CRISPR CONSIDERATIONS: ETHICAL EDITING AND RESPONSIBLE REGULATION

ALLISON C. TUOHY†

CONTENTS

ABSTRACT

CRISPR human genome editing possesses untold potential to cure previously untreatable diseases. However, in the United States, the rapid advancement of science is outpacing national laws and regulations, inhibiting the use of CRISPR in human medicine and creating opportunity for misuse. The enduring nature of germline edits means that current decisions will not only impact those treated, but also their offspring. The concept of "designer babies," or the use of CRISPR for enhancement rather than treatment, poses a threat to social and economic equity as well. The evident tension between innovation and caution leaves lawmakers, ethicists, scientists, and clinicians debating the limits within

† B.A., 2019, University of Michigan; J.D. Candidate, 2022, Wayne State University Law School. I would like to express my great appreciation to Professor Lance Gable for his enthusiastic encouragement and valuable insight during the planning and development of this Article.

which germline editing can operate. This Note calls for a multifactorial and proactive approach to this looming ethical and legal issue including legislation, oversight, and inclusive public discourse on germline editing use.

INTRODUCTION

As the world continues to advance and innovate using new technologies, there are new and unchartered ethical considerations to evaluate. One notable innovation that has brought up many of these questions is human germline editing.[1] Gene editing in embryos is a burgeoning and rapidly progressing public health practice. Using powerful gene editing technology like CRISPR/Cas9 can manipulate genetic code and edit individual genes in one's genome. The technology has the potential to correct mutations in the embryo's genome that may result in inherited diseases and conditions. Genome editing has been an insightful endeavor for the scientific community because of the research it yields for improving biological understanding of early human embryo development and treatment of rare genetic diseases.[2]

With more research on the horizon, it is a possibility that heritable germline editing becomes a reality. Many parents could be relieved at the availability of technology that could prevent their offspring from inheriting genomes with indicators for Huntington's Disease, BRCA1/2 genes, and other genetic diseases. However, "there is significant public discomfort about heritable genome editing, particularly for less serious conditions and for situations in which alternatives exist."[3]

As seen with a plethora of other medical innovations,[4] CRISPR gene editing brings about significant benefits, drawbacks, regulatory considerations, and ethical implications. Specific concerns about the practice of gene editing have been raised regarding germline editing.[5]

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1. There are two different kinds of gene editing: somatic gene editing and germline editing. Somatic editing affects only the patient and his/her cells. On the other hand, germline editing affects all the cells of an organism, including germ (reproductive) cells. By editing the reproductive cells, genetic changes to the germline are then heritable and passed down to future offspring. Somatic cell editing is generally more accepted as a safe practice in the research community than germline editing.

2. *See generally* NUFFIELD COUNS. ON BIOETHICS, GENOME EDITING: AN ETHICAL REVIEW (2016).

3. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, & GOVERNANCE 133-34 (2017).

4. *See generally* NUFFIELD COUNS. ON BIOETHICS, *supra* note 2.

5. *See generally* NAT'L HUM. GENOME RSCH. INST., *What are the Ethical Concerns of Genome Editing?*, https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/ethical-concerns (last updated Aug. 3, 2017).

These concerns stem from the fact that germline gene therapy does not just affect the embryo but transmits any gene alterations to future offspring of that person as well. Researchers highlight some unsettling consequences of gene editing in embryos such as off-target mutations as well as the potential for these technologies to be misused for enhancement purposes rather than therapeutic purposes.[6] CRISPR technology has been a preferred method within the research community because of its relatively low cost and ease of use.[7] This technology can target specific DNA sequences, it is often easily produced in the laboratory setting, and it is available for purchase in commercial kits.

The utilization of CRISPR becomes more of a reality every day. There are several biotechnology companies with gene-editing therapies that expect to launch as early as 2022.[8] While therapies will not become widely available in medicine for some time, these biotechnology companies prompt thoughts about the uses and possible misuses of CRISPR technology. The promise and potential of CRISPR in the field of medicine incentivized many researchers to seek patents over the technology. This battle over the CRISPR patent is ongoing, but many prominent researchers in the field have called for a "peace treaty," so to speak. This would allow all institutions to work together to promote access of CRISPR technology to all parties in an effort to use the technology to solve today's problems.[9] This Note focuses on the developments of CRISPR and the subsequent ethical implications of its use in human germline editing. Further, this Note will suggest a national oversight policy needed to ensure the ethical utilization of human genome editing using CRISPR technology.

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6. Katherine J. Wu, *Crispr Gene Editing Can Cause Unwanted Changes in Human Embryos, Study Finds*, NY TIMES (Oct. 31, 2020), https://www.nytimes.com/2020/10/31/health/crispr-genetics-embryos.html; NUFFIELD COUNS. ON BIOETHICS, *supra* note 2, at 51.

7. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., *supra* note 3, at 133-34; Mark Shwartz, *Target, Delete, Repair*, STANFORD MED. MAG. (Winter 2018), https://stanmed.stanford.edu/2018winter/CRISPR-for-gene-editing-is-revolutionary-but-it-comes-with-risks.html#.

8. Allison Gatlin, *This Biotech Stock Could Launch Its First CRISPR Drug in 2022*, INV. BUS. DAILY (Nov. 30, 2018, 4:14 PM), https://www.investors.com/news/technology/crispr-stock-biotech-stocks-gene-editing/.

9. Jon Cohen, *The Latest Round in the CRISPR Patent Battle Has an Apparent Victor, But the Fight Continues*, SCIENCE (Sept. 11, 2020, 6:40 PM), https://www.sciencemag.org/news/2020/09/latest-round-crispr-patent-battle-has-apparent-victor-fight-continues.

I. BACKGROUND

A. History of CRISPR Policy

Nature Methods recognized genome editing as the 2011 Method of the Year.[10] While CRISPR has been on the radar for some time, *Science* named it Breakthrough of the Year in 2015.[11] It continues to be a significant area of both policy and social interest, as it could potentially serve to modify genes responsible for many fatal genetic diseases. The notion of altering the human genome in embryos has been widely debated by researchers and policymakers;[12] this permanent augmentation of cells poses safety and ethical concerns. Some worry that allowing this sort of unchartered gene editing would open a can of worms that could never be closed again.[13] As research continued in the United States, questions arose surrounding the federal approval and funding.

In 2015, the National Institutes of Health (NIH) put out a statement that they would not fund any use of gene-editing technologies in human embryos citing concerns of safety and ethics.[14] Soon after, Chinese scientists were able to edit the genes of non-viable embryos discarded from in-vitro fertilization (IVF) and attempted to protect the embryos from HIV infection.[15] This novel use of CRISPR to engineer mutations into human embryos started a worldwide ethical discourse on altering the human germline. In 2017, the National Academy of Sciences and the National Academy of Medicine came together to form the Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations. The committee's primary purpose was discussing and publishing a report on the science of genome editing, the possible clinical applications of the

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10. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., *supra* note 3, at xi.

11. John Travis, *Making the Cut: CRISPR Genome-Editing Technology Shows its Power*, 350 SCIENCE 1456, 1456 (2015), https://science.sciencemag.org/content/sci/350/6267/1456.full.pdf.

12. *See e.g.* Jocelyn Kaiser, *CRISPR Debate Fueled by Publication of Second Human Embryo-Editing Paper*, SCIENCE (April 8, 2016), https://www.science.org/content/article/crispr-debate-fueled-publication-second-human-embryo-editing-paper.

13. *See generally* NUFFIELD COUNS. ON BIOETHICS, *supra* note 2.

14. Francis S. Collins, *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT'L INST. OF HEALTH (Apr. 28, 2015), https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos.

15. Alvaro Plaza Reyes & Fredrik Lanner, *Towards a CRISPR View of Early Human Development: Applications, Limitations and Ethical Concerns of Genome Editing in Human Embryos*, 144 DEV. 3, 5 (2017); *See generally* David Cyranoski, *The CRISPR-Baby Scandal: What's Next for Human Gene-Editing*, NATURE, https://www.nature.com/articles/d41586-019-00673-1 (last updated Mar. 11, 2019).

technologies, some possible risks and benefits, standards for quantification of unintended consequences, analysis of current regulatory frameworks, and the general guiding principles to guide human germline editing.[16]

1. Gene Editing and the Development of CRISPR

Genome editing in embryos is an ongoing debate, but with the recent discovery of new gene therapy techniques such as CRISPR, the debate has been reignited. The CRISPR/Cas9 (CRISPR) system is a novel technological development that has, "…made editing of the genome much more precise, efficient, flexible, and less expensive…"[17] Essentially, CRISPR is one of several gene editing technologies that have made human gene editing more easily accessible and streamlined for those who wish to use it. Genome editing is defined as, …the deliberate alteration of a selected DNA sequence in a living cell, in which strands of DNA are specifically cut and altered in a way that can reactivate, deactivate, insert, delete, or alter genes, especially those that cause disease.[18]

2. Balancing Innovation with Precaution

As the capabilities of gene editing have continued to progress, bioethicists and scientists debate whether the positive advancements attributed to genome editing outweigh the potential unintended consequences. Embryonic genome editing is of significant concern to the public health community for a myriad of reasons, one being misuse of the technology. One possibility of CRISPR technology misuse stems from germline editing, in which the genome of an individual's reproductive cells is edited and heritable. Changes made in the germline are permanent and passed down to future generations.

A benefit of germline editing of disease alleles is that "…they will forever be gone from the lineage of the treated individual."[19] Germline editing also has the potential to prevent diseases inherited from parents, which differs from somatic therapies that target non-productive cells and

16. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., *supra* note 3, at 26.

