GENETICALLY EDITED SPERM: AN ETHICAL ANALYSIS OF THE POTENTIAL FOR MODIFIED HUMANS

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INTRODUCTION

People have been striving for human "perfection" for as long as human civilization has existed, sometimes with questionable and even catastrophic results.[1] The idea of perfecting the human population led to eugenics, the nineteenth and early twentieth-century philosophical movement to "breed better people."[2] Eugenics ultimately laid the framework for forced sterilization laws in a number of countries, including the United States, where lawmakers prohibited certain people from procreating.[3] As appalling as forced sterilization was, eugenics took an even darker turn leading up to and during World War II when Nazi Germany murdered millions in the name of creating a superior Aryan race.[4] Adolf Hitler did not come up with the concept of genetic purity on his own.[5] "In fact, [Hitler] referred to American eugenics in his 1934 book, *Mein Kampf*."[6] Although eugenics lost momentum after these atrocities,[7] the idea of human enhancement has continued. Today, scientific advancements in gene-editing technology offer a new take on human modification.

Gene editing is a group of technologies that enable scientists to change an individual's DNA.[8] Genetic material can be added, removed, or altered at

1. David Masci, *Human Enhancement: The Scientific and Ethical Dimensions of Striving for Perfection*, PEW RES. CTR. (July 26, 2016), https://www.pewresearch.org/science/2016/07/26/human-enhancement-the-scientific-and-ethical-dimensions-of-striving-for-perfection [https://perma.cc/NRQ7-XYPU].

2. *Id.*

3. History.com Editors, *Eugenics*, HISTORY (Nov. 15, 2017), https://www.history.com/topics/germany/eugenics [https://perma.cc/Y4HJ-MXBL].

4. Masci, *supra* note 1.

5. History.com Editors, *supra* note 3.

6. *Id.*

7. *Id.*

8. *What Are Genome Editing and CRISPR-Cas9?*, MEDLINEPLUS, https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting [https://perma.cc/ZK6J-66UJ]. Although many ethical

particular locations in the genome.[9] One such gene-editing technique is the revolutionary technology called CRISPR-Cas9, short for "clustered regularly interspaced short palindromic repeats" and CRISPR-associated protein 9,[10] which was discovered in 2012.[11] In 2013, groups of scientists led by Feng Zhang and George Church used CRISPR to edit human cell cultures for the first time.[12] By 2015, Chinese scientist Puping Liang used CRISPR to edit the genes in human tripronuclear zygotes.[13] CRISPR has generated much excitement in the scientific community because it is faster and cheaper, as well as more accurate and more efficient than any other existing method to genetically alter DNA.[14] This is of particular interest in the prevention and treatment of diseases, because CRISPR has the potential to correct mutations associated with single-gene diseases such as cystic fibrosis, sickle-cell anemia, and hemophilia, as well as complex diseases such as cancer, heart disease, and HIV infection.[15]

However, CRISPR has rekindled debates about the numerous social, ethical, and policy concerns of genetic manipulation.[16] These concerns become even more complicated with germline gene editing, which results in changes in sperm, eggs, or embryos that will be passed on to the next generation.[17] Critics of germline editing worry about the potential for "designer babies," children whose traits, including eye color, height, and even athletic ability, are modified by gene editors at the request of their

and policy concerns arise from the application of gene editing in organisms other than humans, such as plants and nonhuman animals, such a discussion is outside the scope of this Note. The focus will remain solely on gene editing as it relates to human beings, as the Cornell experiment is attempting to modify human sperm.

9. *Id.*

10. *Id.*

11. Kara Rogers, *Jennifer Doudna*, ENCYCLOPEDIA BRITANNICA (Dec. 7, 2020), https://www.britannica.com/biography/Jennifer-Doudna [https://perma.cc/Z3LA-K68M].

12. Le Cong, F. Ann Ran, David Cox, Shuailiang Lin, Robert Barretto, Naomi Habib, Patrick D. Hsu, Xuebing Wu, Wenyan Jiang, Luciano A. Marraffini & Feng Zhang, *Multiplex Genome Engineering Using CRISPR/Cas Systems*, 339 SCIENCE 819, 819–23 (2013); Prashant Mali, Luhan Yang, Kevin M. Esvelt, John Aach, Marc Guell, James E. DiCarlo, Julie E. Norville & George M. Church, *RNA-Guided Human Genome Engineering via Cas9*, 339 SCIENCE 823, 823–26 (2013).

13. Puping Liang, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv, Xiaowei Xie, Yuxi Chen, Yujing Li, Ying Sun, Yaofu Bai, Zhou Songyang, Wenbin Ma, Canquan Zhou & Junjiu Huang, *CRISPR/Cas9-Mediated Gene Editing in Human Tripronuclear Zygotes*, 6 PROTEIN & CELL 363, 364 (2015).

14. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 8.

15. *Id.*; *see also* Michael Specter, *The Gene Hackers*, NEW YORKER (Nov. 9, 2015), http://www.newyorker.com/magazine/2015/11/16/the-gene-hackers [https://perma.cc/TY32-S2CS].

16. Nancy M. P. King, *Human Gene-Editing Research: Is the Future Here Yet?*, 97 N.C. L. REV. 1051, 1052 (2019).

17. *Is Germline Gene Therapy Ethical?*, YOUR GENOME, https://www.yourgenome.org/debates/is-germline-gene-therapy-ethical#q4 [https://perma.cc/RDM8-5BLY].

parent-consumers.[18] Genetically modified babies remained speculative until November 2018, when Chinese scientist Dr. He Jankui announced that he had created the world's first "CRISPR babies," twin girls named Lulu and Nana.[19]

To conduct his experiment, Dr. He recruited couples in which the men had HIV infection and the women did not.[20] After creating embryos by fertilizing the eggs with the sperm, Dr. He used CRISPR to edit the embryos and disable a gene that helps HIV enter healthy cells, for the purpose of giving the twin girls resistance to HIV.[21] Notably, however, "Dr. He admitted that the edit was not successful in one of the embryos, and it is unclear whether it was completely or even partially successful in the other."[22] Dr. He's experiment generated an outpouring of criticism and hand-wringing from scientists and bioethicists around the world, who labeled him a "rogue" scientist[23] whose unethical experiment was "amateurish" and "unconscionable."[24] The safety risks and long-term effects of Dr. He's experiment will remain a mystery for years to come, meaning the twins will likely be studied for the rest of their lives.[25] Although Lulu and Nana brought bioethical considerations of gene editing to the forefront, researchers are still striving to advance CRISPR technology, with one of the most recent developments occurring right now in New York City.[26]

Currently, reproductive biologists at Weill Cornell Medicine are making the first attempt at genetically editing the DNA in human sperm

18. Tara R. Melillo, Note, *Gene Editing and the Rise of Designer Babies*, 50 VAND. J. TRANSNAT'L L. 757, 760 (2017).

19. Marilynn Marchione, *Chinese Researcher Claims First Gene-Edited Babies*, ASSOCIATED PRESS (Nov. 26, 2018), https://apnews.com/4997bb7aa36c45449b488e19ac83e86d [https://perma.cc/7QB7-3QML].

20. *Id.*

21. Alice Park, *'They Will Be Studied for the Rest of Their Lives.' How China's Gene-Edited Twins Could Be Forever Changed by Controversial CRISPR Work*, TIME (Nov. 29, 2018, 3:49 PM) https://time.com/5466967/crispr-twins-lives [https://perma.cc/Q3CJ-N9CC].

22. King, *supra* note 16, at 1069; *see also* Marchione, *supra* note 19.

23. Anthony King, *Rogue Chinese Scientist to Be Punished for Creation of First Gene-Edited Humans*, ROYAL SOC'Y OF CHEMISTRY: CHEMISTRY WORLD (Jan. 23, 2019), https://www.chemistryworld.com/news/rogue-chinese-scientist-to-be-punished-for-creation-of-first-gene-edited-humans/3010026.article [https://perma.cc/QD6U-KQK3].

24. Katarina Zimmer, *CRISPR Scientists Slam Methods Used on Gene-Edited Babies*, SCIENTIST (Dec. 4, 2018), https://www.the-scientist.com/news-opinion/crispr-scientists-slam-methods-used-on-gene-edited-babies--65167 [https://perma.cc/3D6A-XGLE].

