostics company – if it is even so lucky as to obtain a patent from the USPTO – can reasonably expect to have its patent invalidated in court, it is hard to imagine how investment in this space can continue. *In vitro* diagnostics and radiopharmaceutical diagnostics take on average 7-10 years and 7-9 years, respectively, to go from invention to market.[3] And the costs associated with research and development through market introduction can range from around 20 million for follow-on diagnostic products to over 100 million for new platforms or tests involving a new biomarker.[4] Without the ability to protect these diagnostic tools once introduced into the market, large sustained investment in this area may not be maintained and, consequently, innovation will diminish. Already, business analysts are characterizing the in vitro diagnostics (IVD) industry as being dominated by a small number of key players, consolidation, and lackluster levels of investment. Between 2016-2019, the IVD industry received only about 3% of all biomedical venture dollars. And the COVID pandemic has brought to light what has been described as a lack of recent innovation.[5] Emerging evidence shows that *Myriad*, *Mayo*, and their progeny have caused the development of molecular tests to be abandoned, have interfered with the ability of small developers to enter into development partnerships, and are driving a pivot to trade secrecy rather than patenting and publication.[6]

Precision medicine – a form of medicine that relies on genetic or other diagnostic testing to optimize treatment for a particular patient – may likewise suffer. A common example of precision medicine is the use of an older, already approved molecule, for targeted treatment in patients who present with a specific genetic mutation. In such a scenario, the patent on the molecule may have already expired but researchers may only learn years later that the compound is more

[3] B.N. Roin, 61 UCLA L. Rev. 672 (2014).

[4] Dolginow et al., "Mystery Solved! What is the Cost to Develop and Launch a Diagnostic?," Jan. 15, 2013, available at https://diaceutics-website.s3.eu-west-1.amazonaws.com/store/2e17552089662dafc17a2597f44463dc.pdf.

[5] https://www.outcomecapital.com/blog/caught-by-surprise-the-diagnostics-industry-in-the-time-of-covid/

[6] Liddicoat, Liddell, and Aboy; The Effects of Myriad and Mayo on Molecular-Test Development in the United States and Europe: Interviews from the Frontline; Vanderbilt Journal of Entertainment and Technology Law 22(4), 2020, available at: https://scholarship.law.vanderbilt.edu/cgi/viewcontent.cgi?article=1031&context=jetlaw

effective in patients with this particular genetic mutation. Society as a whole benefits from incentivizing such research – we all want to take medicine that works for us and to avoid medicines that are less effective – yet the state of patent protection in this area is foggy at best. Without clarity and certainty, we cannot expect scientists, companies, and investors to pursue this costly and timely research and the associated regulatory delays, when in the end there may be no way to prevent competitors from copying these new methods of treatment.[7]

The patent-eligibility of claims to medicines derived from naturally occurring products and related treatments is only slightly less murky than of those to diagnostics and precision medicines. While the 2019 *Natural Alternatives International, Inc.* decision from the Federal Circuit is a step in the right direction regarding the patent-eligibility of these types of claims, the assurance is tenuous at best. In that case, the Federal Circuit reversed a lower court's grant of a motion for judgment on the pleadings that certain claims pertaining to formulations and methods of treatment using naturally occurring beta-alanine were ineligible. The court explained that claims to methods of using natural products are not the same as claims to the natural products themselves, and that a claim to a "manufacture or composition of matter made from a natural product is not directed to the natural product where it has different characteristics and 'the potential for significant utility.'" Nonetheless, the court's holding was tailored to the specific facts of that case and the case was remanded for further proceedings. And as we have seen with the doctrinal drift in this area of patent law, innovators and investors in this space cannot be assured that a different panel of the Federal Circuit on slightly different facts would come out the same way.

10. Please identify how the current state of patent eligibility jurisprudence in the United States impacts the global strength of U.S. intellectual property.

BIO members report that they do not experience the same difficulties establishing the patent-eligibility of their claimed inventions in foreign jurisdictions. BIO is unaware of another jurisdiction that applies a version of the two-step *Mayo/Alice* test developed under U.S. law. Rather, these foreign jurisdictions tend to focus on the technical nature of the claimed invention and whether the subject matter constitutes an enumerated exception from patent eligibility. For example, the European Patent Office (EPO) applies a list of exceptions to patentable subject matter identified in Articles 52 and 53 of the European Patent Convention, which includes subject matter claimed "as such:" discoveries, scientific theories, and mathematical methods; aesthetic creations; schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers; and presentations of information. Rather than handling questions of whether claim limitations are old or new and whether in combination they constitute a transformative inventive concept as a question of patent eligibility like the *Mayo/Alice* test, the EPO applies a patent-eligibility analysis only to claims that claim an exception "as such." In instances where claims combine technical and non-technical features, the EPO proceeds to an inventive step analysis that determines which claim elements contribute to the technical character of the invention and then considers only those elements when analyzing whether the required inventive step is present. In doing so, the EPO seeks to ensure that only claim elements that contribute to the technical character of an invention serve

[7] *See* Lefstin et al., "Final Report of the Berkeley Center For Law & Technology Section 101 Workshop: Addressing Patent Eligibility Challenges," 33 Berkeley Tech L.J. 551, 582-84 (2018) (explaining the relationship between precision medicines and diagnostics, the difficulty in patenting diagnostic technologies, and the associated decrease in investor interest in this area of research and development).

to distinguish the invention over the prior art. The EPO's process is generally viewed as reasonably predictable, internally consistent, and technical in nature, and has generated far less controversy than the U.S. process.

