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Beyond Dr. Frankenstein's Monster: Human Germline Editing and the Implications of Waiting to Regulate

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Beyond Dr. Frankenstein's Monster: Human Germline Editing and the Implications of Waiting to Regulate

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From the birth of bioethics in the United States to the hindrance of advancement caused by laws that claim to remove barriers to innovation, CRISPR and its germline editing abilities simply cannot live up to their full potential in the United States unless current limitations are lifted and a more reasonable approach is taken. While scientific acronyms and analogies to scissors and word processing functions abound in CRISPR-related articles, many focus on the patent for the technology itself. Few seek to resolve the discord that abounds in federal regulations of this emerging biotechnology. This Comment seeks to do just that and advocates for the adoption of the 2017 American Society of Human Genetics position statement as a rational and research-based approach.

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1. J.D. Candidate, Northern Illinois University College of Law, December 2018. I would like to dedicate this article to my patient and ever-faithful family and friends. First to my husband Mark, for his love, reminders to take breaks, encouragement, and provision of writing snacks. Next to my mother, Julie Marshall, without whom this article topic would have never crossed my mind and for her constant willingness to answer science-based questions and simplify difficult topics. Also to my father, David Marshall, for his reminders that he is "button-popping proud" of me, my sisters for their confidence, and my in-laws, Kim and Nelson, for their reassurance that law school was the right choice and for the copious amounts of caffeine. Additionally, I would like to thank Professor Heidi Kuehl for her wonderfully helpful notes; Tara Ramljak, my comment editor, for her kind reminders that although I needed to define more terms, I was on the right track despite my angst; and Margaret Nunne, my research editor, for her willingness to share her abundant Bluebook knowledge at all hours of the night. Finally, much gratitude to my dear friend Bruce Keller, who not only helped inspire my journey into the legal field, but who also reminds me to keep my feet on the ground while reaching for the stars.

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I. INTRODUCTION

Legal scholars, politicians, professors, and law students rarely claim that the law evolves quickly in response to new technology. Science, on the other hand, moves at breakneck paces that are substantially faster than the regulatory bodies that govern it. This leaves such governing bodies at a great disadvantage while many scientists are confined mostly by the ethics imposed upon them by their own profession.[2] New technological and scientific

2. *See generally* World Medical Association General Assembly, *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*, WORLD MED. ASS'N (Mar. 19, 2018), https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ [https://perma.cc/G8F6-FKUE]. The World Medical Association ("WMA") Declaration of Helsinki provides ethical guidelines and principles for medical research that involves human

advances in the world of genetic editing are no different. One of the newest gene-editing innovations–commonly known as CRISPR-Cas9[3]–has far outpaced the legal ties that may bind it.

The idea of changing one's genetics has been around for decades, in everything from literature and entertainment to scientific experiments. While perhaps the most well-known image conjured by the mention of genetic editing, the monster in Mary Shelley's *Frankenstein* was created from an inanimate body and brought to life through chemistry and alchemy, so these edits to the lifeform cannot be considered editing of the genes.[4] The repetitive genetic rewrites of the character Rocket in Marvel's *Guardians of the Galaxy*[5] come much closer to the type of genetic editing that is currently controversial. But it is Aldous Huxley's science fiction novel *Brave New World*, which

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subjects. First adopted in 1964, the WMA's global ethical standards are designed for physicians, but are encouraged to be adopted by all involved in human subject medical research. These standards include an outline of physician duties, aspects of research protocol, and registration requirements. *Id.*

3. *Questions and Answers About CRISPR*, BROAD INST., https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/questions-and-answers-about-crispr [https://perma.cc/WX8S-MCEG]. This technology is sometimes called just CRISPR or is paired with an enzyme other than Cas9. For the purposes of this Comment, the nomenclature used will be CRISPR-Cas9. For more information regarding CRISPR, *see infra* text accompanying notes 45-71.

4. *See generally* MARY WOLLSTONECRAFT SHELLEY, FRANKENSTEIN, OR, THE MODERN PROMETHEUS (1818).

