**STARTING THE CONVERSATION: CRISPR’S ROLE IN INDIA**

**Abstract**: The applications of gene editing technologies such as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) have developed significantly in recent years. Several countries have adopted stances on the regulation of such technology, however India does not have any legally enforceable regulations in place. There is a need for such a development as India’s regulatory, sociocultural, and economic landscape is unique. First, we discuss the uncertainty regarding India’s regulatory capacity to enforce ethical standards for CRISPR use. Then, we discuss unique driving forces that could lead to the misuse of CRISPR in India, such as certain sociocultural norms like preferences for fair skin and public demand for sex determination. Given these previous concerns, we posit the question; where on the priority list does CRISPR stand in the context of public health in India?

**PERSPECTIVE:**

Late in 2018, the world stood by in disbelief as a Chinese scientist reportedly created two genetically engineered human beings using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) gene-editing technology [1]. This development, which was merely just a challenging possibility not so long ago, has led to the resurgence of a host of ethical questions in the scientific community regarding the use of CRISPR, such as those involving off-target effects, access, and regulation [2]. On a global front, the technology has been growing faster than our ability to reach any sort of moral consensus on its use and regulation. The successful genetic modification of human embryos, and now, human beings, has fueled apprehensions that this technology could one day be used to design and pick babies with certain designer character traits. Would it be ethical for parents to customize a baby that could run like Usain Bolt and sing like Beyoncé? While experts discredit these specific applications as being unlikely in the near future, the ability to control for less complex and highly heritable traits, such as skin color and gender, are not [3].

Currently, there are no internationally agreed-upon laws or regulations on gene editing, placing scientific research and application of CRISPR technology under the discretion of individual countries [4]. Although countries like the United States, United Kingdom, Canada, and Germany, have strict rules prohibiting genetic modification of the human germline either experimentally or clinically, other countries like France and Argentina are not as clearly regulated [4, 5]. Only last year did Japan set specific guidelines for use of CRISPR technology and has moved towards furthering research on gene-editing in early human embryo development [6]. As it stands, Indian protocols prohibit human germ-line editing and reproductive cloning, as detailed in the in the National Guidelines for Stem Cell Research by the Indian Council of Medical Research. However, the concerning fact is that these guidelines have not yet been converted into specific laws. [7,8]. This concern was highlighted a few years ago by Japanese bioethicist Tetsuya Ishii, who noted that countries such as China, Japan and India ban genomic editing for clinical use, yet these bans are not legally binding, and are seen as unenforceable due to the immense population and lack of deterrent by criminal law [5]. This, coupled with factors such as the availability of do-it-yourself CRISPR kits and the high number of commercial fertility clinics, have raised red flags because of the potential for misuse and manipulation [5,9].

Based on the management of scientific technology in the past, it is uncertain whether or not the current regulatory landscape in India would be capable of enforcing the regulation of such an immensely powerful technology in a safe and ethical manner. Past developments in genetic technology have been mishandled, demonstrating the capacity (or lack thereof) of India’s regulatory organizations. For example, take the development of genetically modified crops. While the permissibility of these was still being debated in parliament, they were being illegally and prematurely sown in Gujarat in spades due to their perceived profitability [3]. This was largely as a result of corrupt practices in Indian regulatory agencies. In the medical field, India has even gone so far as to ban the clinical use of stem cell therapy due to “rampant malpractice” and the inability to regulate its commercial use [7]. Corruption within such organizations is so rampant that India’s medical administration is said to be one of the most corrupt in the world, with physicians, medical regulatory bodies and even the government playing a part [11].

The Medical Council of India (MCI) and the Indian Medical Association (IMA) have faced numerous scandal regarding bribes for the establishment of ventures and even entire institutions. Efforts to hold them accountable through the legal systems have been null and void due to the backlog of cases and only a small fraction of prosecutions have resulted in legal consequences [12]. Therefore, there is little discouragement against the misuse and manipulation of medical technology for personal or commercial gain. The extensive growth of black markets for human organs and counterfeit medicine in India is the greatest testament to this statement. India’s black market for organs is one of the largest in the world, with hospital administrators, doctors, and even law enforcement officials regularly caught for the procurement and sale of black market organs [13]. This paints an alarming picture of the state of regulation with regard to medical services in India, and raises several concerns when considering the regulation of profitable gene-editing technology.

Translating these discussions into public discourse is of imminent need, as advances in gene-editing technology have already begun to gather momentum. Private companies have already sought to explore the commercial potential of such technology in India and they will surely march forward in due time [10]. On a more positive note, Indian scientists have been making remarkable advancements in research using gene-editing technology on blood disorders like sickle-cell anemia which involves manipulating somatic cell samples from patients [9]. The key question at hand is whether or not research will continue to be conducted in a safe and ethical manner, and this seems dubious without legally enforceable guidelines, and an effective regulatory and legal infrastructure.