17. *Id.* at 1.

18. NUFFIELD COUNS. ON BIOETHICS, GENOME EDITING, *Genome Editing: An Ethical Review – Guide to the Report* (Sept. 30, 2016), https://www.nuffieldbioethics.org/publications/genome-editing-an-ethical-review/guide-to-the-report/genome-editing-in-brief-what-why-and-how.

19. Dana Carroll, *Genome Editing: Past, Present, and Future*, 90 YALE J. OF BIOLOGY & MED. 653, 655 (2017).

therefore do not get passed down to future generations.[20] However, some researchers are concerned about off-target mutations that can occur and contemplate if the risk to correct disease causing genes is worth the possible harms that could present themselves.[21] Some off-target mutations are harmless or unnoticeable; however, others can cause damaging changes to portions of DNA that are not the intended or desired edits depending on their location and effects.[22]

Another risk to gene editing is mosaicism, which presents a significant chance that some of the cells in the embryo would not have any of these intended edits.[23] Additionally, any screening of the edited embryos for mosaicism would not necessarily confirm the "…correct editing of the implanted embryo because a single cell may not reflect the genotype of the other cells of the embryo."[24] Because of this, the germline in the resulting child may be mosaic, indicating that the edit would not be heritable for succeeding generations. This is an undesirable outcome for generations with heritable diseases wishing to be terminated in the succeeding offspring.

B. Application to the Human Genome

As CRISPR gained popularity and prominence, the world began thinking of the endless possibilities that could be achieved through the utilization of the technology. While CRISPR can be utilized for foods, plants, agriculture, and more, many researchers became interested in how

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20. NAT'L HUM. GENOME RSCH. INST., *How is Genome Editing Used?*, https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/How-genome-editing-is-used (last updated Aug. 3, 2017).

21. *See generally* Diane Catherine Wang & Xiangdong Wang, *Off-Target Genome Editing: A New Discipline of Gene Science and a New Class of Medicine*, 35 CELL BIOLOGY & TOXICOLOGY 179, 179-183 (2019). An off-target mutation is an unintended gene modification that can occasionally occur through the uses of various gene editing technologies. These technologies can accidentally send genetic changes to unintended sites in a given genome. While the way these off-target effects occur is complex, researchers are concerned that these off-target effects or mutations occur at a much more frequent rate than initially expected. There has been an effort to eliminate or at least to limit the off-target effects, as the effects are not monitored, measured, or expected. Not much is known about the short-term and long-term side-effects or toxicity in humans.

22. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., *supra* note 3, at 24.

23. *Id*. at 116; Michael Le Page, *Mosaic Problem Stands in the Way of Gene Editing Embryos*, NEW SCIENTIST (Mar. 18, 2017), https://www.newscientist.com/article/mg23331174-400-mosaic-problem-stands-in-the-way-of-gene-editing-embryos/. Mosaicism is an unintended consequence of gene editing where edited germlines may result in mixtures of edited and unedited cells., meaning that children could still potentially "develop the disease that gene editing was supposed to prevent."

24. NAT'L ACADEM. OF SCIENCES, ENG'G, & MED., *supra* note 3, at 116.

human lives could be better optimized or improved. While some pondered how germline editing could end horrible, heritable diseases for families, such as Huntington's Disease, others took a more dystopian route and began exploring the concept of designer babies.

The use of CRISPR in the human genome goes beyond editing out terrible diseases, and it could include using CRISPR technology to regulate certain aspects of the cell germline to create an embryo with the exact traits and DNA desired. In 2019, the House Appropriations Committee took up the issue when approving the 2020 spending bill.[25] The Committee ultimately decided to bar the U.S. Food and Drug Administration (FDA) from considering any requests for approval for clinical trials "…in which a human embryo is intentionally created or modified to include a heritable genetic modification."[26] The House Committee previously wanted to remove this rider to promote a wider, more robust discussion about how the U.S. should regulate genetic modification of human sex cells.[27] Specifically, they were concerned that any restriction on gene editing would hinder the development of potentially life-saving therapies (including using CRISPR) to prevent heritable diseases.[28] This evident tension between innovation and caution is one that repeatedly comes up as lawmakers and ethicists debate the limits within which germline editing can operate.

In addition to the safety aspect of this innovative therapy, ethicists are also concerned about the implications of allowing the gene editing of human germlines, specifically embryos. The ethical concerns focus on the slippery slope that could occur should this gene therapy become widely available for public use. That is, policymakers and ethicists worry that the editing of genes would "…confer advantageous traits not related to avoiding disease or preserving health."[29] Prospective parents trying to prevent their offspring from inheriting a genetic condition are in a clearly different situation from parents wishing to augment their children to have specific genetic traits. As policymakers wrestle with the possible regulations and oversight for gene editing in embryos, there remains a reasonable concern from a societal standpoint that the individual choices

25. Jocelyn Kaiser, *Update: House Spending Panel Restores U.S. Ban on Gene-Edited Babies*, SCIENCE (June 4, 2019, 1:45 PM), https://www.science.org/content/article/update-house-spending-panel-restores-us-ban-gene-edited-babies.