25. Park, *supra* note 21.

26. Rob Stein, *Scientists Attempt Controversial Experiment to Edit DNA in Human Sperm Using CRISPR*, NPR (Aug. 22, 2019), https://www.npr.org/sections/health-shots/2019/08/22/746321083/scientists-attempt-controversial-experiment-to-edit-dna-in-human-sperm-using-cri?utm_medium=RSS&utm_campaign=storiesfromnpr [https://perma.cc/HS4A-GT6M].

using CRISPR.[27] The controversial research is aimed at preventing genetic disorders that are passed down from men, including certain forms of male infertility.[28] The researchers are beginning with a gene that increases the risk of breast, ovarian, prostate and other cancers.[29] Because DNA is packed very tightly inside the head of each sperm, it is difficult to insert the microscopic CRISPR tool.[30] To overcome this challenge, the Cornell scientists electrically shock the sperm with the goal that the shock will cause the cells to loosen up for a moment so that CRISPR can get inside.[31] June Wang, a lab technician conducting the experiments at Cornell, admits that "[i]t's kind of a weird concept" but states that "it works pretty well."[32]

Although the experiments are still underway and are not yet successful, the research raises many of the same hopes—and fears—as editing the genes in human embryos.[33] Nevertheless, the researchers defend their work.[34] Gianpiero Palermo, who runs the lab where the experiment is being conducted, states, "I think it's important from the scientific point of view to investigate in an ethical manner to be able to learn if it's possible."[35] Palermo went on to say, "If we can wipe out a particular gene, it would be incredible."[36] However, Françoise Baylis, a bioethicist at Dalhousie University in Canada who is advising the World Health Organization, expresses the view that editing DNA in sperm raises the same troubling questions as editing DNA in embryos.[37] In addition to safety concerns for resulting babies and future generations in the event that the genetically edited sperm is used, there are profound ethical and social concerns about conducting the research in the first place.[38] As bioethicist Ben Hurlbut put it,

> There's reason to worry about undertaking the research before we've asked the question properly whether we would ever actually want to use those techniques . . . . Once those techniques are developed, it becomes much harder to govern them. If you've done the hard work of developing the recipe, someone else can bake the cake.[39]

27. *Id.*
28. *Id.*
29. *Id.*
30. *Id.*
31. *Id.*
32. *Id.*
33. *Id.*
34. *Id.*
35. *Id.*
36. *Id.*
37. *Id.*
38. *Id.*
39. *Id.*

The willingness of researchers to develop human uses of CRISPR demonstrates the pressing need to regulate such advancements and, in particular, its possible use to genetically edit human sperm. Part I of this Note will provide a scientific background necessary to understand genetically edited sperm, including a brief history of relevant scientific advancements, a discussion of CRISPR-Cas9 technology, and an explanation of somatic cells and germline cells. Part II will analyze various ethical considerations regarding editing human sperm, including safety concerns, informed consent issues, the debate between treatment and enhancement, and the potential for new forms of social inequality. Part III will discuss the most applicable regulations in the United States under the Food and Drug Administration and National Institutes of Health, and ultimately conclude that as it stands, the law is unprepared for the development of genetically edited sperm. Part IV will propose a resolution to address these concerns, including a federal licensing regime, a call for public engagement, and regulations to mitigate equality and accessibility concerns if sperm editing is commercialized.

I. THE SCIENCE: GENE EDITING AND CRISPR TECHNOLOGY

To provide a more comprehensive understanding of the central issues involved with using CRISPR to genetically edit human sperm, this Part will offer a brief scientific background, including a description of the most relevant scientific developments leading up to the advent of modern-day gene editing, an explanation of gene editing today using CRISPR-Cas9 technology, and an explanation of the distinction between somatic editing and germline editing.

A. SCIENTIFIC DEVELOPMENTS THAT LED TO MODERN-DAY GENE EDITING

In order to truly understand the implications of genetically editing human sperm, it is necessary to have a basic understanding of Assisted Reproductive Technology ("ART"). For example, Dr. He genetically edited the embryos during in-vitro fertilization ("IVF"), an ART procedure, before implanting them into the mother to bring the twin girls to term.[40] ART includes "all fertility treatments in which both eggs and embryos are handled."[41] ART refers to alternative methods to achieve pregnancy in

40. AM. SOC'Y FOR REPROD. MED., ASSISTED REPRODUCTIVE TECHNOLOGY: A GUIDE FOR PATIENTS 3 (2015), http://www.fertilityanswers.com/wp-content/uploads/2016/04/assisted-reproductive-technologies-booklet.pdf [https://perma.cc/BWR6-M2VP].

41. *What Is Assisted Reproductive Technology?*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/art/whatis.html [https://perma.cc/8GCV-RJW3].

situations in which naturally conceiving a child is infeasible.[42] The modern era of ART began with the birth of Louise Brown in 1978.[43] Brown was the first "test tube baby" conceived through IVF, a technique in which fertilization is accomplished outside of the woman's body.[44] IVF involves removing eggs from a woman's ovaries, fertilizing the eggs with sperm, and implanting the eggs into a woman's uterus.[45] This is distinguishable from artificial insemination[46] that involves injecting sperm into a woman, meaning fertilization is accomplished inside of the woman's body.[47] Following the birth of Louise Brown, the proliferation of ART has been astounding.[48] The National Academies of Sciences, Engineering and Medicine estimate that more than five million babies have been born as a result of IVF.[49] The Academies also estimate that, although there are no official numbers, more than one million embryos remain frozen in storage across the United States, many of which are left over from IVF procedures and may never be used.[50] Moreover, the Centers for Disease Control and Prevention reported that as of 2015, there were 499 ART clinics operating in the United States.[51]

Scientists made significant advancements in embryonic research after the development of ART. Previously, the notion of "choosing" the genes of potential offspring focused on preimplantation genetic diagnosis ("PGD")—a technique used during IVF that allows doctors to screen embryos for

42. AM. SOC'Y FOR REPROD. MED., *supra* note 40.

43. Raymond C. O'Brien, *The Immediacy of Genome Editing and Mitochondrial Replacement*, 9 WAKE FOREST J.L. & POL'Y 419, 431 (2019).

44. *Id.*

45. *In Vitro Fertilization (IVF)*, MEDLINEPLUS, https://medlineplus.gov/ency/article/007279.htm [https://perma.cc/AJ5B-NCT6].

46. Artificial insemination is not considered an Artificial Reproductive Technology procedure because it only involves the handling of sperm whereas ART procedures involve the handling of both eggs and embryos. *What Is Assisted Reproductive Technology?*, *supra* note 41.

47. O'Brien, *supra* note 43.

48. Today, ART not only includes IVF but also gamete intrafallopian transfer ("GIFT"), when eggs and sperm are transferred into the fallopian tube and fertilization occurs inside the tube; zygote intrafallopian transfer ("ZIFT"), when the egg is fertilized outside the body and the zygote is placed in the fallopian tube before cell division takes place; pronuclear stage tubal transfer ("PROST"); and tubal embryo transfer ("TET"). AM. SOC'Y FOR REPROD. MED., *supra* note 40, at 23–28.

49. NAT'L ACADS. SCI., ENG'G & MED., MITOCHONDRIAL REPLACEMENT TECHNIQUES: ETHICAL, SOC., & POL'Y CONSIDERATIONS 60 (Anne Claiborne, Rebecca English & Jeffrey Kahn eds., 2016) (ebook).

50. *Id.* at 105.

51. CTRS. FOR DISEASE CONTROL & PREVENTION, 2015 ASSISTED REPRODUCTIVE TECHNOLOGY: NATIONAL SUMMARY REPORT 7 (2017), https://www.cdc.gov/art/pdf/2015-report/ART-2015-National-Summary-Report.pdf [https://perma.cc/55W9-R8UM].

genetic predispositions, disorders, and diseases,[52] such as Down syndrome.[53] Parents then select which embryos to implant based on their genetic traits, while embryos with undesired genes are typically discarded or donated to research.[54] Today, the notion of "choosing" the genes of potential offspring is also possible through gene editing, but ART procedures, such as IVF, remain the methods by which a child could be created with the desired traits.

"The idea of using gene editing to treat disease or alter traits dates to at least [1953] and the discovery of the double-helix structure of DNA."[55] By 1972, scientists discovered how to "copy and paste" DNA, making it possible to mix and match genes to create hybrid sequences called recombinant DNA.[56] The ability to create recombinant DNA paved the way for "gene therapy,"[57] which is a technique that uses DNA to treat a genetic disease.[58] The first approved gene therapy clinical trial for treatment of human disease occurred in 1990.[59] Different methods of gene therapy include replacing a mutated gene that causes disease with a functioning copy of the gene, inactivating a mutated gene, and introducing a new gene into the body to help fight a disease.[60]

Although gene therapy is a promising treatment option for various diseases, including inherited disorders, cancer, and viral infections, the technique is still relatively new and safety concerns are not fully resolved.[61]

52. Gregory Katz & Stuart O. Schweitzer, *Implications of Genetic Testing for Health Policy*, 10 YALE J. HEALTH POL'Y L. & ETHICS 90, 93 (2010); AM. SOC'Y FOR REPROD. MED., *supra* note 40, at 10.

53. Jaime King, *Predicting Probability: Regulating the Future of Preimplantation Genetic Screening*, 8 YALE J. HEALTH POL'Y L. & ETHICS 283, 290 (2008).

54. *Id.* at 291.

55. Judith L. Fridovich-Keil, *Gene Editing,* ENCYCLOPEDIA BRITANNICA (June 4, 2019), https://www.britannica.com/science/gene-editing [https://perma.cc/J9XL-66KK]; *see also* O'Brien, *supra* note 43, at 441.