The potential for misuse in an Indian context is driven by a number of sociocultural factors intrinsic to the subcontinent. For example, take the all too familiar preference for fair skin in Indian society. The pervasiveness of general concern over skin color is reflected in consumer markets, with the Indian population having spent over $500 million on ‘fairness’ products in 2014 [14]. This sociocultural obsession translates into discrimination against darker skin tones in the professional sphere. In 2012, close to 70% of the surveyed population preferred partners of fairer complexion, and furthermore, many industries including film, hospitality and aviation are marred with cases of active hiring discrimination against applicants with darker complexions [15,16]. To what extent might these preferences take form in healthcare markets if consumers are able to manipulate such characteristics? The demand for these traits definitely exist, and it would not be unreasonable to be concerned over potential future misuse of technologies like CRISPR to meet such a demand.

Perhaps the sociocultural element that merits the greatest consideration is one that the Indian medical profession has been grappling with for centuries. Preferences for male children drive some of the most severe ethical breaches amongst the medical profession. In fact, fairly recent technological advances have been shown to empower such preferences, contributing to the vastly skewed sex ratios observed in many Indian states [17]. The normal sex ratio observed for children is 952 girls per 1000 boys, yet in states such as Haryana it remains as low as 830:1000, and states like Punjab, Delhi, Bihar, Gujarat, Andhra Pradesh and Madhya Pradesh all fall significantly short of the mark [18]. According to public health scholars, the increased availability of ultrasound machines in rural areas coupled with poor to no regulation of sex determination laws are some of the driving factors behind these skewed ratios [19]. This is a worrisome trend that results in adverse effects to the Indian population as a whole, the effects of which have been extensively studied. From an economic perspective, according to a report by McKinsey & Co., India’s GDP could be 60% higher in 2025 if women played the same role in the workforce as men [20]. While there is no doubt that other factors (sexism in the work force, systematic patriarchy, etc.) also contribute to an unequal workforce, skewed sex ratios are not an insignificant driving factor. From a social standpoint, empirical studies have also linked skewed sex ratios to the increased likelihood of violent sexual crimes, specifically human trafficking and sexual abuse [20]. Therefore, we see that we have a moral and economic imperative to safeguard these ratios and prevent unlawful sex selection. Current trends foreshadow the potential for future misuse and misapplication, and the way medical technology has been misused in the past can serve as important lessons. If past and existing medical technology has been misused because of these driving social-cultural factors, it gives us reason to believe that this could be the case with gene-editing technology as well. Therefore, the efficacious and ethical regulation of CRISPR technology must take these factors into considerations.

Finally, given the unique sociocultural, economic and regulatory landscape of India, we must also ask to what degree we are willing to allocate resources towards the development and application of technologies like CRISPR. Furthermore, to what extent might gene-editing technology further pre-existing injustice and inequality? It is unlikely that the substantial proportion of Indians who live in poverty, 363 million to be exact, would be the direct beneficiaries of CRISPR [21]. In a country where the top 1% is responsible for 73% of the country’s wealth and 60% of women do not have access to hospital care when giving birth, can we justify further reallocating valuable and limited resources that will likely benefit only the wealthy few? [22,23]. Should we also not be even more cautious if this technology could one day lead to cognitive or physical genetic enhancement for its beneficiaries? As the Western world gears up to allocate resources towards the development and application of CRISPR technology, we feel developing countries like India must bear caution. A technology should have an evidenced and favorable risk/benefit ratio in order to justify a higher prioritization of resources. Approximately 423,000 Indians die from tuberculosis, 205,000 die from malaria and 105,000 die from diarrhea each year, to name only a few [24,25,26]. Interventions that are effective and cost effective exist, and we feel these should take priority.

The promises of gene-editing technologies are discussed and disseminated to a great degree, and with good reason. They represent very real, tangible opportunities at positively impacting the lives of certain patients with certain diseases. However, it is important not to generalize this potential across societies and nations, but to recognize that each country is unique and has its own narrative. The sociocultural factors discussed above have been weaved together with medical practice in India for decades, despite best attempts at regulation. Understanding that a technology with such great potential for unethical use requires more caution than optimism, regulatory efforts going forward must pause to consider these issues in depth.

If India is to pursue advancements in gene-editing technology, it is important that they not conform to the laws of other countries, rather, it is crucial that rules and regulations are created that take into account India’s unique professional and sociocultural landscape, and furthermore, the capacity for ensuring that such a technology is handled responsibly and ethically.

**WORKS CITED:**

[1] Belluz, Julia. “Is the CRISPR Baby Controversy the Start of a Terrifying New Chapter in Gene Editing?” Vox.com, *Vox Media*, 3 Dec. 2018, www.vox.com/science-and-health/2018/11/30/18119589/crispr-technology-he-jiankui.

[2] Brokowski, Carolyn, and Mazhar Adli. “CRISPR Ethics: Moral Considerations for Applications of a Powerful Tool.” *Journal of Molecular Biology*, U.S. National Library of Medicine, 4 Jan. 2019, www.ncbi.nlm.nih.gov/pubmed/29885329.

[3] Adashi EY, Cohen IG. The Ethics of Heritable Genome Editing: New Considerations in a Controversial Area. *JAMA.* 2018;320(24):2531–2532.

