CRISPR-CAS9: DESIGNING LAW FOR DESIGNER BABIES

Written by ***Ritwik Prakash Srivastava***

** 2nd Year BA LLB (Hons.) Student, National Law Institute University Bhopal*

The recent years have seen a tremendous advancement in the field of biotechnology. From diagnosing cancer by spit tests[1], to nerve regenerating nano-gels[2], to smart contact lenses helping to administer glaucoma[3], to portable dialysis machines[4], to rocket-powered arms[5]. The list of discoveries and inventions is virtually limitless and ever-expanding. One such technology termed CRISPR-Cas9[6], a gene editing tool, brings with it unique ethical, moral and legal problems. CRISPR[7] enables scientists to alter, delete and/or reposition the genetic material or the DNA of any living organism. The discovery of CRISPR has been widely celebrated and for good measure. The technology has shown promise helping scientists treat mutation[8] and successfully edit genomes[9]. This involves in its study alive subject mattes and

[1] Wong, D.T., 2008. Salivary Diagnostics: Amazing as it might seem, doctors can detect and monitor diseases using molecules found in a sample of spit. *American scientist*, *96*(1), p.37.

[2] Mohanna, P.N., Young, R.C., Wiberg, M. and Terenghi, G., 2003. A composite poly-hydroxybutyrate–glial growth factor conduit for long nerve gap repairs. *Journal of anatomy*, *203*(6), pp.553-565.

[3] Leonardi, M., Pitchon, E.M., Bertsch, A., Renaud, P. and Mermoud, A., 2009. Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes. *Acta ophthalmologica*, *87*(4), pp.433-437.

[4] Plahey, K., Hedmann, F., Klatte, S. and Folden, T., Fresenius Medical Care Holdings Inc, 2006. *Portable apparatus for peritoneal dialysis therapy*. U.S. Patent Application 11/069,195.

[5]Available at https://news.vanderbilt.edu/2007/08/20/rocket-powered-mechanical-arm-could-revolutionize-prosthetics-58519/

[6] Doudna, J.A. and Charpentier, E., 2014. The new frontier of genome engineering with CRISPR-Cas9. *Science*, *346*(6213), p.1258096.

[7] Short for or Clustered Regularly Interspaced Short Palindromic Repeats. See Hwang, W.Y., Fu, Y., Reyon, D., Maeder, M.L., Tsai, S.Q., Sander, J.D., Peterson, R.T., Yeh, J.J. and Joung, J.K., 2013. Efficient genome editing in zebrafish using a CRISPR-Cas system. *Nature biotechnology*, *31*(3), p.227.

[8] Available at https://www.vox.com/science-and-health/2017/8/2/16083300/crispr-heart-disease

[9] Shen, B., Zhang, W., Zhang, J., Zhou, J., Wang, J., Chen, L., Wang, L., Hodgkins, A., Iyer, V., Huang, X. and Skarnes, W.C., 2014. Efficient genome modification by CRISPR-Cas9 nickase with minimal off-target effects. *Nature methods*, *11*(4), p.399.

inevitably, the alteration of genetic identity of an organism. Such alteration is capable of profound impact on humans, plants or animals, their lives and/or the environment. In layman terms, this makes it possible to design babies, giving them desired traits like 20/20 vision and a higher IQ.[10] This arises fundamental questions of ethics and morality.[11] Thus utmost care and caution must be exercised in dealing with and examining such inventions to ensure that their utility, in no way, causes a disruption of public order or morality, or inflicts any harm to the humans, plants, animals or the environment.[12]

Thus, the patentability and its eventual application on human genes needs to be put under the legal microscope. In the international landscape, the patent is being famously contested between two parties. The first contention is by Jennifer Doudna, at the University of California, Berkeley (UC Berkeley), and Emmanuelle Charpentier.[13] The second comes from Feng Zhang of MIT, which claims a priority date of December 12 2012, and has already been issued.[14] The framing of the patent granted to Zhang is quite broad, thus it overlaps with the newer and more efficient methods developed by UCB. If the latter wins, then Zhang's patent would be invalidated without there being any guarantee of the former's patent being granted. However, if the latter lose, then they walk away empty-handed. In any case, due to the scope of biotechnology, if the patent is allowed to move forward, even the most preliminary alteration of gene would invoke the licence. This would therefore put restrictions on academic research on the subject, its clinical use and hamper further advancement.[15] The scope of the patent itself is immense and can easily be commercially exploited. The technique is aimed at editing human genetics. This leaves the field open for even tweaking hereditary carriers and essentially editing the embryo to bring about artificial or designer babies.[16] The motivation of such

[10] Fogleman, S., Santana, C., Bishop, C., Miller, A. and Capco, D.G., 2016. CRISPR/Cas9 and mitochondrial gene replacement therapy: promising techniques and ethical considerations. *American journal of stem cells*, *5*(2), p.39.

[11] V.R. Potter, *Evolving ethical concepts*, 27 BIOSCIENCE 251, 251-253 (1997).

[12] Rule 10, *Guidelines for Examination of Biotechnology Applications for Patent*, Office of the Controller General of Patents, Designs and Trade Marks, Government of India (2013).

[13] Jinek, M. et al. US Patent Application No. PCT/ US2013/032589 (2013).