56. Ariel Bleicher, *Genome Editing Before CRISPR: A Brief History*, MEDIUM (Oct. 23, 2018), https://medium.com/ucsf-magazine/genome-editing-before-crispr-a-brief-history-f02c1e3e2344 [https://perma.cc/77YB-VQSC]; *1972: First Recombinant DNA*, NAT'L HUM. GENOME RES. INST., https://www.genome.gov/25520302/online-education-kit-1972-first-recombinant-dna [https://perma.cc/64VR-F9PT].

57. Bleicher, *supra* note 56. Gene therapy is also referred to as "gene-transfer," "gene augmentation," or "gene-addition" research to distinguish it from gene editing. King, *supra* note 16, at n.25.

58. *What Is Gene Therapy?*, YOUR GENOME, https://www.yourgenome.org/facts/what-is-gene-therapy [https://perma.cc/P2SB-6HPP].

59. Sharon Begley, *Out of Prison, the 'Father of Gene Therapy' Faces a Harsh Reality: A Tarnished Legacy and an Ankle Monitor*, STAT (July 23, 2018), https://www.statnews.com/2018/07/23/w-french-anderson-father-of-gene-therapy [https://perma.cc/S4E2-6B9R].

60. *What Is Gene Therapy?*, MEDLINEPLUS, https://ghr.nlm.nih.gov/primer/therapy/genetherapy [https://perma.cc/88DW-96DD].

61. *Id.*; *Is Gene Therapy Safe?*, MEDLINEPLUS, https://ghr.nlm.nih.gov/primer/therapy/safety [https://perma.cc/472D-2SVM].

Because the transfer of the gene is not a precise technique, copies of the new gene may be added at unpredictable spots in the genome or be delivered into a cell in the wrong organ, creating the potential for major health problems.[62] For example, an inserted gene may interfere with a gene involved in regulating cell division which can result in cancer, or the gene may prompt an adverse cellular response.[63] In 1999, eighteen-year-old Jesse Gelsinger was the first person publicly identified as dying in a clinical trial for gene therapy.[64] Notwithstanding Gelsinger's death, the number of gene therapy clinical trials continues to grow.[65]

Researchers began searching for tools they could better control.[66] Scientists needed to be able to break DNA at precisely the desired location so that the "bad" sequence could be replaced by the "good" sequence at that particular spot.[67] By the mid-2000s, gene editing became possible.[68] Before the discovery of CRISPR-Cas9, two approaches were used to make site-specific breaks in DNA to accomplish gene editing: zinc finger nucleases ("ZFNs") and transcription activator-like effector nucleases ("TALENs").[69] However, these techniques are expensive, complex, and difficult to work with in laboratories, and thus failed to gain widespread traction.[70]

B. MODERN-DAY GENE EDITING WITH CRISPR-CAS9 TECHNOLOGY

One of the reasons that gene editing is of great interest to scientists and researchers looking for means of treating genetic mutations is that it seems to be more precise, accurate, and effective than gene therapy.[71] Gene editing, in contrast with gene therapy, does not involve flooding the organism with new copies of sequence.[72] Rather, gene editing involves removing mutated or damaged DNA sequences from genes, as well as replacing these damaged

62. *What Is Gene Therapy?*, *supra* note 58.

63. *Id.*

64. Sheryl Gay Stolberg, *The Biotech Death of Jessee Gelsinger*, N.Y. TIMES MAG. (Nov. 28, 1999), https://www.nytimes.com/1999/11/28/magazine/the-biotech-death-of-jesse-gelsinger.html [https://perma.cc/AK6W-RM22].

65. *See* ALL. FOR REGENERATIVE MED., QUARTERLY REGENERATIVE MEDICINE SECTOR REPORT 8–10 (2019), http://alliancerm.org/wp-content/uploads/2019/11/ARM_Q3_2019_FINAL-1.pdf [https://perma.cc/NE2K-75DB]. By the end of the third quarter of 2019, there were 370 gene therapy clinical trials in progress. Of the 370, 115 were in Phase I, 223 were in Phase II, and 32 were in Phase III. *Id*. at 8.

66. Bleicher, *supra* note 56.

67. Fridovich-Keil, *supra* note 55.

68. O'Brien, *supra* note 43, at 442.

69. Fridovich-Keil, *supra* note 55.

70. King, *supra* note 16, at 1055.

71. *See* Rodolphe Barrangou & Jennifer A. Doudna, *Applications of CRISPR Technologies in Research and Beyond*, 34 NATURE BIOTECHNOLOGY 933, 933 (2016).

72. *See id.* at 935–36.

sequences with a correctly functioning version of the gene.[73] To accomplish this, a gene-editing tool must be used to break the strands in the mutated or damaged DNA.[74] Gene editing prior to the discovery of CRISPR used ZFNs and TALENs, but these tools "required very precise and painstaking construction of the proteins that break DNA . . . to hit the right places where the DNA should be broken."[75]

Over the past decade, CRISPR-Cas9 has become the most widely used gene-editing tool.[76] The technique uses guide RNA, which is designed to locate and bind to a target sequence of DNA.[77] This is because "the guide RNA has RNA bases that are complementary to those of the target DNA sequence," which means that theoretically the guide RNA will only bind to that particular sequence.[78] The guide RNA "guides" the Cas9 enzyme to the same location in the DNA sequence, and then the Cas9 enzyme acts as a pair of scissors that cuts both strands of the DNA double helix at the specific location in the genome.[79] Once cut, DNA can be added or removed at that particular site.[80]

CRISPR technology is simple enough that "do-it-yourself" CRISPR kits are now sold online, enabling people to experiment with gene editing in their own home.[81] Relative to gene editing in the past, CRISPR is so precise that some researchers have compared it to a "word processor, capable of effortlessly editing a gene down to the level of a single letter."[82] Although there is evidence of its precision, and thus a lower likelihood of harmful "off-target" effects, this risk has not been completely eliminated.[83]

73. *Id.* at 933–34.

74. *Id.*

75. King, *supra* note 16, at 1060.

76. *See* Cong et al., *supra* note 12, at 819–22.

77. *What Is CRISPR-Cas9?*, YOUR GENOME, https://www.yourgenome.org/facts/what-is-crispr-cas9 [https://perma.cc/PZ8S-M6FY].

78. *Id.*

79. *Id.*

80. *Id.* For a video illustrating how CRISPR-Cas9 works, see McGovern Institute, *Genome Editing with CRISPR-Cas9*, YOUTUBE (Nov. 5, 2014), https://www.youtube.com/watch?v=2pp17E4E-O8 [https://perma.cc/6UZY-GTF9].

81. Kevin Curran, *How on Earth Are We Currently Regulating Human Genetic Modification?*, RISING TIDE BIOLOGY (Sept. 15, 2020), https://www.risingtidebio.com/human-gene-therapy-regulations-laws [https://perma.cc/K5GJ-AMPW]; *see also Beginner Kits*, ODIN, https://www.the-odin.com/beginner-kits [https://perma.cc/R6CC-48Z8]. California resident Josiah Zayner operates The Odin, a company that sells "DIY" CRISPR kits. At one point, the company offered a kit to modify a human gene called myostatin, but that kit is no longer for sale. The Odin still offers kits that allow purchasers to modify bacteria DNA, which sell for under two hundred dollars.

82. Jennifer Kahn, *The CRISPR Quandary*, N.Y. TIMES MAG. (Nov. 9, 2015), https://www.nytimes.com/2015/11/15/magazine/the-crispr-quandary.html?_r=0 [https://perma.cc/X7PT-U6MN].

83. Morgan L. Maeder & Charles A. Gersbach, *Genome-Editing Technologies for Gene and Cell*

C. THE DISTINCTION BETWEEN SOMATIC EDITING AND GERMLINE EDITING

Before delving into the implications of using CRISPR on human sperm, it is necessary to understand an ethically relevant division of gene editing: genetically editing somatic cells versus genetically editing germline cells. Somatic cells are "cells other than sperm and egg cells,"[84] such as lung, skin, or blood cells.[85] Changes made to genes in somatic cells only affect certain tissues in that particular individual and are therefore not passed from one generation to the next.[86] Germline cells are egg and sperm cells.[87] Changes made to genes in germline cells, including the genes of an early-stage embryo,[88] affect all the cells in the resultant person and are therefore passed down to future generations.[89] Germline gene editing accentuates the ethical issues inherent in changing the human genome,[90] including whether it would be permissible to use this technology to attempt to enhance human beings, including enhancements that would pass on to future generations.[91]

It is from the combination of the discovery of DNA, ART, and gene editing that we arrive at this point. The reality of modern gene editing now focuses not on whether science could edit inheritable human genes, but instead, whether it should; and if so, how to go about doing it.

II. ETHICAL CONSIDERATIONS OF GENETICALLY EDITING SPERM

The ongoing Cornell research that is attempting to use CRISPR to genetically edit the DNA in human sperm raises many of the same ethical considerations as editing the DNA in human embryos. As Dr. He's experiment in China demonstrated, once a technology is successfully

Therapy, 24 MOLECULAR THERAPY 430, 434–35 (2016).

84. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 8.

