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September 7, 2021

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
600 Dulany Street
Alexandria, VA 22314

Submitted electronically via www.regulations.gov to docket number PTO-P-2021-0032

Dear Commissioner Hirshfeld:

Thank you for the opportunity to provide comments in response to the United States Patent and Trademark Office's (USPTO) request for public input in a Patent Eligibility Jurisprudence Study (PTO-P-2021-0032). The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,500 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from the government, academic, private, and hospital-based clinical laboratories, and the in-vitro diagnostics industry. As professionals that populate most clinical molecular pathology laboratories in the United States, we hold various perspectives as licensees or users of patented technology and developers of innovative laboratory testing.

AMP holds the position that naturally occurring genetic sequences, and any association with diseases and health conditions, should not be patent eligible. Thus, AMP strongly supports the Supreme Court decisions in *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc. (Mayo), Association for Molecular Pathology v. Myriad Genetics (Myriad), Inc., and Alice Corp. v. CLS Bank International (Alice).* As professionals developing, validating, and performing laboratory tests, we see no evidence that these court decisions have had a "dramatic negative impact on investment, research, and innovation" as it relates to molecular laboratory testing. We present the following information to demonstrate that due to the protection afforded by these cases, the field of molecular diagnostics is innovating, growing, and thriving.

Section I—Observations and Experiences

1. *Please explain how the current state of patent eligibility jurisprudence affects the conduct of business in your technology area(s). Please identify the technology area(s) in your response.*

2. *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:*

    a. *Patent prosecution strategy and portfolio management;*
    b. *patent enforcement and litigation;*
    c. *patent counseling and opinions;*
    d. *research and development;*
    e. *employment;*
    f. *procurement;*
    g. *marketing;*
    h. *ability to obtain financing from investors or financial institutions;*
    i. *investment strategy;*
    j. *licensing of patents and patent applications;*
    k. *product development;*
    l. *sales, including downstream and upstream sales;*
    m. *innovation; and*
    n. *competition.*

Our efforts are central to the generation of novel, high quality, molecular pathology procedures that are applied daily in medical decision-making and informing patient care in various areas including molecular oncology, inherited diseases, infectious diseases, and histocompatibility testing. Prior to the *Mayo, Myriad, and Alice* decisions, patents on genetic sequences prevented the development and delivery of up-to-date and effective clinical genetic testing services. In 2001, a survey of 122 clinical laboratory professionals performing genetic testing demonstrated that most felt the patent environment was negatively impacting the cost, access, and development of genetic tests.[1] Ninety-one respondents said that their laboratories needed to obtain a license to use a patented method, device, or reagent. A quarter of the respondents had stopped performing a test altogether because of a patent or license. Moreover, fifty-three percent (53%) of respondents decided not to develop a new clinical genetic test because of a patent or license. In a thorough assessment by the U.S Department of Health and Human Services Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) in 2010, the Committee recognized the burden associated with negotiating numerous licenses and how the cost of these endeavors may render a clinically valuable test unworthy of financial investment.[2] As scientific understanding of genetics and genomics has increased over time, so has an appreciation of the polygenic (involving more than one gene) nature of disease. In 2021, the prospect of negotiating numerous licenses for multiple genes threatens standard medical practices that have evolved since *Mayo, Myriad, and Alice.*

[1] Cho MK, Illangasekare S, Weaver MA, Leonard DGB, Merz JF. Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services. J Mol Diagnostics. 2003;5(1):3-8. doi:10.1016/S1525-1578(10)60444-8

[2] Secretary's Advisory Committee on Genetics, Health, and Society, Department of Health and Human Services. Gene patents and licensing practices and their impact on patient access to genetic tests. https://osp.od.nih.gov/wp-content/uploads/2013/11/SACGHS_patents_report_2010.pdf. Published April 2010. Accessed August 17, 2021.