26. *Id.*

27. *Id.*

28. *Id.*

29. George Q. Daley et al., *After the Storm – A Responsible Path for Genome Editing*, 380 NEW ENGLAND J. MED. 897, 898 (2019).

influenced by cultural and market forces could usher in a new wave of eugenics.[30]

One of the reasons that gene editing using CRISPR technology is such a controversial topic is that, if approved for widespread use by the public, prospective parents may abuse the availability of the therapy to change the makeup of their embryo to create their "ideal child." This poses a myriad of social issues, such as the potential lack of universal availability of the technology to various socioeconomic groups. In a world riddled with social and economic inequities, the concern is that this therapy would only be available to those of a higher socioeconomic class. In essence, if this sort of "designer baby" concept were to come to fruition, inequities would only increase as the ones who could afford this therapy would ultimately have better health outcomes than those who could not.

While the therapy has not reached this level of use yet, opening the door to widespread gene editing may allow for the use of CRISPR for enhancement purposes as opposed to rehabilitation purposes. These ethical issues necessitate a closer analysis of the legal framework in the United States regulating CRISPR.

C. Legal Landscape of CRISPR in the United States

In the United States, gene therapy operates under a regulatory framework similar to that of biological drugs or devices. As such, regulation falls under the guidance of the FDA.[31] Unlike many other countries, the United States does not have an outright ban on human embryo work or research.[32] Some states have chosen to impose laws, prohibitions, or regulations; some states have less clear rules; and some states do not ban it at all.[33] In the states that do not ban research or work on embryos, researchers could theoretically conduct research in embryos using private funding. The United States government and its agencies have been attempting to find a way to strike a balance between supporting

30. Robert Andorno et al., *Geneva Statement on Heritable Human Genome Editing: The Need for Course Correction*, 38 SCI. & SOC'Y 351, 352 (2020).

31. R. Alta Charo, *The Legal and Regulatory Context for Human Gene Editing*, 32 ISSUES SCI. & TECH. 39 (2016).

32. Françoise Baylis et al., *Human Germline and Heritable Genome Editing: The Global Policy Landscape*, 3 CRISPR J. 5 (Oct. 20, 2020), https://www.liebertpub.com/doi/10.1089/crispr.2020.0082.

33. Sara Reardon, *NIH Reiterates Ban on Editing Human Embryo DNA*, NATURE (Apr. 29, 2015), https://www.nature.com/news/nih-reiterates-ban-on-editing-human-embryo-dna-1.17452.

innovations in biomedical research while doing so in a manner that follows well-established scientific and ethical principles.[34]

1. FDA Guidance

The FDA considers CRISPR/Cas9 methods of gene editing in humans to be a form of gene therapy.[35] All gene therapy products are regulated by the FDA's Center for Biologics Evaluation and Research (CBER). [36] In order to study gene therapy in humans in the United States, researchers must submit an investigational new drug (IND) application prior to initiation.[37] Further, any marketing done requires a biologics license application (BLA).[38] The FDA maintains a list of approved clinical trials and gene therapy products so that individuals know which ones have been approved and vetted by the FDA.[39] A present concern for the FDA is that there are many gene therapy products currently on the market that are advertised as "at-home" kits to produce gene therapies for self-administration.[40] According to the FDA, these are potentially dangerous products because they are being made available to the public, but they pose safety risks and have not been approved by the FDA or studied by the appropriate regulatory oversight agency.[41] As the kits' so-called "biohacking" has gained significant traction over the years, the FDA has stated that it regulates CRISPR and other gene editing techniques while also highlighting that it is not legal to sell gene kits to the public.[42]

In 2016, the House of Representatives' spending bill barred the FDA from considering any clinical trial applications that intentionally create or modify the human embryo to include a heritable genetic modification.[43] There is also another rider which prevents the NIH from funding human

34. Collins, *supra* note 14.

35. FDA, *Information About Self-Administration of Gene Therapy* (Nov. 21, 2017), https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy.

36. *Id.*; *See generally* Anna Abram & Scott Gottlieb, *FDA Advancing Beneficial Animal Biotechnology Product Development*, U.S. FOOD & DRUG ADMIN. (April 8, 2019), https://www.fda.gov/news-events/fda-voices/fda-advancing-beneficial-animal-biotechnology-product-development.

37. FDA, *supra* note 35.

38. *Id.*

39. *Id.*

40. *Id.* A DIY (do it yourself) CRISPR Kit is a product for home experimenting that allows for consumers to make precision genome edits in bacteria. These kits include everything a person would need to genetically engineer bacteria at home.

