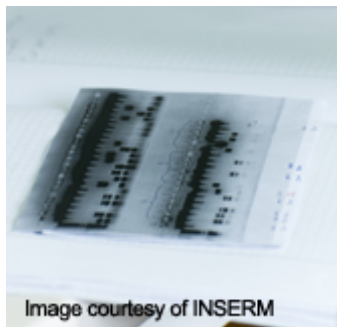


Spotlight on...

Patently controversial: licensing, genes, diagnostics and research

Do gene patents ultimately help or hinder diagnostics and research for rare disorders?



In mid-October, *OrphaNews Europe* spoke with Deborah Heine, creator of the Claire Altman Heine Foundation, a non-profit, publicly-supported charity created in memory of daughter Claire, who died of spinal muscular atrophy type 1 (SMA1) at the age of nine months. Spinal muscular atrophies represent a group of neuromuscular disorders characterised by progressive muscle weakness resulting from the degeneration and loss of the lower motor neurons in the spinal cord and the brain stem nuclei. Around 95% of cases are caused by homozygous deletions in the *SMN1* gene encoding the SMN (survival motor neuron) protein.

The Claire Altman Heine Foundation ([CAHF](#)) dedicates a large part of its energy and funding toward establishing pan-ethnic population carrier screening for SMA that would allow couples to know the risk of giving birth to an affected child and take an appropriate decision. This goal, however, is hindered by a co-exclusive license agreement for the *SMN1* gene, which, Ms. Heine, a lawyer, says seriously hampers access to carrier screening and diagnostics for SMA. Ms. Heine contends that the licensing arrangement between the patent holder of the *SMN1* gene and the licensee(s) is also negatively impacting other forms of potential research involving the *SMN1* gene. A [position paper](#) available on the CAHF website acknowledges that it is not the patent itself that is causing the problem but “*rather how the patent is being used and enforced, resulting in a barrier to clinical access for SMA carrier screening.*” Presently, only two laboratories (in the USA) conduct carrier screening for SMA. No other laboratories or laboratory testing kit manufacturers have been granted licenses. The position paper delineates the detrimental effects of exclusivity in gene licensing for SMA screening and diagnostic testing:

- Causes labs that might have offered SMA carrier screening to avoid offering these services thus limiting clinical access to testing
- Results in a lack of competition and incentive to improve testing services
- Eliminates competition for pricing

- Leaves no opportunity for independent confirmation of a test result (i.e. second opinion or full gene sequencing when needed)
- Dictates and limits clinical access to both physician and patient
- Limits education of medical students and residents due to lack of exposure of patented material
- Limits the ability to use multiplex arrays, gene chips and other emerging technologies
- Hinders scientific and medical advancement of the field and diminishes accrual of knowledge about the molecular basis of the disease (by greatly reducing the number of laboratories with access to the gene)
- Compromises quality assurance because the regular nationwide programs for proficiency testing (CAP/ACMG) are not interested in setting up these programs for a single customer

The complex issue of genetic diagnostic testing patents and licensing is fraught with contention. In March of this year, the United States Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) issued a call for comments on a comprehensive study entitled [Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests](#) (see the 29 April 2009 issue of [OrphaNews Europe](#) for a summary of the contents of the draft paper). Last month the SACGHS held a task force meeting to discuss both the draft report and the comments culled during the public consultation period. An article appearing in [GenomeWeb News](#) reports that the five-year investigation based on studies, case files and the public comments received during the consultation period, has concluded that gene patents may not facilitate innovation, and in fact, may hinder innovation by restricting genetic test utilisation and rendering difficult the process of accessing information for a patented gene or using it for research purposes.