85. G. Owen Schaefer, *Why Treat Gene Editing Differently in Two Types of Human Cells?*, CONVERSATION (Dec. 7, 2015), https://theconversation.com/why-treat-gene-editing-differently-in-two-types-of-human-cells-51843 [https://perma.cc/DST5-E6W2].

86. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 8.

87. *Id.*

88. Henry T. Greely, *CRISPR'd Babies: Human Germline Genome Editing in the 'He Jiankui Affair*,*'* 6 J.L. & BIOSCIENCES 111, 114–15 (2019). Early-stage embryo editing is germline editing, but not all embryo editing will be germline editing. For example, in a later-stage embryo, one could selectively edit only the cells that have already differentiated along a path in which they could not become germline cells. This would be embryo editing, but not germline editing.

89. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 8.

90. This Note focuses on germline gene editing, rather than somatic, because genetically editing sperm involves germline modification.

91. *What Are Genome Editing and CRISPR-Cas9?*, *supra* note 8.

developed, it becomes much more difficult to control its use. This "use" of the technology has the potential for the most profound result—that is, the creation of a living, breathing human being, who was part of an experiment from the moment he or she was conceived.

A. SAFETY

One of the most central issues with using CRISPR to conduct gene editing is whether it is safe. In particular, would it ever be safe to create a human being with genetically edited sperm? Safety concerns are inherent in new scientific developments. For example, although IVF had worked without any problem in many different types of animals, the efforts to produce a human child through IVF raised concerns that the child might have birth defects and even die.[92] However, the birth of Louise Brown served to reduce such fears, leading to the birth of many more IVF babies. Years later, when Brown naturally conceived a healthy son, these fears were largely put to rest.[93] IVF is now a generally accepted procedure;[94] however, in the decades that have passed since Brown's birth, researchers have gained a better understanding of safety risks. For example, studies have shown that children conceived through IVF have a higher risk of low birthweight, perinatal mortality, preterm delivery, preterm rupture of membranes, and induction of labor.[95] Previously, many of these complications were attributed to the higher proportion of multiple pregnancies that often occur with IVF.[96] However, studies in which only singleton pregnancies were considered have likewise shown that these problems occur more frequently in IVF children.[97] One of the reasons Dr. He's experiment was so highly criticized was that the safety of the procedure was entirely unestablished.[98] It seems that Lulu and Nana will provide the first opportunity for doctors to look at the potential consequences of editing human embryos.[99]

92. Arthur Caplan, *New IVF Dilemmas Make Old Fears Seem Quaint*, NBC NEWS (July 24, 2008, 5:24 PM), http://www.nbcnews.com/id/25837220/ns/health-health_care/t/new-ivf-dilemmas-make-old-fears-seem-quaint/#.XcSfvJNKhZg [https://perma.cc/YMZ3-ULJ8].

93. *Id.*

94. *Id.*

95. Shilpi Pandey, Ashalatha Shetty, Mark Hamilton, Siladitya Bhattacharya & Abha Maheshwari, *Obstetric and Perinatal Outcomes in Singleton Pregnancies Resulting from IVF/ICSI: A Systematic Review and Meta-Analysis*, 18 HUM. REPROD. UPDATE 485, 485 (2012).

96. *Id.* at 486.

97. *Id.* at 485.

98. Zimmer, *supra* note 24.

99. New research suggests that Lulu and Nana's ability to learn and form memories may have inadvertently been enhanced due to their CRISPR procedure. For a more detailed explanation, see Antonio Regalado, *China's CRISPR Twins Might Have Had Their Brains Inadvertently Enhanced*, MIT TECH. REV. (Feb. 21, 2019), https://www.technologyreview.com/s/612997/the-crispr-twins-had-their-bra

Although it has been said that CRISPR is an "overwhelmingly efficient and specific" method for editing DNA,[100] it nonetheless poses several safety concerns including off-target genome modifications, unexpected multigenerational side effects, and a debatable reversal mechanism.[101] CRISPR can target the wrong sites in the DNA and make unintended edits, "which could inactivate essential genes, activate cancer-causing genes, or cause chromosomal rearrangements."[102] Researchers have developed a variety of methods to detect off-target edits to reveal the frequency of such off-target modifications.[103]

However, the methods of detection present their own problems, such as missing off-target sites in the genome, presenting false negatives, and being time-consuming and expensive, especially for simple projects.[104] Therefore, scientists are actively trying to improve gene-editing techniques to increase specificity and reduce off-target effects.[105] Even if the CRISPR technique was perfectly "on-target," it could still lead to unexpected multigenerational side effects that present themselves in future generations.[106] These effects would have to be closely studied over time against a diverse backdrop to understand the full range of medical implications.[107] However, multigenerational clinical trials would impose significant time burdens and may be impractical.[108] Lastly, scientists have debated whether CRISPR has a validated reversal mechanism, or in other words, a way to "undo" the edits. Feng Zhang, a biochemist who played a central role in the development of CRISPR, has stated that "[o]nce you go down that path, it may not be so reversible."[109] However, George Church, a geneticist at Harvard Medical School who has conducted substantial research using CRISPR, disagrees.[110]

ins-altered [https://perma.cc/6GQW-74JJ].

100. NAT'L ACADS. SCI. ENG'G & MED., INTERNATIONAL SUMMIT ON HUMAN GENE EDITING: A GLOBAL DISCUSSION 1 (Steven Olson ed., 2015), https://www.nap.edu/read/21913/chapter/1 [https://perma.cc/2PXY-TWXT].

101. Niklaus H. Evitt, Shamik Mascharak & Russ B. Altman, *Human Germline CRISPR-Cas Modification: Toward a Regulatory Framework*, 15 AM. J. BIOETHICS 25, 25–28 (2015).

102. NAT'L ACADS. SCI. ENG'G & MED., *supra* note 100.

103. Xiao-Hui Zhang, Louis Y Tee, Xiao-Gang Wang, Qun-Shan Huang & Shi-Hua Yang, *Off-Target Effects in CRISPR/Cas9-Mediated Genome Engineering*, 4 MOLECULAR THERAPY–NUCLEIC ACIDS e264 (2015).

104. *Id.*

105. NAT'L ACADS. SCI. ENG'G & MED., *supra* note 100, at 2.

106. Evitt et al., *supra* note 101, at 27–28.

107. Sarah Ashley Barnett, Comment, *Regulating Human Germline Modification in Light of CRISPR*, 51 U. RICH. L. REV. 553, 568 (2017).

108. Evitt et al., *supra* note 101, at 27.

109. Specter, *supra* note 15.

110. *Id.*

Church says, "It strikes me as a fake argument to say that something is irreversible . . . . There are tons of technologies that are irreversible. But genetics is not one of them. . . . Eleven generations from now, if we alter something and it doesn't work properly we will simply fix it."[111]

Although the use of gene drives[112] has remained largely theoretical due to technical constraints, Church has proposed that "RNA-guided gene drives could reverse genome alterations that have already spread through populations."[113] He insists that "[t]he ability to update or reverse genomic alterations at the speed of a [gene] drive . . . represents an [] important safety feature."[114] Although "it may be possible to remove germline edits from the population" using this method, "significant research is needed before such [a] reversal mechanism[] [could be] made a reality."[115]

Many researchers and ethicists agree that germline editing should not be used for clinical reproductive purposes until it is shown to be sufficiently safe through research; the risk is not justified by the potential benefit.[116] Other ethicists argue that "there may never be a time when [germline gene] editing will offer a benefit greater than that of existing technologies, such as . . . PGD and . . . IVF."[117] However, there are some instances in which germline editing could address certain needs that PGD cannot.[118] For example, if both parents are homozygous for a disease-causing variant, all of their children would be expected to have the disease,[119] and therefore using PGD to select particular embryos would not fix the underlying problem. It is always possible for the prospective parents to use donor eggs or sperm, but this would not permit them to have children who are genetically related to both parents, and therefore germline editing could provide a viable

111. *Id.*

112. Gene drives are "systems of biased inheritance that enhance the likelihood a sequence of DNA passes between generations through sexual reproduction and potentially throughout a local population and ultimately all connected populations." James P. Collins, *Gene Drives in Our Future: Challenges of and Opportunities for Using a Self-Sustaining Technology in Pest and Vector Management*, 12 BMC PROC. 37, 37 (2018).

113. Kevin M. Esvelt, Andrea L. Smidler, Flaminia Catteruccia & George M. Church, *Concerning RNA-Guided Gene Drives for the Alteration of Wild Populations*, 3 ELIFE 1, 1, 10 (2014).

114. *Id.* at 10.

115. Evitt et al., *supra* note 101, at 26.

116. *What Are the Ethical Concerns of Genome Editing?*, NAT'L HUM. GENOME RES. INST., https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/ethical-concerns#1 [https://perma.cc/AE4R-XT9L].

117. *Id.*; Edward Lanphier, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner & Joanna Smolenski, *Don't Edit the Human Germ Line*, 519 NATURE 410, 410–11 (2015), https://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111 [https://perma.cc/27AD-QALJ].

118. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116.

119. *Id.*

alternative.