Today, in a post-*Mayo, Myriad, and Alice* world, we are fortunate to have an environment where molecular professionals are not restricted by the existence of gene patents when developing and employing clinical laboratory tests in their practice. We implore you consider these experiences and case studies:

Hereditary Breast and Ovarian Cancer (HBOC) Syndrome

HBOC syndrome is an inherited disorder in which genetic alterations in various genes have resulted in a person having an elevated risk of developing breast cancer and ovarian cancer. People with HBOC syndrome may also have an increased risk of other types of cancer, including pancreatic cancer, prostate cancer, and melanoma. Over time, there has been increasing public awareness of the fact that alterations in genes known as *BRCA1* and *BRCA2* can dramatically contribute to a person's susceptibility to developing cancer, and prior to 2013, testing to glean information about a person's inherited risk for developing breast and ovarian cancer was largely focused on analyzing these two genes. As the USPTO is aware, Myriad Genetics, Inc., held patents on the *BRCA1* and *BRCA2* gene sequences and thus, was able to license the intellectual property (IP) for full DNA sequencing for the *BRCA* genes.[3] Myriad Genetics, Inc. unfortunately used the company's control over these patents to reduce competition for testing of the *BRCA* genes. In the study of laboratory professionals from 2001, there were nine reported instances of laboratories being contacted by Myriad Genetics, Inc., which led to those laboratories removing their tests from the market. However, upon the Supreme Court's decision in the 2013 *Myriad* case, five companies began offering testing for HBOC syndrome[4], with many more joining the market by 2014.[5] Today there are 300 clinical tests involving the analysis of *BRCA1*, and 334 clinical tests involving the analysis of *BRCA2*, being performed in CLIA-certified laboratories according to the Genetic Test Registry.[6] This growth in *BRCA1* and *BRCA2* testing alone since the 2013 *Myriad* case decision is tremendous.

The existence of numerous clinical tests for a disease or condition is important for inter-laboratory comparisons, which helps to ensure that testing is high quality and allows patients to have confirmatory testing performed. For example, in 2006, a group of authors reported that approximately 12% of people with breast cancer who had severe family histories of cancer but tested negative for *BRCA1* and *BRCA2* alterations using Myriad's testing strategy at the time, were found by other testing methodologies to carry a large genomic deletion or duplication in one of these genes.[7] In other words, many patients that could have benefited from additional testing methods to detect these large rearrangements were being missed by the only clinical test that was available to them. That same year, Myriad Genetics, Inc., responded by offering testing for large rearrangements in *BRCA1* and *BRCA2*. It is speculated that this change was largely the result of considerable pressure from the scientific community consequent to the release of the critical study.

[3] University of Utah Research Foundation, et al. v. Ambry Genetics Corp. Case No. 2:13-cv-00640-RJS (D.Utah, filed July 9, 2013)
[4] https://www.nytimes.com/2013/06/14/business/after-dna-patent-ruling-availability-of-genetic-tests-could-broaden.html
[5] Cook-Deegan R, Niehaus A. After Myriad: Genetic Testing in the Wake of Recent Supreme Court Decisions about Gene Patents. Curr Genet Med Rep. 2014;2(4):223. doi:10.1007/S40142-014-0055-5
[6] Data accessed on August 17, 2021 from Genetic Testing Registry; https://www.ncbi.nlm.nih.gov/gtr/
[7] Walsh T, Casadei S, Hale Coats K, et al. Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. JAMA. 2006;295(12):1379-1388. doi:10.1001/JAMA.295.12.1379

Our scientific understanding of HBOC syndrome has evolved and now molecular pathologists know that many more genes are involved in this disorder. For instance, the Current Procedural Terminology (CPT) code 81432 used for the billing of genomic sequence analysis panel (panel tests) for hereditary breast cancer-related disorders must include the sequencing of 14 genes including *ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11,* and *TP53*. A separate CPT code, 81433, is used for the payment of a duplication/deletion analysis panel that must include analyses for *BRCA1*, *BRCA2*, *MLH1*, *MSH2*, and *STK11.* In 2018[8], Concert Genetics reported that there were 374 panel tests that included *BRCA1* and *BRCA2* which compared to the 172 panel tests in 2016[9]. These highly complex tests greatly improve patient care by simultaneously evaluating multiple genes that can lead to similar disease presentations and Concert Genetics attributes the explosion of panel testing directly to the 2013 *Myriad* decision.[10] Panel tests are only possible because burdensome patents and/or licensing agreements do not interfere with the study of these genes, nor with the translation of scientific understanding into clinically actionable diagnostic tests. Furthermore, as the understanding of inherited genetic risk for cancer evolves, laboratories can readily update their testing to account for new scientific and medical information and deliver appropriate care to their patients.