5. *See generally* GUARDIANS OF THE GALAXY (Marvel Studios 2014). Rocket, a greedy and vengeful talking raccoon who walks on his hind legs, is the result of unauthorized genetic and cybernetic experiments. *Id.* When taunted about his background, Rocket states, "Well I didn't ask to get made. I didn't ask to be torn apart and put back together over and over and turned into some, some little monster." *Id.* at 54:07. Human germline editing critics share ethical concerns similar to this statement because germline editing is completed before a child is born – therefore the child cannot give consent to the procedure and must rely on its parents to make a choice in its best interest – and that genome edit is passed down to the next generation. *See Genome Editing: What are the Ethical Concerns About Genome Editing?*, NAT'L HUM. GENOME RES. INST. (Aug. 3, 2017), https://www.genome.gov/27569225/what-are-the-ethical-concerns-about-genome-editing/ [https://perma.cc/S4L6-G5B8]. For a discussion on germline editing, see *infra* Part II, Section A. For a discussion on the ethical concerns posed by scientists regarding germline modification on embryos, see *infra* Part III, Section A(2).

addresses a severe form of in vitro eugenics[6] in a totalitarian future,[7] that makes the capabilities of science a little less fictional.

While Shelley's tale of scientific hubris focuses on a scientist consumed by his creation,[8] some in the scientific community view it as an early warning sign.[9] In the name of "improving" society, compulsory sterilization laws were legal in the state of Virginia until 1974.[10] The Supreme Court upheld such a law in *Buck v. Bell* in an eight to one decision, justifying sterilizations of "feeble-minded" women as benefits to the public welfare.[11] The theory of eugenics continued during World War II when German physicians experimented on thousands of nonconsenting concentration camp prisoners.[12]

The advent of CRISPR-Cas9 brings the fictional and the cruel closer to reality. Patients on the organ transplant wait lists could receive life-saving surgery without having to wait years.[13] The ability of parents to choose advantageous traits for their unborn child is within reach.[14] Genetic diseases could be eradicated.[15] Once-extinct animals could come to life outside a

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6. Eugenics is a form of "science that deals with the improvement (as by control of human mating) of hereditary qualities of a race or breed." *Eugenics*, MERRIAM-WEBSTER'S COLLEGIATE DICTIONARY (11th ed. 2003). The term "eugenics" was coined in 1883 by British scientist Francis Galton. Galton advocated for rewarding marriages amongst "superior" members of society to promote selective breeding. The work of American eugenicists was later used by the Nazis in justifying their sterilization programs in the 1930s. *See* Steven A. Farber, *U.S. Scientists' Role in the Eugenics Movement (1907-1939): A Contemporary Biologist's Perspective*, 5 ZEBRAFISH 243, 243-44 (2008).

7. *See generally* ALDOUS HUXLEY, BRAVE NEW WORLD (1932).

8. *See generally* SHELLEY, *supra* note 4.

9. *See* Kai Kupferschmidt, *The Long Shadow of Frankenstein*, SCIENCE, Jan. 12, 2018, at 147.

10. *See* Matthew Wills, *When Forced Sterilization was Legal in the U.S.*, JSTOR DAILY (Aug. 3, 2017), https://daily.jstor.org/when-forced-sterilization-was-legal-in-the-u-s/ [https://perma.cc/M36A-JC8S].

11. *See* Buck v. Bell, 274 U.S. 200, 207 (1927) ("Three generations of imbeciles are enough."). This decision bolstered the American eugenics movement, which was led in Virginia by Dr. Albert Priddy and Harry Laughlin. *See* Michelle Oberman, *Thirteen Ways of Look at Buck v. Bell: Thoughts Occasioned by Paul Lombardo's "Three Generations, No Imbeciles."* 59 J. LEGAL EDUC. 357, 359-60 (2010).

12. United States Holocaust Memorial Museum, *Nazi Medical Experiments*, HOLOCAUST ENCYCLOPEDIA, https://www.ushmm.org/wlc/en/article.php?ModuleId=10005168 [https://perma.cc/J9MD-N3TU]. One goal of the experiments was to advance the "master race" through sterilization of many Jews, Roma, and other "undesirable" groups. This racist ideology involving eugenics was not new, but the Nazis brought it to the forefront. *Id.*

13. See discussion *infra* Part I, Section D.

14. *See* Paul Knoepfler, *The Ethical Dilemma of Designer Babies*, TED (Oct. 2015), https://www.ted.com/talks/paul_knoepfler_the_ethical_dilemma_of_designer_babies/details [https://perma.cc/262U-AGN7].

15. *See generally* Heidi Ledford, *CRISPR Fixes Embryo Error*, 548 NATURE 13 (2017); Emily Mullin, *Arming Bodies with CRISPR to Fight Huntington's Disease and ALS*,

movie theater.[16] The mixed opportunities presented by new technology bring both advocates and critics.