"Theoretically, editing DNA in sperm could be somewhat safer than editing DNA in . . . embryos" because "in sperm any changes would be present in every cell of any resulting offspring," whereas "in embryos it is possible to inconsistently edit and miss certain cells,"[120] resulting in "mosaicism."[121] Mosaicism is essentially a "patchwork" edit where some cells carry the edit but others do not.[122] To the contrary, if a change has unexpected deleterious effects, its presence in every cell in the body would be worse than if it were only present in some cells.[123] In its current state, the safety concerns of CRISPR remain a major issue, and the technique is still far from ready to modify the human germline.[124] As we have seen, however, this may not stop overly-ambitious scientists.

B. INFORMED CONSENT

Ethical human experimentation requires obtaining the informed consent of the subject prior to the research.[125] This stems from the idea of recognizing the intrinsic value of human beings, as well as respecting personal autonomy and protecting those with diminished autonomy.[126] Informed consent requires that both foreseeable risks and potential benefits be adequately expressed to the participant-subject.[127] Bioethicists assert that informed consent is not possible for germline genetic editing because, in addition to the risks being unknown, the future subjects of the current experiment are nonexistent at the time of the experiment.[128] In other words, it is impossible to receive informed consent from sperm. Although all biomedical research carries a degree of uncertainty and risk, germline editing specifically involves a divergence between the people giving consent and the people that ultimately bear the risks—that is, the resulting children who will have to live

120. Stein, *supra* note 26.

121. Heidi Ledford, *CRISPR Babies: When Will the World Be Ready?*, 570 NATURE 293, 295 (2019), https://www.nature.com/articles/d41586-019-01906-z [https://perma.cc/KEJ9-YVLR]; *see also* Eli Adashi & I. Glenn Cohen, *Heritable Genome Editing: Edited Eggs and Sperm to the Rescue?*, 332 JAMA 1754, 1754 (2019).

122. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116.

123. *See id.*

124. Barnett, *supra* note 107, at 567–68.

125. Mark McQuain, *Informed Consent and Genetic Germline Engineering*, TRINITY INT'L U.: BIOETHICS AT TIU (Feb. 19, 2019), http://blogs.tiu.edu/bioethics/2019/02/19/informed-consent-and-genetic-germline-engineering [https://perma.cc/4K4Q-TUQL].

126. Nicholas Geringer, *Sequencing the Regulations on Human Germline Editing Research*, 37 J. YOUNG INVESTIGATORS 22, 22 (2019).

127. *Id.*

128. *Id.*; McQuain, *supra* note 125.

with the genetic changes.[129] Moreover, because editing sperm would introduce heritable genetic changes into the germline, the problem of being unable to obtain consent from the persons affected stretches out infinitely to all future generations.[130]

The counterargument is that parents are already allowed to provide informed consent for decisions that affect their future offspring, including similarly complicated and ethically trying decisions such as PGD during IVF.[131] Is hand-selecting genetically favorable embryos and discarding the rest really that much different from creating a favorable embryo by using genetically edited sperm? Furthermore, one can argue that informed consent from subsequent generations is not warranted because nonexistent beings do not have that right, and therefore parental informed consent can suffice.[132] However, because informed consent requires knowledge of the potential risks, it may not be possible for parents to give truly informed consent to genetically altering their sperm so long as the risks of germline editing are unknown.[133]

Tina Rulli asserts that parental permission for therapy of a child rests on treating an existing disease.[134] Rulli argues that germline uses of CRISPR cannot be considered a cure or treatment because they fail to meet the counterfactual requirement that without the intervention, a person will suffer more or die earlier from a disease or disorder.[135] This is because if parents forego using CRISPR for reproductive purposes, it is not inevitable that a diseased child will exist.[136] Rather, it remains the parents' independent choice to bring the child into existence in the first place.[137] Therefore, it may be theoretically impossible for parents to consent to using CRISPR to genetically edit sperm because it does not involve an entity that is *already* suffering from a disease. In other words, although editing sperm can benefit a later-born child, that child did not exist at the time of the edit and did not have an ethical claim on such "treatment." Using CRISPR to genetically edit sperm may lack the therapeutic justification to balance the risks of gene editing.[138]

129. Geringer, *supra* note 126.
130. Evitt et al., *supra* note 101, at 27.
131. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116.
132. Evitt et al., *supra* note 101, at 27.
133. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116.
134. Tina Rulli, *Reproductive CRISPR Does Not Cure Disease*, 33 BIOETHICS 1072, 1076 (2019).
135. *Id.*
136. *Id.* at 1077.
137. *Id.*
138. *Id.* at 1074–76.

C. TREATMENT OR ENHANCEMENT?

Some bioethicists are concerned that any gene editing, even for therapeutic uses, will lead us down a slippery slope to making nontherapeutic "enhancements" in offspring.[139] Others, such as Australian philosopher and bioethicist Julian Savulescu, argue that once such techniques are proved safe and effective, there is a "moral imperative" to treat genetic disease and that concerns about enhancement should simply be managed through policy and regulation.[140] Much debate has focused on the distinction between treatment and enhancement, which is a difficult line to draw and necessarily involves making value judgments about which human characteristics are desirable and undesirable. With regard to the Cornell experiment, is editing human sperm to prevent male infertility in resulting offspring considered treatment or enhancement?

This question was similarly considered with regard to Lulu and Nana. If successful, would giving HIV-immunity be considered treatment or enhancement? Notably, Dr. He first "washed" the sperm to separate it from semen, which is the fluid where HIV can lurk, before using it to fertilize the eggs.[141] Studies have shown that the "washing" process makes it virtually impossible for the sperm to transmit HIV to the embryo.[142] Additionally, the fathers were on anti-HIV medications, making it unlikely they would infect their children in the first place.[143] Considering that the embryos were not diseased in any way, let alone infected with HIV, giving the twins resistance to HIV for personal encounters later on in life looks much more like enhancement rather than treatment.[144]

The President's Council on Bioethics distinguished "therapy" and "enhancement" in their report *Beyond Therapy* as follows:

> "Therapy" . . . is the use of biotechnical power to treat individuals with known diseases, disabilities, or impairments, in an attempt to restore them to a normal state of health and fitness. "Enhancement," by contrast, is the

139. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116; *see also* Masci, *supra* note 1.

140. Julian Savulescu, Jonathan Pugh, Thomas Douglas & Christopher Gyngell, *The Moral Imperative to Continue Gene Editing Research on Human Embryos*, 6 PROTEIN & CELL 476, 476–478 (2015).

141. Marchione, *supra* note 19.

142. Maryam Zafer, Hacsi Horvath, Okeoma Mmeje, Sheryl van der Poel, Augusto E. Semprini, George Rutherford & Joelle Brown, *Effectiveness of Semen Washing to Prevent Human Immunodeficiency Virus (HIV) Transmission and Assist Pregnancy in HIV-Discordant Couples: A Systematic Review and Meta-Analysis*, 105 FERTILITY & STERILITY 645, 647–50 (2016).

143. Park, *supra* note 21.

144. King, *supra* note 16, at 1070.

> directed use of biotechnical power to alter, by direct intervention, not disease processes but the "normal" workings of the human body and psyche, to augment or improve their native capacities and performances.[145]

Even if it were settled that therapy entails treating diseases, disabilities, and impairments, what if many people with a condition do not regard it as a disability? Take genetic deafness, for example. If a person is perfectly healthy in all other respects and does not view deafness as a disability, then giving them hearing may be considered enhancement. On the other hand, one could argue that using gene editing to ensure hearing is simply treatment, in the sense that retaining all of the human senses is a "normal state of health." The fact that a deaf person has means of communicating that do not involve the sense of hearing—and hence does not feel "disabled" or in need of "therapy"—is not inconsistent with classifying a cure for deafness as therapy rather than enhancement.[146]

The preceding line of reasoning can also be applied to human qualities or abilities that exist along a spectrum, such as intelligence. For example, using gene editing to increase a person's IQ from 55, which is associated with developmental or learning disabilities, to 100, which is an approximately average IQ, could arguably be considered treatment. Increasing the person's IQ to 100 could be equated to restoring a person's hearing, in the sense that both uses of gene editing would allow for a "normal," or average, state of health and being. However, would using gene editing to increase a person's IQ from 100 to 145, which is associated with extreme giftedness, be considered treatment or enhancement? Such an application of gene editing would likely amount to enhancement because the individual did not originally have a disease, disability, or impairment and thus was not "restored" to a "normal state of health." One could imagine a scenario in which the genetic editing of peoples' intelligence becomes a regular occurrence, creating a new, much higher average IQ. These two examples consider the opposite extremes of IQ scores and thus clearly demonstrate the difference between treatment and enhancement. However, a scenario in which gene editing is used to increase a person's IQ that falls in between the extremes demonstrates that the line between treatment and

145. The President's Council on Bioethics, *Beyond Therapy: Biotechnology and the Pursuit of Happiness* (Oct. 2003), https://bioethicsarchive.georgetown.edu/pcbe/reports/beyondtherapy/chapter1.html [https://perma.cc/683A-UH33].