41. *Id.*

42. *Id.*

43. Kaiser, *supra* note 25.

germline editing.[44] While these trials can also be performed legally through private funding, the researchers are also required to get FDA approval to run a clinical trial using germline editing.[45]

2. Governmental Discourse and Legal Precedents

Given the serious and numerous potential safety issues posed by editing the human germline, the government and legislative bodies have enacted multiple legislative and regulatory prohibitions. Passed in 1996, the Dickey-Wicker Amendment effectively prohibited the use of appropriated funds for "…work that destroys human embryos or creates them for the purposes of research."[46] However, any appropriations, riders, or laws that limit researchers' foray into biotechnology have the potential to eventually become outdated. The amendment has had long-standing effects on science's progress since its inception.[47] The Dickey-Wicker Amendment has remained a large roadblock for clinical researchers who wish to study germline editing in embryos through CRISPR. Attempts have been made to overturn the Dickey-Wicker Amendment, yet it continues to be included in every spending bill since its passage.[48]

After an executive order was passed by President Obama in 2009, the NIH had permission to fund embryonic stem cell research and, in turn, had to promulgate guidelines on how they planned to handle stem cell research.[49] The United States Court of Appeals weighed in on how the Dickey-Wicker Amendment should be analyzed by the NIH in *Sherley v. Sebelius*.[50] In *Sherley*, the Court of Appeals held that executive orders "react to the progress of science," and since the discovery of CRISPR, there have not been executive orders or legislation relating to CRISPR.[51] Based on these rulings, many companies that work with CRISPR have tried to utilize private funding to operate under fewer restrictions and regulations.[52] This convention is potentially problematic since CRISPR remains a relatively controversial technology needing more extensive government oversight than what is currently provided.[53] These

44. *Id.*
45. *Id*.
46. Reardon, *supra* note 33.
47. Matthew D. Hebert, *Opening a Can of Genetically Modified Worms: Funding and Regulating CRISPR Technology*, 52 VAL. U.L. REV. 505, 516 (2018).
48. *Id*.
49. *Id*.
50. *See* Sherley v. Sebelius, 689 F.3d 776, 780-83 (D.C. Cir. 2012).
51. Hebert, *supra* note 47, at 519.
52. *See* Anna Zaret, *Editing Embryos: Considering Restrictions on Genetically Engineered Humans*, 67 HASTINGS L.J. 1805, 1829-1830 (2016).
53. Hebert, *supra* note 47, at 520-21.

circumventions and loopholes that companies utilize essentially render any CRISPR government oversight useless. The concern is that privately funded companies will competitively continue to work around the restrictions and regulations to keep up with the emerging technologies and research.

In a time when there are rapidly developing technologies, rapidly developing policies must follow. "On March 14, 2019, the NIH director issued a statement supporting the call for an international moratorium on research establishing human pregnancies using germline-edited embryos."[54] While this statement has no bearing on the legal framework of research regulations in the United States, it illustrates the fear and hesitation toward this type of research until more is known about its effects. A moratorium would prevent the clinical use of human germline editing, but it would not apply to germline editing for research use so long as the studies do not involve an embryonic transfer to a uterus.[55] Prominent researchers in the field have been critical of the idea of a moratorium because there is "…no pathway toward possible responsible use."[56] An open-ended moratorium could slow scientific inquiry, withhold potential medical care, and promote cross-border medical tourism; these consequences of a moratorium must be weighed against other potential options for regulation. If a moratorium were to be put in place, it would hopefully bear some sort of international governance framework. Until then, the United States is left to regulate domestically.

Soon after the NIH's statement, the first CRISPR law was passed in California on July 30, 2019.[57] This new consumer protection law addressed the concerns about at-home gene therapy kits called "DIY CRISPR Kits." This new law requires all sellers of these kits to include a "…notice prior to the point of sale, in addition to a label, stating that CRISPR kits are not intended for self-administration."[58] Based on these

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54. NAT'L INST. OF HEALTH, *Gene Editing – Digital Media Kit*, https://www.nih.gov/news-events/gene-editing-digital-press-kit (last visited Nov. 5, 2020).

55. Eli Y. Adashi & I. Glenn Cohen, *Heritable Genome Editing: Is a Moratorium Needed?*, 322 JAMA 104, 104 (2019).

56. *Id*. (statement of Jennifer Doudna, PhD, a prominent genome editing researcher stated her misgivings of a potential moratorium: "The word moratorium implies enforcement…I don't want to drive others underground with this" and statement Dean of Harvard Medical School George Q. Daley, MD, PhD: "A moratorium complicates future discussions rather than clarifies them," noting that it is unclear who gets to decide how and when they end).

57. S.B. 180, 2019-2020 Leg., Reg. Sess. (Cal. 2019), https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=201920200SB180.

