



ASSOCIATION FOR MOLECULAR PATHOLOGY

Providing global expertise in molecular testing that drives patient care
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January 19, 2024

The Honorable Bill Cassidy
Ranking Member, Senate Committee on
Health, Education, Labor, and Pensions
455 Dirksen Senate Office Building
Washington, DC 20510

Re: Request for information from Stakeholders on Improving Americans' Access to Gene Therapies

Submitted electronically at GeneTherapyCoverage@help.senate.gov

Dear Senator Cassidy,

On behalf of the Association for Molecular Pathology (AMP), we thank you for the opportunity to provide input to you and your colleagues on the Health, Education, Labor, and Pensions Committee as you explore ways to improve and protect access to gene therapies for Americans with ultra-rare diseases. AMP is an international medical and professional association representing approximately 2,900 physicians, doctoral scientists, and medical laboratory scientists (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 medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry.

We are pleased that you intend to consider policy that ensures access to potential life-saving gene therapies and we are grateful for the opportunity to provide input for your consideration. We provide the following comments below in response to questions relevant to our expertise and to raise related policy issues that may impact your efforts.

How Do Physicians Provide Access to These Therapies?

How does a physician or health system initiate the process of prescribing a patient with an ultra-rare disease or disorder one of these therapies?

The first step to treating a patient with an ultra-rare disease or disorder is obtaining an accurate and timely diagnosis. The absence of a timely or correct diagnosis may have detrimental consequences for both the patient and relatives. Importantly, any delay in diagnosis will often lead to worsening of the disease condition and lack of proper treatment and support. Clinical laboratory testing is often used by healthcare providers to efficiently establish a diagnosis and enable the identification of treatments or therapies most likely to succeed. A pivotal component of this assessment is genetic testing as it is estimated that 80% of rare diseases are genetic in origin. As you understand, these tests are performed by highly trained laboratory professionals in clinical laboratories across the country.

Pathologists and laboratory professionals use their education, training, and deep expertise to develop novel, high quality, molecular pathology testing procedures in an effort to define the disease at a genetic level or by alterations in biochemical pathways. This will further support clinical decision-making and inform patient care across numerous medical specialties including, but not limited to, gene-based therapeutical approaches approved by medical agencies or in clinical trials.

One model example that highlights the importance of clinical genetic testing in the context of ultra-rare disorders and potential implications for gene therapies is Canavan disease. This is a rare “gene-linked neurological disorder in which the brain degenerates into spongy tissue riddled with microscopic fluid-filled spaces” according to the National Institutes of Health (NIH).¹ The disease develops when a child inherits two genetically altered copies of the *ASPA* gene,² leading to a deficiency of an essential enzyme (*ASPA*) and resulting in the progressive deterioration of white matter in the brain (demyelination). Children with Canavan disease present in early childhood with neurodevelopmental impairments, lack head control, reduced visual responsiveness and abnormal muscle tone such as stiffness or floppiness.³ Over time, children can also experience seizures, become paralyzed, blind, and deaf. 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 Canavan disease and 100 other inheritable autosomal recessive and X-linked conditions.⁴ The prognosis for Canavan disease is poor, with a life expectancy around 10 years of age. While, at present, there is no cure, technological advances in genetic and clinical screening are allowing accurate and more prompt diagnoses and thus access treatments to help alleviate symptoms and improve their quality of life.⁵ Novel treatment approaches such as gene therapy are actively being investigated in clinical trials with promising preliminary clinical data including improvement in myelination as well as positive trends in motor and functional outcomes^{6,7}. Notably, in this context, early diagnosis would be an important component for therapeutic intervention as to allow implementation prior to irreversible impairment ensues.

What is the Future of Access for These Therapies?

What is the appropriate role of the federal government in ensuring access to these therapies in the commercial market? How can any steps be taken on the federal level ensure expanded access while not hurting innovation in this area?

Maintaining Broad Access to the Human Genome

It is imperative that the federal government continue to ensure that policy supports the development and availability of biomarker testing, including genetic testing for all patients and encompassing those with rare and ultra rare diseases or conditions. Today, we are fortunate to have an environment where molecular professionals and pathologists are not restricted by the existence of patents on

¹ <https://www.ninds.nih.gov/Disorders/All-Disorders/Canavan-Disease-Information-Page>

² <https://rarediseases.info.nih.gov/diseases/5984/canavan-disease>

³ https://www.canavanfoundation.org/about_canavan_disease

⁴ 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

⁵ <https://www.huntershope.org/family-care/leukodystrophies/canavan-disease/>

⁶ <https://clinicaltrials.gov/study/NCT04998396>

⁷ <https://clinicaltrials.gov/study/NCT04833907?term=NCT04833907%20&rank=1>

naturally occurring genetic sequences and their association to diseases and health conditions. This is in part because in 2013, the Supreme Court decided unanimously in the *Association for Molecular Pathology v. Myriad Genetics (AMP v. Myriad)* suit which argued that naturally occurring DNA, including when isolated from the body, is a product of nature and therefore not patent eligible. However, this has not always been the case; over a decade ago, patents on genetic sequences and their association with diseases and health conditions were enormously disruptive to patient care. We raise this issue, and the following examples, of how patents can restrict care for those with rare diseases because, if enacted, **the Patent Eligibility Restoration Act (S. 2140) would restrict the ability to develop and perform genetic testing in the United States.** The legislation would effectively abrogate 150 years of judicial decision on patent eligibility, including important court cases like *AMP v. Myriad*, and would once again allow patents on DNA and its association with health status. We are deeply concerned that this legislation, if enacted, would run counter to your efforts by creating monopolies on genetic and genomic testing and research, restricting access to care, and dramatically driving up healthcare costs.