Although current use of gene-editing technology on human embryos is sparse, many CRISPR-Cas9 opponents advocate for a total ban on the technology.[17] A January 2016 poll done by the partnership of Harvard T.H. Chan School of Public Health and STAT reported that eighty-three percent of Americans oppose gene editing that is done only to improve physical or intellectual characteristics, while approximately sixty-three percent oppose genetic edits to fetuses.[18] Opposition on this level breaches the pro-life, pro-choice debate. Critics are wary of "designer baby" possibilities and fear parents may "prevent or cure" certain physical differences in order to exact social change.[19] Other opponents are averse to any human experimentation, regardless of the stage of life.[20] At this point in time, the long-term implications of genome editing technology such as CRISPR-Cas9 are yet to be found and fuel some of the controversy.[21]

Legal scholarship is lacking in the area of germline editing. One can presume that the complex scientific terminology and principles are daunting to non-scientists in the legislative and legal divisions.[22] To date, the Supreme

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MIT TECH. REV. (Oct. 5, 2017), https://www.technologyreview.com/s/608967/arming-bodies-with-crispr-to-fight-huntingtons-disease-and-als/ [https://perma.cc/J6UN-CXF7].

16. *See* Simon Worrall, *We Could Resurrect the Woolly Mammoth. Here's How.*, NAT'L GEOGRAPHIC (July 9, 2017), https://news.nationalgeographic.com/2017/07/woolly-mammoths-extinction-cloning-genetics/ [https://perma.cc/Z9M4-9BNX] (discussing the possible resurrection of the woolly mammoth and the accompanying ethical concerns).

17. *See* Sarah Karlin, *Gene Editing: The Next Frontier in America's Abortion Wars*, POLITICO (Feb. 16, 2016, 5:21 AM), https://www.politico.com/story/2016/02/gene-editing-abortion-wars-219230 [https://perma.cc/AU6U-UNLE].

18. *Id.*

19. *See* Knoepfler, *supra* note 14.

20. *See* Karlin, *supra* note 17.

21. *See, e.g.*, Emily McManus, *Scientists are Trying to Use CRISPR to Fix Everything. What's Wrong with That?*, TED (May 5, 2016), https://ideas.ted.com/scientists-are-trying-to-use-crispr-to-fix-everything-whats-wrong-with-that/ [https://perma.cc/26JP-3ZCM]; *see also* Jennifer Kahn, *The CRISPR Quandry*, N.Y. TIMES MAG. (Nov. 9, 2015), https://www.nytimes.com/2015/11/15/magazine/the-crispr-quandary.html?_r=0 [https://perma.cc/GB7U-224N].

22. Oral arguments in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* are a prime example of non-scientists in the legal field trying to make sense of these complex scientific principles. *See generally* Transcript of Oral Argument, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576 (2013) (No. 12-398), https://www.supremecourt.gov/oral_arguments/argument_transcripts/2012/12-398_h3dj.pdf [https://perma.cc/LX2A-RFJP] [hereinafter Transcript of Oral Argument]. "Do you -- you've really lost me when you say that it's nature that does the alteration rather than the scientist. I mean, whenever a scientist does an alteration, he does it, you know, by some force of nature." *Id.* at 21:14 (Scalia, J.).

"[M]y understanding is that here, what's involved, obviously through scientific processes, but we're not talking about process. Here, what's involved is snipping. You've got the thing there

Court has been faced with a CRISPR-Cas9 issue only regarding patent issues.[23] This Comment focuses on the scientific background of human germline editing, current regulations, and the need for evolving regulations for the use of CRISPR-Cas9 in the human medical products arena.

While complicated, it is necessary to explore the rather recent history of human germline editing and CRISPR-Cas9. Science and biotechnologies evolve at a sometimes-alarming rate and regulators need to be aware of how far science has come in such a short time. The sources of current regulations covering human germline editing are varied. The FDA, USDA, National Institutes of Health, and funding restrictions through tax appropriations bills all touch on germline editing, but none address it fully or directly. Due to the lack of direct and relevant law regarding human germline editing and biotechnologies such as CRISPR-Cas9, it is time for change. The American Society of Human Genetics (ASHG) issued a position statement in 2017 that addressed the lack of regulation and proposed a set of guidelines for regulators to consider.[24] This Comment advocates that this statement should be adopted in full. Section II of this Comment deals with the scientific background of human germline modification, CRISPR-Cas9, and current uses of gene editing technologies. Section II explores the current regulations in place for genetic editing and genetically altered products and why they are inadequate. Section III of this Comment discusses the need for evolving regulations and why the suggestions outlined the ASHG's position statement should be adopted.