58. Ling Ling Chang, *First CRISPR Law: Selling "Gene-Therapy Kits" Will Be Illegal in California Unless They Carry a Warning*, TECH. NETWORKS (Aug. 16, 2019), https://

various laws and moratorium considerations, policymakers and researchers have no clear consensus on how to proceed with the clinical application of CRISPR on human germlines.[59] While more research needs to be done, more policymaking also needs to be prepared to ensure the safe use of this potentially life-saving therapy.

II. ANALYSIS

CRISPR technology has advanced the science of gene editing and made the process easier and more precise. While the clinical research world is still in agreement that research on germline editing of human embryos should be paused until there is more knowledge on the subject, calls for total avoidance of germline editing "are increasingly in the minority."[60] This inclination toward learning more about germline editing highlights the need for decisiveness and certainty on the limits of its use. Some believe that the use of CRISPR for germline editing would be instrumental for the prevention of serious monogenic diseases that are likely to be transmitted such as cystic fibrosis, sickle cell anemia, and Tay-Sachs disease.[61] Given the heritable nature of these edits, others are concerned about the ethical, moral, and medical issues that may come up if this sort of genetic alteration becomes commonplace in society.

A. Safety and Ethical Concerns

Greater amounts of research must occur to ensure that the use of gene editing in embryos does not lead to any undesired results such as off-target effects or mosaicism. An international commission of the U.S. National Academy of Medicine, U.S. National Academy of Science, and the U.K.'s Royal Society discussed heritable human genome editing in a report stating that the initial uses of germline editing of the human genome

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www.technologynetworks.com/genomics/news/first-crispr-law-selling-gene-therapy-kits-will-be-illegal-in-california-unless-they-carry-a-322889.

59. Françoise Baylis and Marcy Darnovsky, *Scientists Disagree About the Ethics and Governance of Human Germline Editing*, HASTINGS CTR. (Jan. 17, 2019), https://www.thehastingscenter.org/scientists-disagree-ethics-governance-human-germline-genome-editing/.

60. Nancy M.P. King, *Human Gene-Editing Research: Is the Future Here Yet?*, 97 N.C.L. REV. 1051, 1085 (2019).

61. Megan Lowry & Alex Matthews-King, *Heritable Genome Editing Not Yet Ready to Be Tried Safely and Effectively in Humans; Initial Clinical Uses, If Permitted, Should Be Limited to Serious Single-Gene Diseases*, NAT'L ACAD. SCIS., ENG'G & MED. (Sept. 3, 2020), https://www.nationalacademies.org/news/2020/09/heritable-genome-editing-not-yet-ready-to-be-tried-safely-and-effectively-in-humans-initial-clinical-uses-if-permitted-should-be-limited-to-serious-single-gene-diseases.

should be done "…incrementally and cautiously" in an effort to balance possible harms and benefits.[62] The committee articulated that there must be a translational pathway from research to clinical use that is supported by preclinical evidence proving that clinical use would be feasible, efficient, and highly accurate.[63] Until such translational pathway is proven with confidence, more research is needed to ensure the safety of genome editing in human embryos.

With few precedents or a process to draw from, public education, discussion, and approval continue to develop.[64] The best way to gain a comprehensive understanding should involve international conversation discussing any ethical or safety concerns. At the very least, the United States should domestically engage in discussions with various stakeholders including ethicists, clinical researchers and geneticists, public health professionals, policymakers, social scientists, physicians, advocacy groups (Center for Genetics and Society), and patient communities (e.g. Cystic Fibrosis Foundation, Huntington's Disease of America).

An open forum with these various experts and stakeholders will illuminate the benefits and risks associated with germline editing in embryos. These open forums, or consensus conferences, are public meetings that facilitate dialogues between experts and citizens to deliver consensus-based input.[65] A critical ethical issue in clinical research is that the benefits must be greater than the risks since living things and ecosystems could be damaged in the process.[66] Some of the risks are off-target mutations, cell death, or cell transformation. The efficient and safe delivery of CRISPR/Cas9 into cell types or tissues that are difficult to transfect/infect compound the chance for negative impact.[67] By allowing discussion through a consensus conference model, any policy decisions or oversight given will be made with all interests in mind and facilitate discussion and opportunity to ask questions and take notes.[68] As one scholar articulated, "We need public education, engagement and

62. *Id.*

63. *Id.*

64. Adashi & Cohen, *supra* note 55, at 105.

65. EPA, *Public Participation Guide: Consensus Workshops*, https://www.epa.gov/international-cooperation/public-participation-guide-consensus-workshops (last accessed on Jan. 3, 2022).

66. E. Rodriguez, *Ethical Issues in Genome Editing Using Crispr/Cas9 System*, 7 J. CLINICAL RSCH. & BIOETHICS, Mar. 24, 2016, at 2 (2016).