Canavan Disease

The National Institutes of Neurological Disorders and Stroke describes Canavan disease as a "gene-linked neurological disorder in which the brain degenerates into spongy tissue riddled with microscopic fluid-filled spaces."[11] This starts in infancy due to the lack of an essential enzyme resulting in deterioration of white matter in the brain. Children with Canavan disease lack head control, have reduced visual responsiveness and abnormal muscle tone such as stiffness or floppiness.[12] Over time, children can also experience seizures, become paralyzed, developmentally delayed, blind, deaf, and have trouble swallowing. The prognosis for Canavan disease is poor with death usually occurring before the age of 10. This disease is caused when a child inherits two genetically altered copies of the *ASPA* gene.[13] Genetic testing is performed not only for diagnostic purposes, but the American College of Genetics and Genomics (ACMG) also recommends that all pregnant patients and those planning pregnancy should be offered carrier screening for over 100 inheritable autosomal recessive and X-linked conditions including Canavan disease.[14]

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[8] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/02/10_ConcertGenetics_CurrentLandscapeofGeneticTesting_2017Update.pdf Accessed August 31, 2021.

[9] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[10] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[11] https://www.ninds.nih.gov/Disorders/All-Disorders/Canavan-Disease-Information-Page

[12] https://www.canavanfoundation.org/about_canavan_disease

[13] https://rarediseases.info.nih.gov/diseases/5984/canavan-disease

[14] Gregg AR, Aarabi M, Klugman S, et al. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med 2021. 2021;10:1-14. doi:10.1038/s41436-021-01203-z

In 1993, a patent application relating the sequence and genetic alterations associated with *ASPA* was filed by Dr. Reuben Matalon, and others, who at the time was affiliated with Miami Children's Hospital Research Institute, Inc.[15] A review by Colaianni et al. in 2010 described the actions of Miami Children's Hospital following being awarded a patent in 1997. The authors report that Miami Children's Hospital sent letters to laboratories and hospitals informing them that they would have to license access to the sequence or risk an infringement lawsuit. Findings from a survey conducted in 2001 confirm this report, indicating that at least four respondents stopped performing testing on *ASPA* as a result of receiving a patent enforcement letter.[16] Former AMP President, Dr. Debra Leonard, was the recipient of one letter, which indicated the Miami Children's Hospital would charge $12.50 per test and warned that volume limitations would likely be placed on her institution.[17] Unfortunately, Dr. Leonard was ultimately no longer able to perform testing for Canavan disease, in addition to other genetic diseases, because of patent enforcement actions taken by various entities.[18]

As reported by Colaianni et al. (2010), the Canavan disease community found this narrowing of access to affordable testing problematic, and in response formed the Canavan Disease Screening Consortium to advocate for 1) removal of a testing volume cap, 2) reduction of royalty fees, 3) development of an educational program focused on carrier screening, and 4) a dedication of funds to assist families unable to afford carrier testing. Miami Children's Hospital did not agree to the requests of the Consortium and instead pursued a plan to establish a single, large-volume licensee. The controversy culminated in a lawsuit being filed against Miami Children's Hospital which resulted in the United States District Court for the Southern District of Florida concluding that Miami Children's Hospital enriched itself at the expense of the patients and families who had donated tissue which aided in research for Canavan disease.[19]

Today, in the absence of gene patents, there are 117 tests that include an analysis for *ASPA* being performed in 26 CLIA-certified laboratories in the United States.[20] It is also important to emphasize that testing for *ASPA* is often incorporated into panel testing that evaluates an array of genes. This serves two clinical purposes: 1) it offers patients a single, broad, symptom-based approach to diagnosing heritable conditions especially when it is not clear that a child has Canavan disease, and 2) it allows for affordable and efficient comprehensive carrier testing for many diseases and disorders to be performed so that patients can make informed reproductive decisions. If efforts to establish a single, large volume testing entity just for *ASPA* had been successful, efforts to provide optimal patient care would have been disrupted and fragmented across multiple laboratories. Notably, the clinical and financial impact would have been disproportionate on those with elevated risk of carrying an *ASPA* genetic alteration based on their ancestry. For this reason (among others), ACMG now recommends that

[15] Colaianni A, Chandrasekharan S, Cook-Deegan R. Impact of Gene Patents and Licensing Practices on Access to Genetic Testing and Carrier Screening for Tay-Sachs and Canavan Disease. Genet Med. 2010;12(4 Suppl):S5. doi:10.1097/GIM.0B013E3181D5A669

[16] Cho MK, Illangasekare S, Weaver MA, Leonard DGB, Merz JF. Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services. J Mol Diagnostics. 2003;5(1):3-8. doi:10.1016/S1525-1578(10)60444-8

[17] Terry M. Storming the Molecular Diagnostic IP Fortress. Biotechnol Healthc. 2006;3(1):49. /pmc/articles/PMC3571035/.

