VIEWPOINT

Governing Human Germline Editing Through Patent Law

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In the wake of the heritable human genome editing (HHGE) experiments carried out by He Jiankui in China,[1] widely condemned as unethical and scientifically ill grounded, attention has shifted to questions concerning hard law and regulation. The World Health Organization (WHO) recently released a report along with several auxiliary documents exploring international governance tools for human genome engineering.[2] However, as long as such governance occurs only at the national legal level, the possibility of medical tourism to circumvent domestic prohibitions remains a risk.

The risk is not merely theoretical. As with the case of mitochondrial replacement techniques, patients have left their home country for seemingly more permissive regimes in Greece, Spain, Mexico, and Ukraine to access such therapy.[3] The 2019 announcement of possibly establishing a germline-editing clinic in Russia is a case in point.[4] One solution would be an approach like an international treaty on genome editing. But the most recent report from the WHO did not pursue that avenue.

Instead, the WHO largely relied on national implementation of governance tools to provide a translational pathway for potential HHGE uses as well as a way to publicly disclose and report on uses that deviate from established guidelines.[2] Even though these proposed mechanisms are important, nations should also give more attention to another underappreciated governance tool emphasized in the WHO report—patent law as a governance instrument.

> Even though patents are not a perfect solution to the ethical challenges of germline editing, they are a useful supplement to many of the approaches currently available, especially given fractured international regulation.

Patents constitute rights to exclude others from practicing the particular technology claimed in a patent. This includes the right to stop others from using the patent holder's technology in a way the holder finds objectionable. The power of patents to regulate HHGE lies in their use in infringement lawsuits. A successful assertion of a patent infringement suit may result in a court order against the infringer so as to stop the objectionable activity in question (often called an injunction) or financial penalties, some of which can be quite severe.

To avoid infringement, a party must secure a license, essentially getting permission from the patent holder to practice the technology under a set of agreed upon terms. Because a patent holder can impose licensing restrictions as it sees fit, the patent holder can include ethical restrictions on using the technology as a condition of the license.[5] That is, unless the licensee practices the patented technology in an ethical manner, the licensee may be viewed as an infringer and can therefore be sued accordingly.

In this way, patents can be used as an instrument of ethical governance for HHGE, albeit by the patent holder not by the government. Ethical licensing restrictions are already being used by the Broad Institute of MIT and Harvard University, among others, for some applications concerning the genome-editing technology of clustered regularly interspersed short pandemic repeats (CRISPR), including some facets of using CRISPR for human germline editing. These include a prohibition on using CRISPR for gene drive technology and oversight for the editing of certain genes.

This is a particularly important moment to consider "ethical governance by patent." In the US, there exists a growing movement to patent HHGE technology. In May 2021, a researcher at the Oregon Health & Science University (OHSU) filed for a patent disclosing methods of "correcting a mutant allele of a gene of interest in a primate cell" that include HHGE.[6] Earlier, in April 2021, another researcher at Columbia University filed for a patent covering "using CRISPR-based methods to perform gene editing to correct frame shift mutations" in embryos.[7] If granted, these patents would afford these researchers and their institutions significant power over the ethical limits of using such technologies. For institutions committed to the ethical use of these technologies, it is essential to build that element into the patent licensing process.

Although this solution will work in the US, this may not hold true for many other countries. Other nations refuse to issue patents on controversial technologies because, in the specific language of the European Patent Office, these patents would violate the *ordre public*, the prohibition on patents for technologies that "offend human dignity." Importantly, this policy does nothing to prevent the unethical uses of technology, and indeed, absent patents, allows anyone in such a jurisdiction to use the technology as they see fit, at least without fear of patent infringement. This includes unethical uses. The *ordre public* limitation, and others like it, limit ethical governance by patent.

Extricating patents from this important societal role is especially significant in places with unified patent standards but divergent regulatory mechanisms, like Europe. The Czech Republic, for example, grants patents under the rules of the European Patent Convention—that is, it cannot issue patents on germline editing—but has

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a permissive regulatory approach to in vitro fertilization–based technologies, like HHGE. In that country, patents cannot be used meaningfully to curb germline editing should the Czech Republic wish to rely on such a mechanism.

The US, meanwhile, allows such patents but largely bans practicing the technology. This ultimately encourages HHGE technology development in the US (as with patent applications by the researchers at OHSU and Columbia University) but risks medical tourism elsewhere in a manner analogous to that for mitochondrial replacement technology. Patents, used judiciously and well, could get around this absence of harmonized reproductive standards, analogous, perhaps, to an ethical "patent thicket" around human genome editing.

To be sure, using patents as ethical tools for HHGE governance has its limits. This approach relies on private enforcement to bear the costs and vigilance of policing the social harms of what is largely a private activity. Patents also allow private entities, such as research institutions, to set the limits of social policy. This, too, is undemocratic: why should patent holders above all others be able to determine which germline editing procedures are or are not objectionable? Ethical governance by patent could be viewed as an additional approach for regulators to use.

Even if not a panacea, governance by patent may fill some missing gaps in current regulatory approaches, such as the difficulty or unwillingness to police "circumvention tourism" wherein a patient travels abroad for something that is unavailable at home. This approach may also allow for a nimbler response to changing conditions than legislation, which can be especially controversial in this area. It is also true that patents are limited in time; they expire 20 years from when they are filed, making them a depreciating if not decaying governance tool. But perhaps this is a feature and not a flaw; society may think differently about germline editing 20 years from now and most likely will know more about its safety.

Even though patents are not a perfect solution to the ethical challenges of germline editing, they are a useful supplement to many of the approaches currently available, especially given fractured international regulation. Policy makers, and the European Patent Organization, in particular, should consider eliminating the *ordre public* exception, which has not been especially effective in prohibiting unethical research or commercialization of novel technologies, whether human germline editing or otherwise.

Notably, no international patent treaties, which govern harmonization, require such a clause. Ethical patent licensing standards could similarly guide patent holders toward ethical restrictions on their technologies. There are currently some models in existence for CRISPR, but they could easily go further and be more detailed.

Patents present an opportunity to combine the tools of commercialization and ethical behavior in a manner not readily present in other fields. It is an opportunity that should not be wasted; the perfect should not be the enemy of the good.

ARTICLE INFORMATION

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