67. *Id.*

68. *See e.g.* Maria Powell & Daniel Lee Kleinman, *Building Citizen Capacities for Participation in Nanotechnology Decisionmaking: The Democratic Virtues of the Consensus Conference Model*, 17 PUB. UNDERSTANDING SCI. 329 (2008).

empowerment to reach 'broad societal consensus' on whether, not how, to pursue heritable genome editing."[69] To further support science and research in a safe and ethical way, the United States should create a regulatory body or independent mechanism to monitor the potential paths toward clinical implementation, to draw a clear line of unacceptable use of the technology, and to penalize those who misuse CRISPR for human genome editing.[70]

In weighing the safety and ethical concerns, there should be concerted efforts from geneticists, policymakers, government agencies, researchers, ethicists, and other stakeholders to determine that the technology is completely safe to begin work on the human germline. If there were to be some injury or unintended negative side effect of the editing on an embryo, it would raise the question of who would be liable for the damages to the future generations as well.[71] As clinical researchers and the respective committees ponder the ethical and safety considerations, challenges continue for those struggling with untreatable genetic diseases. These questions must be answered sooner rather than later to certify that the "prevention of otherwise untreatable genetic maladies is not being held up."[72]

B. Enhancement vs. Rehabilitation

What makes regulation especially challenging in the United States is that while there are very strong controls in place prior to approval, this control becomes significantly weaker once a therapy like this hits the market or is approved for use.[73] Consequently, while gene editing could potentially be approved for therapeutic reasons, nothing stops doctors or biogeneticists from using the technology for a different purpose or in a way not imagined by those who approved it. As mentioned in the Geneva Statement on Heritable Human Genome Editing, the concern is that the collective of individual choices made to pursue human genome editing will generate a new wave of eugenics.[74]

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69. Françoise Baylis, *Questioning the Proposed Translational Pathway for Germline Genome Editing*, 3 NATURE HUM. BEHAV. 200, 200 (2019).

70. Lowry & Matthews-King, *supra* note 61.

71. Rodriguez, *supra* note 66, at 3.

72. Adashi & Cohen, *supra* note 55, at 105.

73. Charo, *supra* note 31.

74. Andorno et al., *supra* note 30, at 353. Some dismiss these eugenics concerns stating that it would be impossible for parents to genetically alter or enhance traits in their children such as eye color, appearance, athletic ability, or intelligence since the genetic makeup is far too complex. However, just because this is not an immediate possibility or concern, it may be in the future as CRISPR technology becomes more commonplace. Fertility clinics and companies may take advantage of this futuristic aspect in their marketing pursuits.

A genetics professor explained permissible use by saying, "Should they ever be used, it is vitally important that these technologies are used for medically justified interventions, based on rigorous understanding of how the pathogenic variant leads to disease."[75] While uncertainty regarding how this technology could be misused persists, gene editing the human germline could "…revolutionize the treatment of genetically transmitted human disease."[76] The hope of germline editing in human embryos is that CRISPR technology will correct defective genes and potentially remove the genetic errors from the germline to prevent the genes from appearing in human gametes and embryos in the present, and down the generational line.[77]

One of the promising aspects of CRISPR technology is its ability to rid from the gene pool what scientists, clinical researchers, and society deem to be horribly debilitating diseases that lead to pain, suffering, and high rates of mortality. To aid in reaching a balance between enhancement and rehabilitation capabilities, some suggest that when the world is ready, CRISPR in germline editing be limited to only the "…most serious and devastating diseases that are caused by DNA variants in a single gene that could lead to premature death."[78] The line between enhancement and rehabilitation is a thin one, but with government and agency oversight coupled with explicit clinical limits, germline editing can be used to prevent devastating genetic diseases in children while protecting the world from eugenics.

C. Equity and Access

Tied to the concern about eugenics is the possibility that human germline editing could lead to further social inequality, discrimination, and inequitable distribution of lifesaving technologies. One of the most difficult endeavors in CRISPR research is balancing public good and private benefit. There will always be consumers who will pay large sums of money so they can benefit from the technology. Moreover, governing bodies must be insulated from this monetary influence impacting regulation. Giving experts the right to evaluate risk "…strips away many features of the social context that shape technologies and eventually give

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75. Lowry & Matthews-King, *supra* note 61.

76. J. Benjamin Hurlbut, Krishanu Saha & Sheila Jasanoff, *CRISPR Democracy: Gene Editing and the Need for Inclusive Deliberation*, ISSUES SCI. & TECH. 25, 26 (2015).

77. *Id.*

78. Alex Keown, *Panel Lays Out Gene Editing Guidelines, Condemns Risk of Creating 'CRISPR' Babies*, BIOSPACE (Sept. 4, 2020), https://www.biospace.com/article/panel-lays-out-gene-editing-guidelines-condemns-risk-of-creating-crispr-babies/.

rise to disparities in health and health care access."[79] A suggested method for solving the equitable concerns of germline editing would be to create a more inclusive deliberation process to allow for potential users and consumers to "define the harms and benefits of interest."[80] In a world where health equity is already a concern, the government must employ significant oversight of any clinical use of CRISPR editing technologies to ensure that the services are not being disproportionately given to those of high socioeconomic status. Strong governance and inclusive public deliberation prior to clinical implementation can remedy these equity issues.