[18] Leonard D. Medical practice and gene patents: a personal perspective. Acad Med. 2002;77(12 Pt 2):1388-1391. doi:10.1097/00001888-200212001-00010

[19] Fla SD, editor. Greenberg v. Miami Children's Hospital Research Institute, Inc. 264 F. Supp. 2d 1064 (S. D. Fla. 2003). https://pubmed.ncbi.nlm.nih.gov/15776537/

[20] Data accessed on August 18, 2021 from Genetic Testing Registry; https://www.ncbi.nlm.nih.gov/gtr/

carrier screening be offered in an "ethnic and population neutral" approach to ensure those approaches are inclusive of diverse populations and promote equity and inclusion.

The current environment for development of comprehensive carrier screening is robust. In 2016, 20 laboratories offered comprehensive carrier testing.[21] Additionally, several market analyses indicated that North America was the highest-revenue-generating carrier screening market from 2014-2019 and will continue to dominate the market into the future.[22,23,24] One report emphasizes that a number of partnerships have been formed to improve testing solutions and advance technology. If naturally occurring genetic sequences and their association to diseases and health conditions remained patent eligible, the rapid expansion of the carrier screening market would have not occurred, and patients would face restrictions in access to testing as evidenced in the case of Canavan disease.

Comprehensive Genomic Profiling in Cancer/Whole Genome or Exome Sequence for Pediatric Conditions

Technological advancements in genetic sequencing that allowed for the development of a comprehensive genomic profile of a person's cancer have dramatically improved patient care. Comprehensive Genomic Profiling, or CGP, is when molecular professionals use sequencing technology to simultaneously detect various classes of genomic alterations, which include base substitutions, insertions and deletions, copy number alterations, and rearrangements or fusions, across hundreds of genes with a single test on a patient's sample. Not only can CGP detect actionable mutations in any one of hundreds of genes, but it can also provide information about microsatellite instability and tumor mutational burden, which are properties of the cancer genome and are not specific to any one gene. This approach allows clinicians to match patients with advanced cancer to targeted therapies already in clinical use and investigational therapies being evaluated in clinical trials.

Increasingly, CGP has been adopted as an efficient and effective approach in advanced cancer care. Moreover, as the number of targeted therapies associated with genomic targets increases over time, CGP will only become more essential. In oncology, the percentage of clinical trials incorporating biomarkers has risen from 18 percent in 2000 to 61 percent in 2019.[25] This important work has led to the availability of 286 targeted therapies for patients in 2020, a greater than 350% increase from the 81 therapies available in 2012. Taken together, this indicates that more comprehensive approaches to cancer testing will be a focus for molecular professionals well into the future.

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[21] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[22] https://www.researchandmarkets.com/reports/5128884/carrier-screening-market-research-report-by Accessed August 18, 2021.

[23] https://www.psmarketresearch.com/market-analysis/carrier-screening-market Accessed August 18, 2021.

[24] https://www.marketwatch.com/press-release/carrier-screening-market-key-companies-business-opportunities-competitive-landscape-and-industry-analysis-research-report-by-2027-2021-08-11?siteid=bigcharts&dist=bigcharts&tesla=y Accessed August 18, 2021.

[25] Personalized Medicine Coalition, "The Personalized Medicine Report: 2020, Opportunity, Challenges, and the Future." 2020. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_and_Significance_of_Progress_in_2019.pdf Accessed August 19, 2021.

Similarly, using whole exome and genome sequencing (WES/WGS), which evaluates a large number of genes or the full genome, is an important option for pediatric genetic testing for rare diseases. These testing approaches may be appropriate when 1) the gene or genes involved in a disease are not obvious or known in a patient who is undergoing a diagnostic odyssey, 2) the patient has complex clinical presentations or multiple diagnoses, 3) the patient has a disorder associated with a large number of genes, and/or 4) the patient is in need of immediate critical care.