One illuminating example of the distinction between U.S. patent eligibility law and the approaches in foreign jurisdictions is the case of Sequenom's patents on its diagnostic method for diagnosing chromosomal abnormalities in babies in utero. Prior to Sequenom's inventions, mothers and their unborn children had to undergo invasive and at time dangerous procedures (e.g., amniocentesis) to diagnose chromosomal abnormalities before birth. Sequenom discovered an innovative method for sampling a mother's blood, identifying and separating fetal DNA from the blood sample, and analyzing the fetal DNA for certain abnormalities. There was no dispute that this was a significant advance in prenatal care. Nonetheless, the Federal Circuit in 2015 struck down Sequenom's patent covering this innovative method under the *Mayo-Alice* test for lack of patent eligibility. Several ex-U.S. courts came to the opposite conclusion. Australia, the U.K., and some other European countries have upheld Sequenom's patents on this diagnostic method.[8]

Accordingly, for certain biotech inventions, BIO's members can more readily procure patents in ex-U.S. jurisdictions and can be more confident that they will not be invalidated for lack of subject matter eligibility years down the road. It has been established that medicines are introduced in countries with strong IP protections before they are in other countries. Applying the same logic, if the course of patent eligibility jurisprudence is not righted in the U.S., we can expect to see diagnostics, precision therapeutics, and possibly even medicines derived from natural sources introduced into foreign countries well in advance of the United States.

11. Please identify how the current state of patent eligibility jurisprudence in the United States impacts the U.S. economy as a whole.

The biotechnology industry in the United States is a vital engine of innovation, investments, and economic development. In 2020 biopharmaceutical companies had almost 4,500 potential medicines in development, part of the more than $100 billion in research and development spending annually by our U.S. biotechnology industry.[9] Biotech jobs in the U.S. are robust: accounting for 1.87 million jobs with an average salary of $107,000 per year.[10] Our industry is vital to both the future health and wellbeing of our population and, in many respects, the health and wellbeing of our economy.

Instability in the area of patent subject matter eligibility threatens the continued viability of this business model. Vitiating biotech patents on important medicines and other biotech products will only decrease the incentives our manufacturers and their investor partners have to develop the

[8] Adam Houldsworth, "Australian diagnostic method judgment shows US to be the eligibility outlier," IAM, Jul. 26, 2019, available at https://www.iam-media.com/law-policy/australian-diagnostic-method-judgment-shows-us-approach-be-outlier.

[9] Pharmaceuticals in Perspective, PhRMA, available at https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/ChartPack_Biopharmaceuticals_in_Perspective_Fall2020.pdf

[10] Transforming Ideas into Advances: Best Practices in State and Regional Bioscience Economic Development Initiatives, BIO, available at https://www.bio.org/sites/default/files/legacy/bioorg/docs/BIO_BestPracticesReport2019vF.pdf

next generation of cures and treatments. The high paying jobs supported by the biotech industry will likewise suffer.

More generally, it is also important to bear in mind that the impact of the current state of patent eligibility is disparate not only by technology, but also by categories of patentees. Thus, while manufacturing businesses and academic institutions, for example, are all to some degree affected, it has been shown that the "bite" of Section 101 jurisprudence is felt most acutely by independent inventors and small inventor-started businesses.[11] In an economy that values individual entrepreneurship and startup company formation, the long-term effects of this phenomenon, if allowed to continue, need to be better-understood.

Finally, the fact that U.S. eligibility jurisprudence produces systematically different patentability outcomes as compared to other industrialized countries is likely to have implications for U.S. international competitiveness. As a simplified proposition, when U.S. companies seek to enter e.g. the Chinese or EU markets, they will have to contend with relevant patents that may exist in those jurisdictions. Conversely, when Chinese or European companies seek to enter the U.S. market they will encounter a form of free-for-all. In this way, by denying patents on valuable inventions that are patentable in other countries, U.S. eligibility jurisprudence invites imitators and copyists into the United States while coaxing U.S.-based innovators to focus more on jurisdictions where patents can be obtained and enforced.

BIO is hopeful that the USPTO's study will help inform policy makers of the negative impacts judicial decision-making in this area has had on the biotech industry and spur corrective action, and we look forward to engaging further with the USPTO on this important topic.

Respectfully submitted,

/s/ Hans Sauer

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Biotechnology Innovation Organization

[11] Lemley and Zyontz, Does Alice Target Patent Trolls? Available at : https://onlinelibrary.wiley.com/doi/full/10.1111/jels.12275