The opinion submitted by the CAHF on the draft paper reflects the frustration and sense of injustice the current patenting and licensing system can incur. The CAHF opinion recounts the particularities of the patent for the *SMN1* gene:

In the case of SMA, the patent holder did not even bear the financial burden of the discovery, rather an advocacy group and patients and families suffering from the disease donated funds and tissue samples to a researcher who then patented her discovery and sold it. The cost of gene discovery was born by patients and families suffering from the disease (a group truly motivated for innovation) and the "rewards" of their investment are not returning to them. Instead, patients and families affected by SMA are at the mercy of the patent holder. This is the case in many gene patents (familiar example, Canavan Disease).

Based on testimony such as this, the task force analysis of the report finds that *"In the realm of therapeutics, strong arguments can be made that patents enable innovation, drive progress and serve an important role"*. However, *"In the realm of diagnostics, patent-enabled exclusivity primarily results in a narrowing of offerings to patients and physicians"*.

A presentation of the final draft report and recommendations from the Chair of the SACGHS Task Force on Gene Patents and Licensing Practices, James P. Evans, MD, includes two critical recommendations culled from the findings:

The creation of an exemption from liability for infringement of patent claims on genes for anyone making, using, ordering, offering for sale, or selling a test developed under the patent for patient care purposes"; and

The creation of an exemption from patent infringement liability for those who use patent-protected genes in the pursuit of research. Related health care and research entities also should be covered by this exemption.

The task force also issued the recommendation to “discourage the seeking, the granting, and the invoking of simple association patent claims” and counsels the development of “mechanisms to promote voluntary adherence to the principles reflected in NIH’s Best Practices for the Licensing of Genomic Inventions; the Organisation for Economic Co-Operation and Development’s (OECD) [Guidelines for Licensing of Genetic Inventions](#); the NIH Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-wide Association Studies; and In the Public Interest: Nine Points to Consider in Licensing University Technology”.

The recommendation goes on to advise that the US Secretary of Health and Human Services “should also advocate that professional organizations involved in intellectual property policy and practice in this area work together to build on those norms and practices as they relate to gene-based diagnostics by articulating more specific conditions under which exclusive licensing and nonexclusive licensing of uses relevant to genetic testing are appropriate. Professional societies should work cooperatively to forge consensus positions with respect to gene patenting and licensing policies”.

Dr. Evans cites the public comment of a laboratory director who observes that “Patents on genes associated with rare diseases may discourage investment”.



These observations and recommendations echo earlier findings by the European Society of Human Genetics ([ESHG](#)). As was reported in the 30 April 2008 issue of [OrphaNews Europe](#), the ESHG last year issued a set of recommendations for genetic testing patenting and licensing that seeks to encourage fairness and ultimately improve service provision to patients. The recommendations limit patent attribution in certain areas of genetic testing by limiting the patentable subject matter. As with the SACGHS recommendations, the ESHG evokes the guidance issued by the Organisation for Economic Cooperation and Development, which discourage license exclusivity and promotes practical and financial access to licensing. The ESHG recommendations were published in the *European Journal of Human Genetics*. ([Consult the PubMed abstract](#)).

The SACGHS task force recommendations are not unanimously endorsed, however. The

Biotechnology Industry Organization (BIO), the world's largest biotechnology organisation with more than 1,200 members in over 30 countries, qualified the proposed SACGHS policies as “*over-reaching*” and “*restrictive*”. The BIO strongly disagrees with the conclusions the task force drew from its findings, and in a published [statement](#) argues that the task force recommendations would “*do more harm to patients than good, particularly the patients of tomorrow who are relying on biotech innovation to bring the promises of personalized medicine to reality*”. In reference to rare disorder testing and research, the BIO statement observes that “*...some of the Committee's own findings and case studies show how patenting and exclusive licensing practices can, indeed, be necessary to foster the development of these valuable tests for patients, particularly those with rare disorders, and that they have other positive impacts – such as incentives to promote physician and patient education, broader insurance coverage, and improved compliance*”.