[14] Zhang, F. US Patent No. 8,697,359 (2014)

[15] 35 USC § 271(e) (2012)

[16] Quintavalle (on behalf of Comment on Reproductive Ethics) v. Human Fertilisation and Embryology Authority, [2005] 2 AC 561.

predetermination is often absolutely unrelated to the health of the child and is a consequence of cosmetic desires.[17] Such genetic modification is a serious ethical violation. It is only by the accidental nature of our genetic make-up that we can 'grow from nature' and live autonomously.[18] Moreover, trials of similar germ line gene editing techniques show that almost always, unintended changes were made to large segments of the genome.[19]

CRISPR, as described, is a technique for germ line gene editing. In accordance with the provisions[20] given in a Directive of the European Union on biotechnological inventions[21], processes for modifying the germ line genetic identity of humans are not patentable. The Directive conforms to the TRIPS agreement[22] to which all WTO members are party.[23] Before such a technology is put to medicinal use, it will have to test to be fit for human consumption. This would have to be done through clinical trials. However, should such a situation arise it would put the subjects thereby selected to be experimented upon under serious prejudice danger for as much as biotechnology is promising, it is unpredictable.[24] There have been numerous problems reported in the test phases of the technique and its equivalent international counterparts like CRISPR/Cas9 like cleaving of unintended DNA strands,[25,26] problems with efficient delivery into cell types.[27] The international science community therefore does not see this technology as developed enough for any clinical use in making inheritable changes to humans.[28]

[17] AB and Another v. Minister of Social Development, [2016] ZACC 43.
[18] Jonathan Pugh, *Autonomy, natality and freedom: A liberal re-examination of Habermas in the enhancement debate*, 3 BIOETHICS 29 145,, 145-152 (2014).
[19] Christopher Gyngell et al., *The Ethics of Germline Gene Editing*, 34 J. OF APP. PHIL. 498, (2017)
[20] Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological inventions art. 6 (1) (b), Jul. 3, 1998.
[21] Id. 27.
[22] TRIPS: Agreement on Trade-Related Aspects of Intellectual Property Rights art. 27, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299, 33 I.L.M. 1197 (1994) [hereinafter TRIPS Agreement].
[23] Available at http://www.wipo.int/wipolex/en/other_treaties/parties.jsp?treaty_id=231&group_id=22
[24] Ledford, H., 2017. CRISPR studies muddy results of older gene research. *Nature News*.

[25]Y. Fu et al., *High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells*, 31 NAT. BIOTECHNOL. 822, 822-826 (2013).
[26] X.H. Zhang et al., *Off-target Effects in CRISPR/Cas9-mediated Genome Engineering*, 4 MOL. THERAPHY-NUCLEIC ACIDS e264, (2015), https://www.sciencedirect.com/science/article/pii/S216225311630049X.
[27] P.D. Hsu et al., *DNA targeting specificity of RNA-guided Cas9 nucleases*, 31 NAT. BIOTECHNOL. 827, 827-832 (2013).
[28] Edward Lanphier et al., *Don't edit the human germ line*, 519 NAT. 410, 410-411 (2015).

In the absence of any codified regulations, Stem Cell Research and Genome Therapy involving human specimen in India is regulated by the Indian Council of Medical Research and Department of Biotechnology through National Guidelines for Stem Cell Research and Ethical Guidelines for Biomedical Research on Human Participants. The framework of regulations is such that it disallows such research.[29] the guidelines laid down in the NGSCR are applicable to all stakeholders including individual researchers, organizations, sponsors, oversight/regulatory committees and all others associated with both basic and clinical research involving any kind of human stem cells and their derivatives.[30] The NGSCR casts a fence around research on genome modification, restricting it only to in-vitro studies, using only spare embryos.[31] The guidelines explicitly ban any other form of research related to human germ line therapy[32] including in-vitro culture of intact human embryos[33] and use of genome modified human embryos, germ line stem cells and gametes for developmental propagation[34] along with research involving implantation of the human embryo[35] under the head of Prohibited Areas of Research.[36] The BRHP (*Ethical Guidelines for Biomedical Research on Human Participants)* states that Germ Line Therapy is prohibited under the present state of knowledge in such areas.[37]

It is hence concluded that the existing jurisprudence, especially in India, lacks significantly when it comes to regulating something like CRISPR-Cas9 and biotechnological practices in general. The current Indian approach, putting a blanket ban on the research of a promising field, puts the Indian scientists and medicine industry in a disadvantageous position as compared to the rest of the world. While at the same time human beings cannot be used like guinea pigs for the experimentation and pleasure of researchers. The law and policy makers need to adopt a contextual approach, balancing scientific progress and the individual rights of citizens. Technology is evolving at a fast pace and law in comparison, is running out of breath.

[29] 8.2.1., *National Guidelines for Stem Cell Research*, Indian Council of Medical Research (2017).
[30] Aims and Scope, supra note 27.
[31] Id. at 8.2.8.
[32] Id. at 8.3.1.
[33] Id. at 8.3.2.
[34] Id. at 8.3.5.
[35] Id. at 8.3.6.
[36] Id. at 8.3.
[37] Therapeutic Trials including Gene Therapy, *Ethical Guidelines for Biomedical Research on Human Participants*, Indian Council of Medical Research (2006).