Another consideration is the erasure of certain disabled communities and the stigmatization of disabled bodies. In the past, prenatal genetic testing enabled parents to prevent the birth of children with serious illnesses. However, this made advocacy groups, stakeholders, and disability rights groups wary that disabled individuals would be stigmatized as "accidents who should have never been born."[81] This concern lingers with the promise of germline editing as parents and disability rights groups wonder if their communities will be completely eliminated and further stigmatized moving forward.[82] As the Geneva Statement promulgated, "It is clear that social inequality and discrimination can be spurred by the mere perception that some humans are biologically 'better' than others."[83]

D. Modification Moving Forward into the Future

As the possibilities for CRISPR continue to manifest and grow, it is obvious that the current structure of regulation and oversight needs to be bolstered in preparation for the novel ways in which gene editing will be used. While some of these issues may not be pressing at the moment, new legislation should be introduced and enacted now to provide funds to be leveraged specifically for CRISPR research and to put forth an oversight committee or regulatory body to monitor safe and ethical use. This foresight will allow clinical researchers to be fully abreast of the risks and benefits while also ensuring that they are operating ethically and safely within the realm of the law prior to clinical implementation. In addition to new legislation, the government should eliminate legal roadblocks such as

79. Hurlbut, Saha & Jasanoff, *supra* note 76, at 31.

80. *Id.*

81. *Id.* at 28.

82. *See generally* Sandy Sufian, *The Threat That CRISPR Poses to Disabled People*, BRINK NEWS (Mar. 15, 2021), https://www.brinknews.com/the-threat-that-crispr-poses-to-the-disabled/.

83. Andorno et al., *supra* note 30, at 353.

the antiquated Dickey-Wicker amendment. These legal roadblocks have been preventing researchers from obtaining federal funds for CRISPR research connected to embryos and the human germline. Creating a more robust and flexible set of laws that can be amenable to scientific progress and innovation would be extremely beneficial to realize the positive aspects of germline editing.

Uniformly high standards for research and therapy are required to move forward. The oversight of this technology requires a robust policy conversation about which human values are shared across the nation and how a regulatory body can best serve and protect those values. Being transparent about these considerations is crucial to safeguard the health and safety of those who may benefit from gene editing in the future. A professor of law and bioethics explained it well: "The more that we have effective systems for responsible oversight in the development and deployment of a technology, the more we can take chances."[84] Due to competition in the race to clinical application, attention to some of the basic principles of "careful and deliberate knowledge-generating research" can ensure that the pivot from "bench to bedside" is safe, ethical, and responsibly executed.[85] Through thorough research, more will be discovered about how CRISPR works, which can aid in expediting any next steps with more certainty.

CONCLUSION

In discussing the development of CRISPR germline editing and some of the safety, ethical, and equity concerns that may follow, this **Note** also calls for a more robust and centralized framework of oversight and laws to prevent any misuse of human germline editing. After the rising popularity of CRISPR/Cas9, the scientific community as a whole not only praised the potential medical advances of the technology but also expressed some potential ethical concerns that could result from widespread use and acceptance of CRISPR in its gene editing capacity.[86] Germline editing remains controversial due to its perpetuating genetic

84. Charo, *supra* note 31 ("We can move a technology quickly because we have a chance to back up at the end and change course"). It is noteworthy that this author also understands innovation as something that can be synchronous and complimentary of precaution. Both facilitate innovation and give confidence to continue developing novel and courageous technologies.

85. King, *supra* note 60, at 1088; *See generally* Steven Joffe & Franklin G. Miller, *Bench to Bedside: Mapping the Moral Terrain of Clinical Research*, 38 HASTINGS CTR. REP., Feb. 08, 2012, at 30.

86. Mary Todd Bergman, *Perspectives on Gene Editing*, HARV. GAZETTE (Jan. 9 , 2019), https://news.harvard.edu/gazette/story/2019/01/perspectives-on-gene-editing/.

impact and the lack of international governance. The current debate over germline editing concerns the balance between scientific innovation and ethical ramifications of misuse.

A major issue facing the United States is that rapidly advancing science is outpacing any relevant laws or regulations promulgated on a national level. Similarly, outdated laws often hinder clinical researchers from advancing technologies like CRISPR to research novel therapies or treatments for debilitating genetic diseases. However, well-developed laws and governmental oversight are critical to prevent private companies or individual clinical researchers from pursuing heritable germline editing before the world is prepared for it. Enacting modern laws and bolstering the current regulatory system will save time for researchers to be fully informed and for a meaningful public discourse to be held on the matter. While this may be challenging and difficult to facilitate at times, there is no better course to take when the societal consequences are so broad-reaching, permanent, and future-shaping.