146. For a discussion of gene editing technologies that can provide therapeutic approaches for hearing impairment and recent applications of gene editing in the inner ear, see Wen Kang, Zhuoer Sun, Xingle Zhao, Xueling Wang, Yong Tao & Hao Wu, *Gene Editing Based Hearing Impairment Research and Therapeutics*, 709 NEUROSCIENCE LETTERS 134326 (2019).

enhancement necessarily blurs.

D. EQUALITY

If gene editing is expensive, it may only be accessible to the wealthy. If the changes permitted by gene editing are beneficial, the current gap between the rich and the poor would be widened, embedding new forms of social inequality, discrimination, and conflict in human DNA.[147] This could potentially create a scenario in which society's elite simply go to a fertility clinic to have their sperm genetically edited to ensure the desirable traits of their children, leaving the poor and even middle class with their natural deficiencies.

To some extent, purchasing "superior" sperm from exclusive sperm banks—a widespread practice that is largely accepted by society[148]—already presents equality concerns regarding the ability to pay for "better" sperm. California Cryobank, the largest sperm bank in the country, sells one vial of "cream of the cup" sperm for approximately one thousand dollars.[149] Less than one percent of the twenty thousand men who apply to be donors each year are accepted, and the company brags that "[i]t's tougher to get into California Cryobank than it is Harvard or Stanford."[150] The donors are screened for 280 genetic conditions and must provide a three-generation family medical history to check for an array of diseases and conditions.[151] Aside from health considerations, the bank requires all donors to be college-educated and prefers men who are over six feet tall with light eyes and brown hair, stating that these samples tend to sell faster.[152]

Nevertheless, the equality concerns with being able to purchase expensive sperm may be insignificant. The Society for Assisted Reproductive Technology states that the average cost of an IVF cycle in the United States is between ten thousand and fifteen thousand dollars.[153] While paying one thousand dollars for sperm may be out of reach for indigent people, it only represents a portion of the expense of fertility treatments and

147. *What Are the Ethical Concerns of Genome Editing?*, *supra* note 116.

148. Barnett, *supra* note 107, at 573.

149. Hailey Eber, *This L.A. Sperm Bank Is More Exclusive Than an Ivy League College*, L.A. MAG. (Apr. 2, 2019), https://www.lamag.com/citythinkblog/sperm-bank-california-cryobank [https://perma.cc/AZA8-59TY]. The cost per vial for all ID Disclosure donors is $995. Anonymous and Open donors are priced slightly less at $855.

150. *Id.*

151. *Id.*

152. *Id.*

153. *Frequently Asked Questions*, SOC'Y FOR ASSISTED REPROD. TECH., https://www.sart.org/patients/frequently-asked-questions [https://perma.cc/E6W6-VTR4].

therefore may not significantly affect who can use the "better" sperm to conceive a child. Moreover, the scope of equality concerns with expensive sperm banks may be narrower than equality concerns with genetically editing sperm using CRISPR. Donor sperm is generally purchased by couples who have fertility problems, such as when the male partner is sterile, as well as by single women or same-sex couples who wish to conceive a biological child,[154] whereas the people willing to pay money to edit their own sperm for desirable traits may not be limited to these subsets of the population.

On the other hand, if gene editing is inexpensive, or even covered by insurance, it is possible that the playing field would be somewhat leveled. If access to gene editing was largely independent of wealth, the presence of certain diseases, disabilities, and impairments could be reduced throughout the population, therefore decreasing the inequality gap between the rich and poor.

III. THE WILD WEST: A LACK OF EXISTING REGULATION IN THE UNITED STATES

As previously stated, Dr. He's experiment with Lulu and Nana demonstrates the grave reality that once a scientific development has been created, it becomes much more difficult to regulate its use. The Chinese Society for Cell Biology called the research "a serious violation of the Chinese government's laws and regulations and the consensus of the Chinese scientific community."[155] In light of Dr. He's premature use of CRISPR-Cas9 to genetically edit human embryos in disregard of the Chinese regulations, it becomes apparent that in the United States there needs to be stringent regulations to govern the coming biomedical developments—including the ability to genetically edit sperm using CRISPR. Although the Cornell experiments are not yet successful, and the safety concerns are still at issue, it is critical to begin implementing a mechanism of oversight due to the rapid advancements in gene-editing technology to date. This Part will focus on the most applicable current regulations under the Food and Drug Administration ("FDA") and the National Institutes of Health ("NIH"), as these organizations are the most relevant federal regulatory agencies within the United States, and will ultimately conclude that as it stands, the law is

154. NAT'L COLLABORATING CTR. FOR WOMEN'S & CHILDREN'S HEALTH, FERTILITY: ASSESSMENT AND TREATMENT FOR PEOPLE WITH FERTILITY PROBLEMS 389 (2d ed. 2013) (ebook).

155. Dennis Normile, *CRISPR Bombshell: Chinese Researcher Claims to Have Created Gene-Edited Twins*, SCI. MAG. (Nov. 26, 2018, 1:10 PM), https://www.sciencemag.org/news/2018/11/crispr-bombshell-chinese-researcher-claims-have-created-gene-edited-twins [https://perma.cc/L4AW-UN5V]. A discussion of the Chinese regulations is outside the scope of this Note. This Part will focus on the regulations of the United States and the United Kingdom.

unprepared for the development of genetically modified sperm.

A. THE FOOD AND DRUG ADMINISTRATION

Human germline gene editing, which includes genetically edited sperm, would be regulated in the United States within the framework for gene-transfer research and, once approved, for gene therapy.[156] The FDA made this position clear in its November 2017 statement, which was made in response to advances with CRISPR,[157] by stating the "FDA considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy. Gene therapy products are regulated by the FDA's Center for Biologics Evaluation and Research (CBER)."[158]

Generally speaking, researchers conducting a clinical trial of a new biological product must go through an application process with the FDA to have the product approved for use in a trial with human beings.[159] This process requires researchers to submit an Investigational New Drug ("IND") application, which must be approved by the FDA prior to the beginning of each trial.[160]

However, on June 4, 2019, the full Appropriations Committee of the United States House of Representatives restored a rider to a 2020 spending bill that bars the FDA from considering applications for any clinical trial "in which a human embryo is intentionally created or modified to include a heritable genetic modification."[161] This rider serves as a "de facto U.S. ban on germline editing to create a baby," which is actually explicitly barred in other countries.[162] Previously, House Democrats removed the rider because they were concerned that banning the FDA from deciding whether germline clinical trials should be allowed would limit important scientific research and hinder the development of helpful therapies.[163] Sean Tipton, an officer at the American Society for Reproductive Medicine, states that removing the ban

156. NAT'L ACADS. OF SCI., ENG'G & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 34 (Rona Briere & Helaine Resnick eds., 2017) (ebook).

157. Curran, *supra* note 81.

158. *Information About Self-Administration of Gene Therapy*, FDA (Nov. 21, 2017), https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy [https://perma.cc/R7J8-Q6CD].

159. NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 156, at 42.

160. *Id.*

161. Jocelyn Kaiser, *Update: House Spending Panel Restores U.S. Ban on Gene-Edited Babies*, SCI. MAG. (June 4, 2019, 1:45 PM), https://www.sciencemag.org/news/2019/06/update-house-spending-panel-restores-us-ban-gene-edited-babies [https://perma.cc/39CJ-UQHH].

162. *Id.*

163. *Id.*

"allows the FDA to do its job."[164] In other words, the FDA would simply review research requests, as it does for any other innovative therapy.[165] Others dislike the rider because it means that partisan politicians, rather than scientific or regulatory experts well-versed in the field, decided to ban germline clinical trials.[166]

House Republicans, on the other hand, have shown support for the ban on FDA-approved clinical trials involving germline modifications.[167] Concerns center around opening the door to clinical trials involving babies with genetic modifications that will pass down to future generations.[168] Alabama Representative Robert Aderholt said that the "prohibition on gene editing of human embryos . . . is a tremendous victory for those who are concerned about life."[169]

B. THE NATIONAL INSTITUTES OF HEALTH

The NIH sets regulations and requirements for certain types of experiments, including research with human cells that takes place entirely within a laboratory and does not involve either preclinical testing on nonhuman animals or clinical testing on humans.[170] At first glance, this would seemingly apply to the Cornell experiment that is attempting to genetically edit human sperm within a laboratory. Research that is subject to the "NIH Guidelines" must be reviewed and approved by an Institutional Biosafety Committee ("IBC").[171] The IBC assesses the research for risks to human health and the environment, and ensures that the researchers are adequately trained to conduct the work.[172] Importantly, however, the NIH Guidelines only apply to research that is conducted at or sponsored by an institution that receives NIH funding for such research.[173]

The NIH manages federal funding for gene-transfer research through its Recombinant DNA Advisory Committee ("RAC"). The RAC is a panel comprised of scientists, physicians, lawyers, ethicists, and laypersons.[174]

164. *Id.*

165. Andrew Joseph, *Congress Revives Ban on Altering the DNA of Human Embryos Used for Pregnancies*, SCI. AM. (June 5, 2019), https://www.scientificamerican.com/article/congress-revives-ban-on-altering-the-dna-of-human-embryos-used-for-pregnancies [https://perma.cc/JJ2A-J6LG].