To illustrate the disruption that patents on human DNA have previously had on patient care, we bring up again the *ASPA* gene associated with the aforementioned Canavan disease. Historically, the *ASPA* was patented and, in the 1990s, the patent holder sent “cease and desist” letters to laboratories and hospitals informing them that they would have to license access to the sequence the gene or risk an infringement lawsuit. Dr. Debra Leonard, a renowned molecular pathologist, was the recipient of one letter which indicated that the patent holder would charge \$12.50 per test in royalty fees and warned that volume limitations would likely be placed on her institution.⁸ Unfortunately, Dr. Leonard and many other institutions were forced to stop offering testing for Canavan disease at that time.⁹ The Canavan disease community found this narrowing of access to affordable testing problematic and, in an effort to mitigate the harms of patent on the gene, 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. The controversy ultimately culminated in a lawsuit filed against the patent holder and, fortunately, the United States District Court for the Southern District of Florida concluded that the patent holder enriched itself at the expense of the patients and families who had donated tissue that aided in research for Canavan disease.¹⁰ Because of the 2013 *AMP v. Myriad* ruling that prohibited patents on genetic sequences, there are now over a hundred tests for Canavan disease and many other genetic diseases being performed in many CLIA-certified laboratories in the United States, giving patients widespread access to genetic testing from many different providers.

It is also important to emphasize that testing for genes relevant to rare and ultra-rare diseases is now often incorporated into more comprehensive testing, thus offering patients a single, broad, symptom-based approach for diagnosis of heritable conditions. This is a critical advancement as many diseases may present with overlapping signs and symptoms and benefit from upfront comprehensive testing rather than numerous tests that are piecemealed and add to overall cost of testing. For instance, whole exome and genome sequencing (WES/WGS) evaluates tens of thousands of genes

⁸ Terry M. Storming the Molecular Diagnostic IP Fortress. *Biotechnol Healthc.* 2006;3(1):49. /pmc/articles/PMC3571035/.

⁹ 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

¹⁰ 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/>

that encode for proteins or the full human genome. 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 that can be associated with a large number of different genes, and/or 4) the patient needs immediate critical care. Prior to important cases like *AMP v. Myriad*, WES/WGS would not be possible as it would have required for a laboratory to obtain a license for every patent that existed on genes in the human genome. Instead of promoting an environment for growth and innovation, patents on genetic information siloed testing, increased the cost of testing, and inhibited patient access to more comprehensive testing options.

Importantly, not only does WES/WGS allow molecular professionals to evaluate whether the underlying reasons for a patient's symptoms can be attributed to known pathogenic or likely pathogenic DNA sequence alterations, the results of genomic sequencing analysis sometimes implicate new genes and genetic alterations that have not been previously associated with a disease.¹¹ Using this information, molecular professionals share data via public databases such as the National Institutes of Health's ClinVar and work to improve testing and interpretation of findings. 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."¹² Additionally, AMP has recently released a 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.¹³ 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 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." If Congress were to advance legislation that would allow patents on laws and products of nature, such as associations between biomarkers and health status, this type of data sharing would come to a standstill, dramatically slowing the pace of precision medicine research, not only in the development of diagnostics, but also for development of curative therapies for ultra-rare disorders that are based on the underlying genetic cause of the disease.

Given that any gene therapy requires the confirmation of an accurate diagnosis first, we are greatly concerned that efforts like the Patent Eligibility Restoration Act would undermine all of the advances that have been made in developing successful interventions and therapies for patients with ultra-rare disorders. As you know, late last year the Food and Drug Administration (FDA) authorized two new gene therapies for the treatment of sickle cell disorder, an inherited condition caused by a mutation in the gene encoding for hemoglobin.¹⁴ Had someone patented the sequence of that gene, then the

¹¹ As one example, see <https://www.wired.com/story/one-scientists-quest-to-bring-dna-sequencing-to-every-sick-kid/>

¹² 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>

¹³ 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

¹⁴ <https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease>

patent holder could have charged exorbitant licensing fees or restricted access not only to test for the mutation, but also to conduct the very research that led to these groundbreaking and novel treatments.

We have made so much progress in precision medicine since the *AMP v Myriad* decision in 2013¹⁵ and for these reasons, we urge Congress to protect the current state of subject matter eligibility. As you consider policy to expand access to gene therapies, we encourage you to work with your Senate colleagues to make sure that legislation on patent eligibility does not impede the research and development of this emerging innovative therapeutic approaches.

Thank you again for the opportunity to submit these comments to help improve American's access to gene therapies. If AMP may be of further assistance, please do not hesitate to contact Annie Scrimenti, Associate Director of Public Policy and Advocacy at ascrimenti@amp.org.

Sincerely,

Maria E. Arcila, M.D.
President, Association for Molecular Pathology