[4] Vogel, Kathleen. “Crispr Goes Global: A Snapshot of Rules, Policies, and Attitudes.” *Bulletin of the Atomic Scientists*, 28 June 2018, thebulletin.org/2018/06/crispr-goes-global-a-snapshot-of-rules-policies-and-attitudes/?fbclid=IwAR3-0mnLFEag9bRgjXSliNqeih9LDvKrwoym2-zLzQO3BLr87X2lqKAas9g

[5] Ledford, Heidi. “Where in the World Could the First CRISPR Baby Be Born?” *Nature News*, Nature Publishing Group, www.nature.com/news/where-in-the-world-could-the-first-crispr-baby-be-born-1.18542.

[6] Cyranoski, David. (2018). Japan set to allow gene editing in human embryos. Nature. 10.1038/d41586-018-06847-7.

[7] Jayaraman, K. S. “India Bans Commercial Use of Stem Cells for Therapy.” *Nature India*, Oct. 2017, www.natureasia.com/en/nindia/article/10.1038/nindia.2017.130.

[8] ndian Council of Medical Research. “National Ethical Guidelines for Biomedical Research Involving Human Participants .” *Https://Icmr.nic.in/Sites/Default/Files/Guidelines/ICMR\_Ethical\_Guidelines\_2017.Pdf*, Oct. 2017.

[9] Priyadarshini, Subhra. “Armed with CRISPR Scissors, Indian Scientists Look at Curing the Incurable.” *Nature India*, Aug. 2018, www.natureasia.com/en/nindia/article/10.1038/nindia.2018.100.

[10] TV Padma. “It's Time India Has a Conversation about Ethics of Gene Editing”. *https://Www.hindustantimes.com/*, Hindustan Times, 17 Dec. 2017

[11] Mahajan Vijay. "White coated corruption." Indian Journal of Medical Ethics [Online], 7. 1 (2010): 18. Web. 19 Mar. 2019

[12] Mahajan, Vijay. “White Coated Corruption .” *White Coated Corruption* , Indian Journal of Medical Ethics, 2010, ijme.in/articles/white-coated-corruption/?galley=html.

[13] Not first time for Dr Amit. *Hindustan Times* [Internet]. 2008 Jul 7[cited Aug 31]. Available from: http://www.hindustantimes.com/FullCoverage/FullCoverage.aspx?Special=TheKidneyScam

[14] Ahuja, Amit. “Fair Chance: How Indian Voters Use Skin Colour To Choose Candidates.”*Huffington Post India*, Huffington Post India, 28 July 2017

[15] Times, Collin Rodrigues Hindustan. “India's Unfair Obsession with Fair Skin, Its Impact on Relationships.” *https://www.hindustantimes.com/*, Hindustan Times, 20 Mar. 2015

[16] Dasgupta, Piyali. “Piyali Dasgupta 29 Sep 2016 . 6 Min Read.” *Discrimination Based on Skin Color at Workplace*, SHEROES, 29 Dec. 2016

[17] Mackenzie, Debora. “Technology Driving Rise in Abortions of Girls in India.” *New Scientist*, 4 Feb. 2010

[18] “Seven Brothers.” *The Economist*, The Economist Newspaper, 9 Apr. 2011, www.economist.com/node/18530371.

[19] Tripathi, Amrita. “Sex Determination in India: Doctors Tell Their Side of the Story.” *Scroll.in*, Https://Scroll.in, 3 Jan. 2017

[20] Iwamoto, Kentaro. “Asia's Gender Imbalance Is Bad News for Growth.” *Nikkei Asian Review*, Nikkei Asian Review, 13 Apr. 2017, asia.nikkei.com/Features/Too-many-men/Asia-s-gender-imbalance-is-bad-news-for-growth.

[21] Katyal, Ritika. “India Census Shows Extent of Poverty.” *CNN*, Cable News Network, 3 Aug. 2015, www.cnn.com/2015/08/02/asia/india-poor-census-secc/index.html.

[22] BusinessToday.in. “Income Inequality Gets Worse; India's Top 1% Bag 73% of the Country's Wealth, Says Oxfam.” *Business News - Latest Stock Market and Economy News India*, Living Media India Limited

[23] Balarajan, Yarlini, S Selvaraj, and S V Subramanian. “Health Care and Equity in India.” *Lancet* 377.9764 (2011): 505–515. *PMC*. Web. 25 Jan. 2018.

[24]Govt Mass Media Campaign Highlights the Link between Tobacco and TB - ET HealthWorld.” *ETHealthworld.com*, 15 Mar. 2018, health.economictimes.indiatimes.com/news/policy/govt-mass-media-campaign-highlights-the-link-between-tobacco-and-tb/63316056.

[25]Lyn, Tan Ee. “New Malaria Estimate Says 205,000 Die in India.” *Reuters*, Thomson Reuters, 20 Oct. 2010, www.reuters.com/article/us-malaria-india/new-malaria-estimate-says-205000-die-in-india-idUSTRE69J6BX20101020.

[26]“42 Per Cent Global Child Deaths Due to Diarrhoea in India, Nigeria.” *The Economic Times*, 2 June 2017, economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/42-per-cent-global-child-deaths-due-to-diarrhoea-in-india-nigeria/articleshow/58966874.cms.