166. Kaiser, *supra* note 161.

167. Joseph, *supra* note 165.

168. *Id*.

169. Adashi & Cohen, *supra* note 121.

170. NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 156, at 39.

171. *Id.*

172. *Id.*

173. *Id.*

174. The President's Council on Bioethics, *Reproduction and Responsibility: The Regulation of*

This panel determines whether to approve gene-editing proposals that seek government funding.[175] In addition to reviewing specific research proposals, the RAC also recommends changes to the NIH Guidelines.[176] Although the RAC discusses implications of gene-transfer research, "such deliberation tends to focus on safety issues, not on the broader ethical issues relating to the character of human procreation or the significance of increasing the genetic control of parents over offspring."[177]

C. DICKEY-WICKER

Each year since 1996, Congress has included the Dickey-Wicker Amendment as a rider to the appropriation bill for the Department of Health and Human Services ("HHS").[178] The Amendment prohibits the HHS from using any appropriated funds for creating, destroying, or knowingly injuring human embryos.[179] HHS funding also includes the funding for the NIH.[180] The Dickey-Wicker Amendment does not prohibit conducting the research itself, but only prohibits federal funding of the research.[181] In pertinent part, Dickey-Wicker prohibits federal funds from being used for "the creation of a human embryo or embryos for research purposes . . . [or] research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research" under applicable Federal regulations.[182]

The Dickey-Wicker Amendment demonstrates that congressional action has historically centered on embryos, with no mention of gene editing or the potential for germline editing.[183] This is likely attributable to the fact that, until recently, the possibility of human genetic modification was purely speculative.[184] Because Dickey-Wicker is only concerned with human embryos, the Amendment does not apply to using CRISPR to genetically

New Biotechnologies, (Mar. 2004), https://bioethicsarchive.georgetown.edu/pcbe/reports/reproductionandresponsibility/chapter4.html [https://perma.cc/Y9JP-6R2N].

175. *Id.*

176. *Id.*

177. *Id.*

178. Megan Kearl, *Dickey-Wicker Amendment, 1996*, EMBRYO PROJECT ENCYCLOPEDIA (Aug. 27, 2010), https://embryo.asu.edu/pages/dickey-wicker-amendment-1996 [https://perma.cc/Q9NX-CZZJ].

179. *Id*.

180. KAVYA SEKAR, CONG. RESEARCH SERV., R43341, NATIONAL INSTITUTES OF HEALTH (NIH) FUNDING: FY1995-FY2021 (2020), https://fas.org/sgp/crs/misc/R43341.pdf [https://perma.cc/5YF9-LZAP].

181. Balanced Budget Downpayment Act, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

182. *Id.*

183. O'Brien, *supra* note 43, at 451.

184. The President's Council on Bioethics, *supra* note 174.

edit sperm so long as the experiments occur before implantation. In other words, although Dickey-Wicker would apply if edited sperm were used for the "creation of a human embryo," simply editing the sperm is not covered. Additionally, because Dickey-Wicker only restricts federal funds, privately funded projects remain untouched.[185]

D. CRITICISMS OF THE CURRENT REGULATORY SCHEME IN THE UNITED STATES

More than forty countries around the world have laws that explicitly prohibit inheritable genetic modifications of humans.[186] In the United States, however, there is no outright, explicit ban on germline editing.[187] In fact, the United States has often been referred to as the "Wild West" of reproductive technology.[188] While it is true that the United States' regulatory landscape has imposed certain restrictions on researchers,[189] the current regulations under the FDA and NIH focus on clinical trials and federal funding, and place particular emphasis on the human embryo. Funding restrictions and recommendations are not barriers to experimentation.[190] Therefore, the current regulatory scheme fails to adequately regulate the potential to use CRISPR to genetically edit human sperm.

Given that the FDA is currently banned from considering clinical trials in which embryos would have heritable genetic modifications,[191] the FDA is prohibited from allowing clinical trials in which edited sperm would be used to create a child. However, as long as the research on sperm remains preclinical—that is, there is no creation of an embryo or transfer for gestation—it falls outside of the FDA's purview. Therefore, the only federal

185. NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 156, at 43.

186. CTR. FOR GENETICS & SOC'Y, HUMAN GERMLINE MODIFICATION SUMMARY OF NATIONAL AND INTERNATIONAL POLICIES (2015), https://www.geneticsandsociety.org/sites/default/files/cgs_global_policies_summary_2015.pdf [https://perma.cc/QJQ7-78VW]; *see also* Motoko Araki & Tetsuya Ishii, *International Regulatory Landscape and Integration of Corrective Genome Editing into In Vitro Fertilization*, 12 REPROD. BIOLOGY & ENDOCRINOLOGY 108 (2014).

187. CTR. FOR GENETICS & SOC'Y , *supra* note 186; *see also* O'Brien, *supra* note 43, at 453.

188. David Magnus & Nicole Martinez, *In Embryo Research We Need Laws First, Then Science*, TIME (Feb. 2, 2016, 4;07 PM), https://time.com/4204059/crispr-regulation [https://perma.cc/RV5W-SHDC].

189. Bhaargavi Ashok & Jack Karsten, *Is There a Responsible Way Forward for Gene Editing?*, BROOKINGS (Oct. 29, 2019), https://www.brookings.edu/blog/techtank/2019/10/29/is-there-a-responsible-way-forward-for-gene-editing [https://perma.cc/B6QN-NXUT].

190. O'Brien, *supra* note 43, at 452.

191. Kaiser, *supra* note 161. For further information, see Adashi & Cohen, *supra* note 121, at 1755 ("Given that the editing of eggs and sperm is not mentioned in the statutory federal moratorium, limited political and doctrinal opposition to this approach may be assumed.").

restrictions on editing the DNA in human sperm relate to funding.[192]

Moreover, because NIH regulations only apply to research that receives NIH funding, and the NIH is banned from funding human germline editing, editing the DNA in human sperm is permissible with private funding.[193] Considering that CRISPR is easy to use and highly affordable, especially when compared to past gene-editing technologies, "it would not take an outrageous amount of money to try to do it privately."[194] This is particularly concerning because private research may not be subject to public scrutiny, which often encourages an evaluation of risk, morality, and process.[195] Aside from private sources, individual states can fund germline gene editing as well.[196] In fact, California, Connecticut, Maryland, New Jersey, and New York have all funded research projects that did not qualify for federal funds.[197]

In sum, unlike in some countries, such as the United Kingdom, in which regulations generally fall under a single statutory framework or regulatory agency,[198] in the United States the individual rules related to each stage of work or source of funding overlap, interact, and leave gaps.[199] As a result, the current regulatory scheme may discourage transparency and encourage private, unmonitored research. If a researcher can secure private funding and does not wish to conduct an FDA-approved clinical trial, it seems that this will obviate the need to go through stringent regulatory and ethical approvals.

IV. A PROPOSED RESOLUTION

Once research on genetically editing human embryos was "successful," in the sense that it became feasible to modify human cells, Dr. He exploited the possibility by prematurely using these methods to create "edited" human embryos in violation of Chinese regulations. Research on genetically editing human sperm, although not yet successful, thus presents the same opportunity for premature application at the moment when it becomes physically possible to modify human sperm. In light of the current regulatory

192. *See* NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 156, at 39–43.
193. Kaiser, *supra* note 161.
194. Barnett, *supra* note 107, at 579.
195. O'Brien, *supra* note 43, at 453.
196. NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 156, at 43.
197. *Id.* This Note will not discuss state law. Rather, the states' ability to fund research independently is mentioned to further demonstrate the incohesive regulatory framework within the United States.
198. *Id.* at 35.
199. *Id.*

gap that allows for preclinical privately funded research, as well as the risk that scientists will prematurely use scientific capabilities achieved through research despite the profound ethical concerns about using genetically edited sperm (discussed in Part II), this Part will propose the adoption of stringent regulations on conducting the research itself. The proposed regulations will be modeled after the United Kingdom's research rules for IVF. Furthermore, this Part will also propose regulations to address the equality and accessibility concerns about using CRISPR to edit sperm, which need to be addressed if sperm editing is commercialized.

Although an in-depth constitutional analysis is outside the scope of this Note, Congress likely has the authority to federally regulate genetically edited sperm under the Commerce Clause. Gene editing will likely have a significant economic impact throughout the country, especially in the event of widespread commercialization, and therefore have substantial effects on interstate commerce.

A. REGULATING THE RESEARCH

The United Kingdom has created rigorous yet flexible legislation and therefore has been at the forefront of scientific innovation regarding ART and associated technologies.[200] The Human Fertilisation and Embryology Act, which was first adopted in 1990, established the Human Fertilisation and Embryology Authority ("HFEA"), which regulates all research involving human embryos in the United Kingdom.[201] Some of the HFEA research regulations, although tailored toward embryos, can provide a framework for regulating research on genetically editing human sperm within the United States.

1. Establishing Licensure Requirements in the United States

The United States should establish a federal licensing system, based on that of the United Kingdom, to regulate both private and public research on genetically editing sperm. A licensing regime is a practical and tested solution that can promote scientific advancements, especially with regard to treating disease, while addressing safety risks and ethical concerns as they arise and are solved.