WES/WGS allows molecular professionals to explore whether the underlying reasons for a patient's symptoms can be attributed to any known pathogenic or likely pathogenic alterations, and also sometimes the results of a test implicates new genes and genetic alterations that have not been previously associated with a disease.[26] Using this information, molecular professionals work to improve testing – when evaluating the number of new genetic tests in 2017, one report found that the number of pediatric and rare disease tests grew faster than any other domain.[27] Moreover, they reported that between January 2016 and March 2018, the number of exome sequencing tests in the market grew from 72 to 125 (a 74 percent increase).

CGP, WES, and WGS are made possible because information about thousands of genes and the role of various segments of genetic sequences in human health and disease can be incorporated into a single test. Prior to *Mayo, Myriad, and Alice*, this was not possible as it would have required a laboratory to obtain a license for every gene patent that existed or to exclude potentially clinically relevant genes from the analysis. Instead of promoting an environment for growth and innovation, patents on genetic information would have siloed testing and inhibited patient access to more comprehensive testing options. In fact, since these court decisions, there has been increasing support by researchers and genetic testing laboratories to share and provide open access to information on genetic variants.

In 2017, the ACMG published a statement on data sharing, noting that "information that underpins health-care service delivery should be treated neither as intellectual property nor as a trade secret when other patients may benefit from the knowledge being widely available."[28] Additionally, AMP has recently released its own position statement on data sharing outlining numerous recommendations for hospitals, academic medical centers, commercial diagnostic laboratories, patient organizations, policymakers, and others, to support and facilitate the sharing of molecular genetic variant data.[29] As relayed in the statement, data sharing is "essential both for understanding the contribution of genetic and genomic variation to disease and conditions, and for translating that information through the development, validation, and interpretation of clinical testing… Submissions of de-identified data to [curated databases] accelerates the process for re-assignment of variants of unknown

[26] As one example, see https://www.wired.com/story/one-scientists-quest-to-bring-dna-sequencing-to-every-sick-kid/
[27] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.
[28] American College of Medical Genetics and Genomics Board of Directors, "Laboratory and clinical genomic data sharing is crucial to improving genetic health care: a position statement of the American College of Medical Genetics and Genomics." Genetics in Medicine January 5, 2017. https://www.nature.com/articles/gim2016196
[29] Association for Molecular Pathology, "Association for Molecular Pathology Position Statement: Variant Data Sharing." July 29, 2021 https://www.amp.org/AMP/assets/File/advocacy/AMP_Position_Variant_Data_Sharing_7_29_2021.pdf

significance (VUS) to clinically actionable categories (e.g., benign or pathogenic), which [the National Institutes of Health] considers a critical aspect of the quality assurance process for accurate genetic and genomic testing."

Should associations between observed variants and health conditions once again become patent eligible, this type of data sharing would come to a standstill, dramatically slowing the pace of precision medicine research, harming quality genetic variant interpretation, and restricting the ability of molecular professionals to keep their tests current – the latter being a hallmark feature of their work using laboratory developed testing procedures. Ultimately, these effects would render CGP, WES, and WGS unusable, to the detriment of patient care.

COVID-19

Lastly, we call attention to the current pandemic and the response effort which is largely reliant upon highly effective and broadly accessible testing for SARS-CoV-2. AMP shares the concerns expressed by others about how, if allowed, patents on the SARS-CoV-2 genetic sequence would have greatly hampered the United States' response efforts[30], and joined thirty-seven other organizations in calling President Biden's attention to how this current situation compares to the 2003 outbreak of severe acute respiratory syndrome (SARS).[31] As described in our letter, during the 2003 outbreak, biotechnology and pharmaceutical companies raced to patent everything from the genetic sequences within the virus' genome to the virus itself.[32] In competition with these companies was the CDC which sought to defensively patent the virus and its entire genetic content "to make sure access to the virus remains available to anyone" as stated by then CDC Director Julie Gerberding.[33]