Furthermore, *GenomeWeb News* reported that a “*particularly scathing critique*” was made by Brian Stanton, a molecular oncologist and ad hoc member of the SACGHS task force who formerly served as Director of Policy for the NIH's Office of Technology Transfer and as a Practice Specialist for the United States Patent and Trademark Office. In a letter of dissent, Stanton accused the draft report of being “*based on flawed assumptions*” and that “*...the data demonstrates no evidence that intellectual property laws or licensing practices are the cause of general harm, a lack of technology development, or any systemic lack of public access to genetic testing,*” according to the *GenomeWeb News* report.

Meanwhile, new research brings fresh information to the debate. In the October issue of *Nature Biotechnology*, the article *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, describes the analysis of the patents for 22 molecular diagnostic tests for monogenetic disorders (fragile X; cystic fibrosis; familial breast and ovary cancer; hereditary hemochromatosis; factor V Leiden thrombophilia; factor II thrombophilia; beta thalassemia; hereditary nonpolyposis colon cancer; Prader-Willi syndrome; Angelman syndrome; Charcot-Marie-Tooth neuropathy; myotonic dystrophy; GJB2-related hereditary hearing loss and deafness; Duchenne muscular dystrophy; Huntington disease; spinocerebellar ataxia; spinal muscular atrophy; familial adenomatous polyposis; attenuated familial adenomatous polyposis; facioscapulohumeral muscular dystrophy; Friedreich ataxia; and Rett syndrome). This study ultimately demonstrates that, while there is not a widespread problem of patent thickets (defined as “*overlapping set(s) of patent rights requiring that those seeking to commercialise new technology obtain licenses from multiple patentees*”) in genetic diagnostics, there is “*a problem of lack of transparency and clarity, leading to legal uncertainty.*” The study reveals that while there are fewer claims on genes than has been indicated, questions of legal uncertainty abound. For genetic diagnostic testing, seven of the 22 diseases are covered by patents (granted and/or applications) in Europe, whereas in the USA 12 of the 22 diseases are covered by granted patents or pending patent applications.

In the USA, “*most genetic diagnostic patents are exclusively licensed out to Athena Diagnostics*”, the laboratory that holds a license for the diagnostic test for SMA, and which according to the CAHF, “*significantly limits clinical access to testing*”.

The authors of the *Nature Biotechnology* study observe that proposals that seek to ban patents on human genes are not useful since not many gene patent thickets exist. However, a ban on patents for “*broad genetic diagnostic methods as such*” could be useful. The authors recall the ESHG recommendation to avoid “*patenting of the pure link between a mutation and disease*” and call for ‘responsible’ licensing practices, cautioning that, “*...Otherwise, the risk*

exists that the control by owners of patents containing those broad claims with respect to genetic diagnostic testing may in the future dissociate actual genetic diagnostic testing from genetic counselling and clinical investigation, which is to the detriment of progress of the genetic diagnostic service and public healthcare system”.

Though they seem to be coming from opposite poles, at the end of the day, the common ground between the various stakeholders is that they all want a similar end result: quality innovation that pushes the envelope of research. Biotechnology firms want the financial freedom and incentive to create products and services that foster further discovery. Patients and their caregivers want affordable access to this quality innovation. Non-profit watchdogs such as the SACGHS and the ESHG want to see innovation go forward fairly, with best practices employed, quality assured, and access guaranteed. How to tweak the patent system to best achieve these overlapping goals? Can gene patenting for diagnostics work for all interested parties: innovators who want to be rewarded for their efforts; patients and medical professionals who need access to the fruits of this labour for screening and diagnostic purposes; and other researchers who want to further the momentum of discovery? In their comments directed to the SACGHS draft paper, the CAHF observes: *“The current patent system is jeopardizing the benefits of years of collective discovery and research and adversely affecting the populations that were meant to be assisted and served. ... Change is needed now.”* How such change is to be accomplished so all sides benefit urgently needs to be determined. The BIO urges caution in issuing recommendations to change long-established policies, especially *“in the context of biotechnology ... which promises solutions to so many of the world’s gravest human and environmental challenges”*. The question remains: can the current genetic diagnostics patent and licensing system be modified in a way that will please all stakeholders?