"The HFEA requires that researchers obtain a license for every

200. *See* Melillo, *supra* note 18, at 774.

201. *See generally* Department of Health, Human Fertilisation and Embryology Act 1990 – An Illustrative Text, DEP'T HEALTH, https://webarchive.nationalarchives.gov.uk/20130103041211/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_080205 [https://perma.cc/JV4J-QPWX].

project."[202] Before the researcher may submit an application for a license, an ethics committee must approve the research.[203] The HFEA also conducts inspections to ensure that certain standards are met.[204] A License Committee then decides whether to grant a license, which is valid for up to four years with the option to renew.[205] The Committee may also condition a license on researchers improving particular aspects of the research.[206] After granting a license, the HFEA continues to conduct inspections every two years and can even do so unannounced.[207] The findings from the inspections are presented to the License Committee, which decides whether to continue or to revoke the license.[208] Moreover, all inspection reports are publicly available and accessible online,[209] which promotes transparency of research. Just like the HFEA, all researchers applying for licenses in the United States should meet strict requirements, including educational standards, practical experience related to the research, and payment of a fee.[210] This will help respond to safety concerns and, in particular, do-it-yourself "garage" science.

2. Composition of the Licensing Committee

The ethics and licensing committees should be comprised of disinterested and well-trained scientific experts such as bioethicists, biologists, and researchers, as well as nonscientific members such as elected officials, lawyers, and laypersons. To promote objectivity, committee members should not have a conflict of interest with the proposed research. In addition to representing diverse disciplines and backgrounds, the committees should be somewhat adaptable to the project at issue. This can be likened to FDA regulations for Institutional Review Boards ("IRBs"), which are groups of people responsible for ensuring the ethical and responsible treatment of human subjects in research.[211] For example, if an IRB reviews research that involves a vulnerable category of human subjects, such as children, prisoners, or handicapped, the IRB is advised to include

202. Tracey Tomlinson, *A CRISPR Future for Gene-Editing Regulation: A Proposal for an Updated Biotechnology Regulatory System in an Era of Human Genomic Editing*, 87 FORDHAM L. REV. 437, 471 (2018).

203. *Id.*

204. *How We Regulate*, HUM. FERTILISATION & EMBRYOLOGY AUTHORITY, https://www.hfea.gov.uk/about-us/how-we-regulate [https://perma.cc/D8MX-EWCG].

205. *Id.*

206. *Id.*

207. *Id.*

208. *Id.*

209. *Id.*

210. Human Fertilisation and Embryology Act 2008, c. 22, § 16 (UK).

211. *See* 21 C.F.R. § 56.107 (2020).

one or more members who are knowledgeable about and experienced in working with that class of subjects.[212] The FDA regulations even consider the race, gender, cultural backgrounds, and community attitudes of IRB members.[213]

Similarly, the composition of the ethics and licensing committees should be tailored toward any sensitive aspects of the proposed research project to promote complete and adequate review. Because CRISPR presents a variety of safety concerns which require a scientific understanding of the technology, groups of scientific experts will be in the best position to balance the risks against the potential benefits and decide whether we can justifiably proceed. Likewise, each research experiment may present its own set of ethical concerns which should be debated amongst bioethicists and members of the public. Involving both scientific and nonscientific members is a superior means of reaching decisions over having members of Congress decide which research projects should be approved. A licensing system will create a flexible framework that can monitor the safety and morality of research on a case-by-case basis, while simultaneously adapting and responding to new scientific discoveries, ethical considerations, and cultural norms.

B. PROMOTING PUBLIC ENGAGEMENT

In addition to including nonscientific members and laypersons on the ethics and licensing committees, the United States should explore ways of engaging the public in discussions about gene editing. The United Kingdom's British Society for Gene and Cell Therapy hosts an annual "Public Engagement Day" to foster discussion and debate among various members of the public, such as students, patients, and caregivers.[214] Likewise, the United Kingdom and China held a public engagement training workshop, where government regulators, researchers, and members of the public discussed gene editing.[215]

The United States should follow the precedent set by the United Kingdom and China and similarly strive to promote public engagement and awareness with regard to gene editing. For example, the United States should hold annual summits in major cities across the United States that are open to

212. *See id*.

213. *Id.*

214. NAT'L ACADS. OF SCI., ENG'G & MED., *supra* note 156, at 58.

215. Steven Olson, *Second International Summit on Human Genome Editing: Continuing the Global Discussion Proceedings of a Workshop–in Brief*, NAT'L ACADS. SCI., ENG'G & MED. 6 (2019), https://www.nap.edu/read/25343/chapter/1#6 [https://perma.cc/F3ZY-ZWFW].

the public. These summits could be partially funded via a fee that is incorporated into the application process when a researcher applies for a license. To encourage attendance, admission should be free to all members of the public. To promote constructive discussion and debate, researchers should be encouraged to send representatives to the summit. One such incentive could be a reduction or partial refund of the application fee if a representative attends.

By encouraging members of the public to actively participate in discussions and become familiar with CRISPR technology and gene editing, citizens can better advocate on behalf of their communities and convey their opinions to elected officials. Public officials are considered a "vehicle for expressing the values and preferences of citizens, communities, and society as a whole."[216] Because societal values and preferences change over time,[217] especially with regard to rapidly advancing scientific developments and procedures, it is pertinent to be inclusive of both the public and elected officials to ensure that gene editing evolves with society, rather than ahead of it.

C. REGULATING THE POTENTIAL COMMERCIALIZATION

If genetically editing sperm becomes commercialized, the law should address associated equality and accessibility concerns. Although the idea of widespread use of edited sperm may seem foreign, it can be likened to the normalization of IVF. Since the birth of Louise Brown, more than five million babies have been born through IVF,[218] showing a general acceptance of the once-criticized procedure. The law should strike a balance between promoting widespread accessibility of genetically edited sperm to people of all socioeconomic backgrounds, while preserving parental autonomy to choose not to use the technology.

Insurance providers should not be permitted to adjust premiums based on whether an individual is a product of genetically edited sperm. If insurance companies were allowed to consider whether a person or their ancestors have received germline editing, those who choose to conceive naturally or were born before the advent of such technology would be financially disadvantaged.[219] One can imagine insurance providers seeking to lower deductibles for insureds who are predictably "cheaper" due to their

216. Jocelyne Bourgon, *Responsive, Responsible and Respected Government: Towards a New Public Administration Theory*, 73 INT'L REV. ADMIN. SCI. 7, 7 (2007).

217. *Id.*

218. NAT'L ACADS. SCI., ENG'G & MED., *supra* note 49, at 60.

219. Evitt et al., *supra* note 101, at 27.

modified germline. Likewise, insurance providers may be incentivized to increase deductibles for people with certain genetic conditions, rationalizing that they could have simply been avoided with edited sperm. These policies should remain true even if paying for a CRISPR procedure is significantly less expensive than the additional costs, such as medical expenses and specialized education, that are associated with diseases and disorders. Regardless of the morality of choosing to conceive a child with a disorder, it is still a matter of parental autonomy.[220]

CONCLUSION

Gene editing, and CRISPR technology specifically, are significant scientific advancements on which researchers are continuing to make rapid progress. These developments present a wide range of social, ethical, and policy concerns that must be carefully considered. Gene editing using CRISPR presents several safety concerns, including off-target genome modifications, unexpected multigenerational side effects, and a debatable reversal mechanism. It may not be possible to obtain informed consent for germline genetic editing because, in addition to the risks of the procedure not being fully understood, the resulting children who would ultimately bear the risks of the genetic changes would be unable to consent at the time the editing occurs. Using gene editing to correct diseases, disabilities or impairments also presents the difficulty of distinguishing treatment from enhancement, which inherently involves making value judgements about which human characteristics are desirable and undesirable. Lastly, if gene editing is expensive, the gap between the rich and the poor will widen, creating new forms of social inequality, discrimination, and conflict in human DNA.

As Dr. He's experiment with Lulu and Nana demonstrated, scientists may seek to prematurely use gene editing techniques in disregard of the future consequences or consensus among scientific and legal communities. The Cornell research attempting to genetically edit the DNA in human sperm thus demonstrates the pressing need to implement regulations in the United States, especially in light of the current regulatory gap which allows for preclinical, privately funded research.

A proposed resolution must take a forward-thinking approach, considering both the research itself and the potential use and commercialization of edited sperm. Similar to the United Kingdom, the United States should establish a federal licensing system that requires all researchers to obtain a license prior to conducting their research. The

220. *Id.* at 27–28.

licensing committee should be comprised of both scientific and nonscientific members and, if necessary, tailored toward any sensitive aspects of the proposed research project. The United States should also promote awareness and public engagement of gene editing so that citizens can better advocate on behalf of their communities and convey their opinions to elected officials. Lastly, the law should strike a balance between promoting accessibility of CRISPR technology and preserving parental autonomy. Together, this regulatory framework will help prevent premature experimentation, while encouraging the ethical progression of gene editing and CRISPR technology.