The necessity for molecular professionals to operate, innovate, and developed testing for patients in an environment free of considerations related to the patent-status of SARS-CoV2 and COVID-19 disease are crystalized when considering the necessity of frequent shifts in testing strategy due to external challenges experienced repeatedly since February 2020. AMP members have been on the frontlines of responding to the COVID-19 pandemic by developing and providing molecular-based diagnostics for patients across the United States. We surveyed our membership multiple times over the course of 2020 and collected over 250 responses from molecular laboratory professionals to understand their successes and hurdles when developing and providing the crucial and timely diagnostic services that patients needed during the COVID-19 pandemic.[34] In August and April of 2020, respondents reported that supply chain interruptions were having a significant impact on their work – in August, over 90% reported that interruptions delayed and/or decreased testing. Similar responses across all laboratory types indicated that additional resources were needed to implement and/or maintain testing, with commercially-available testing kits and platform-specific laboratory consumables identified as the most needed items. To overcome testing supply shortages and maintain their testing capacity, molecular professionals deployed multiple testing methodologies, i.e. they built redundancy in test protocols

[30] As an example: Park, S. "The Dangers of Expanding What Can Be Patented In the Age of COVID-19." October 30, 2020. https://www.aclu.org/news/privacy-technology/the-dangers-of-expanding-what-can-be-patented-in-the-age-of-covid-19/ Accessed August 19, 2021.
[31] https://www.amp.org/AMP/assets/File/advocacy/Coalition%20Letter%20to%20Biden%20Administration%20on%20Patent-Eligibility_6_8_2021.pdf
[32] https://apnews.com/article/145b4e8d156cddc93e996ae52dc24ec0
[33] https://www.wsj.com/articles/SB105226807345954200
[34] https://www.amp.org/advocacy/sars-cov-2-survey/

within their laboratories in order to switch to a different testing platform when a shortage compromised use of another one. Many used more than three methods, which were often a combination of both commercially available testing kits and laboratory developed testing procedures that they designed and validated in their own laboratories. Our findings indicated that testing diversity continues to play an important role in the public health emergency to meet the clinical need. If laboratories and manufacturers needed to navigate multiple patent and licensing arrangements related to SARS-CoV-2 RNA sequence with each assay adjustment or introduction, the observed testing response would not have been possible.

The response to SARS-CoV-2 by the laboratory community was restricted by unfortunate regulatory decisions early in the pandemic, a situation which would only have been exacerbated by the imposition of patent protections on the sequence of the SARS-CoV-2 virus. In February, the Food and Drug Administration (FDA) granted an emergency use authorization (EUA) for one test kit. With only one test kit available for clinical use, the country's entire response relied upon it and unfortunately, due to contamination during the manufacturing process, the kits failed to perform correctly leaving the country without any testing for weeks. For a considerable amount of time, laboratories stood by, ready to act as SARS-CoV-2 was silently transmitted within the United States but were unable to do so until the FDA modified its regulatory policy in late February.

SARS-CoV-2 is made up of ribonucleic acid (RNA, a similar material to DNA) that contains all the genes the virus needs to function within a human cell, and on January 10, 2021, scientists in China made the full sequence of the virus' genomic available to the public. Fortunately, genetic sequences and their association to health conditions are not patentable in the United States, which has allowed for hundreds upon hundreds of molecular tests for SARS-CoV-2 to be developed and performed in CLIA high complexity certified laboratories across the United States.[35] Current patent eligibility jurisprudence has allowed molecular professionals to be adaptable, to rapidly detect different emerging strains, and to ensure that testing in a geographic area is sensitive and specific for that particular population. Flexible regulatory policy during the emergency and the lack of patents on the virus' RNA sequence are the reason why our members are now able to meet the testing needs of this nation.

Moreover, innovation for diagnostic and public health testing has flourished over the past two years. Innovation has brought about methods that allow patients to collect their own specimens, thus circumventing the need for scarce personal protective equipment (PPE). Test developers have validated the use of saline instead of viral transport media, which is in extremely limited supply. Similarly, they have validated testing so saliva could be used as a specimen type to alleviate the swab shortage. Moreover, the range of projects funded by the Biomedical Advanced Research and Development Authority (BARDA) provides a public glimpse into other advancements that have been made in diagnostic testing.[36] Additionally, earlier this year, FDA announced that the Agency had authorized the first ever molecular at-home test that did not require a prescription.[37] These successes, and the resulting population health and economic benefits, should be factored into the USPTO's analysis – all of them made possible with the current state of patent eligibility jurisprudence.

[35] https://chs.asu.edu/diagnostics-commons/testing-commons
[36] https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx?filter=diagnostic
[37] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-authorization-first-molecular-non-prescription-home-test

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

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

Taking a broader view than specific case studies and the experiences of molecular professionals, AMP believes it is critical to also take into consideration how genetic testing and the field of molecular pathology have grown over time. We know from public reports from Concert Genetics that as of October 2020, there were over 160,000 genetic tests in the US market[38] -- a nearly 175 percent increase compared to the number of genetic tests in 2016.[39] It has been estimated that 14 genetics tests are entering the market *every day*.[40] As articulated previously, we also know that genetic tests are becoming more complex. For instance, during the 12 months ending March 1, 2018, a net total of 801 new genetic testing panels entered the market.[41] This growth is also having a tremendous positive impact on the economy. According to a 2019 report issued by the American Society of Human Genetics (ASHG), human genetics and genomics contributed $265 billion to the US economy in that year alone, and for every federal dollar invested in human genetics and genomics research in 2019, it yielded a $4.75 return.[42]

AMP believes it is also critically important to consider how this rich environment impacts molecular professionals. The ASHG report on the economy found that US human genetics and genomics research and industrial domain employs nearly 166,000 workers which includes researchers, medical geneticists, and genetic counselors, as well as many workers in adjacent, corporate, or operational roles in firms developing lab equipment and software, performing clinical genetics and genomics testing, or manufacturing pharmacogenomic drugs. Moreover, the analysis determined that the US human genetics and genomics domain supported an additional 684,000 jobs (indirect and induced effects) within the US economy for a total employment impact of more than 850,000 workers. Nearly 63,000 of those jobs were at medical testing/diagnostics companies. While these talented scientists and professionals may not be able to patent naturally-occurring entities and associations, many patents applying to novel innovations and approaches are filed on a regular basis, protecting the critical IP that was developed with hard work and insight.

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[38] Concert Genetics, "The Genetic Test Unit *GTU) -- A unique identifier for every genetic test, accessible royalty-free by all." 2021. http://www.concertgenetics.com/wp-content/uploads/2021/06/Concert-Genetic-Testing-Unit-GTU-Unique-Test-Identifier-Whitepaper-June-2021.pdf

[39] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[40] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.

[41] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.

[42] American Society of Human Genetics, "The Economic Impact and Functional Applications of Human Genetics and Genomics." May 2021 https://www.ashg.org/wp-content/uploads/2021/05/ASHG-TEConomy-Impact-Report-Final.pdf. Accessed August 19, 2021

Taken together, **we find that the current state of patent eligibility jurisprudence in the United States has had an extremely positive impact on the state of innovation, research, and the US economy, especially since the relatively-recent decisions made in *Myriad*, *Mayo*, and *Alice***. The field has come a long way -- Past AMP President, Dr. Margaret Gulley, recently recalled the term "molecular pathologist" being laughed at a pathology conference in 1989.[43] Even with all these developments, however, the field of molecular pathology is still nascent and should be strongly supported to ensure that this positive growth continues. The ability of our members to develop and offer these groundbreaking tests for patients is built upon the current patent eligibility jurisprudence and we fear that attempts to widen patent eligibility to include laws of nature and natural phenomena would have drastic repercussions, both for our members and the patients they serve. AMP members, who were recently described as "invisible" heroes at the front lines of pandemic response[44], continue to be inspired and eager to make a difference. AMP is confident that their work will continue to significantly impact the economy, but more importantly, the lives of patients, provided their work is not blocked by drastic changes to patent eligibility jurisprudence.

As the USPTO continues its efforts to evaluate how current patent eligibility jurisprudence has impacted investment and innovation, AMP members are pleased to be a resource. If you have any questions or wish to discuss the information provided, please contact Tara Burke at tbuke@amp.org. Thank you for your consideration of these comments.

Sincerely,

Mary Steele Williams, MNA, MT(ASCP)SM, CAE
Executive Director, Association for Molecular Pathology

[43] https://www.amp.org/about/who-we-are/25-years-of-innovation/
[44] https://www.nytimes.com/2020/12/03/health/coronavirus-testing-labs-workers.html