II. SCIENTIFIC BACKGROUND

A. Human Germline Modification Explained

When the Human Genome Project[25] consortium first announced the publication of a reference genome in 2001, they predicted that this freely-

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and you snip – snip off the top and you snip off the bottom and there you've got it." *Id.* at 41:10 (Roberts, C.J.).
"I'm sorry, I still don't understand what – in what sense it's different than just snipping along – along the line." *Id.* at 42:23 (Roberts, C.J.).

23. *See, e.g.*, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576 (2013) (holding that isolated DNA segments occurring naturally are not patent eligible, but cDNA may be patented); *In re* Schlich, 2017 U.S. Dist. LEXIS 151060 (S.D.N.Y. Sept. 17, 2017) (denial of a discovery request for pending litigation before the European Patent Office regarding the patent battle for CRISPR/Cas9 biotechnology).

24. Kelly Ormond, et al., *Human Germline Genome Editing*, 101 AM. J. HUM. GENETICS 167 (2017) [hereinafter ASHG Statement].

25. The National Institutes of Health (NIH) and Department of Energy, in conjunction with international partners, formed the Human Genome Project in 1990. Their goal was to sequence all three billion DNA letters – also called base pairs – in the human body in order

released "Book of Life"[26] would aid researchers in identifying and treating diseases.[27] This was a culmination of projects that were launched in the early 1980s, the goal of one being "to locate disease genes of unknown function based solely on their inheritance patterns."[28] The mapping of the human genome took science one step closer to editing the DNA of many organisms and is a noble pursuit.[29]

There are two types of gene editing, somatic[30] and germline.[31] Edits done to somatic cells affect only individuals that receive the treatment.[32] This type of gene editing is less controversial because edits are not passed on to future generations and undergo rigorous evaluation.[33] The National Institutes of Health Common Fund is in the process of developing the Somatic Cell Genome Editing Program to provide researchers with tools to safely and effectively edit the genomes of human patients.[34] Scientists in the United Kingdom used somatic gene therapy in 2015 to help a one-year-old girl, Layla, fight leukemia.[35] The newest technology, CRISPR-Cas9, was not the method

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to provide researchers with more information to understand, treat, and prevent genetic diseases. The complete set of a person's DNA is referred to as their genome. *See Fact Sheet: Human Genome Project*, NAT'L INSTS. HEALTH 1 (Oct. 2010), https://report.nih.gov/NIHfactsheets/Pdfs/HumanGenomeProject(NHGRI).pdf [https://perma.cc/6U82-J4YH].

26. All discoveries made and data compiled by the Human Genome Project were made available free of charge on the Internet. *Id.*

27. *See International Human Genome Sequencing Consortium Publishes Sequence and Analysis of the Human Genome*, NAT'L HUM. GENOME RES. INST. (Feb. 12, 2001), https://www.genome.gov/10002192/2001-release-first-analysis-of-human-genome/ [https://perma.cc/J2MU-TM54].

28. Int'l Human Genome Sequencing Consortium, *Initial Sequencing and Analysis of the Human Genome,* 409 NATURE 860, 862 (2001) [hereinafter Initial Sequencing].

29. *See generally id.*

30. Somatic cells do not transfer their genome to the next generation. *Gene Editing in Clinical Disease: Scientific, Ethical and Societal Questions*, CTR. FOR GENETICS & SOC'Y (Nov. 14, 2017), https://www.geneticsandsociety.org/internal-content/gene-editing-clinical-disease-scientific-ethical-and-societal-questions [https://perma.cc/PQM3-J3JX].

31. *See* discussion *infra* note 37.

32. *Id.*

33. *Id.*

34. *See Somatic Cell Genome Editing*, NAT'L INSTS. HEALTH OFF. STRATEGIC COORDINATION – COMMON FUND, https://commonfund.nih.gov/editing [https://perma.cc/DH5W-JCCT]. Funding for this program, approximately $190,000,000 over the next six years, will be awarded through the NIH Common Fund and does include CRISPR-Cas9 technology. *See* Alex Philippidis, *NIH Commits $190M to Somatic Gene-Editing Tools/Tech Research*, GENETIC ENGINEERING & BIOTECHNOLOGY NEWS (Jan. 24, 2018), https://www.genengnews.com/gen-news-highlights/nih-commits-190m-to-somatic-gene-editing-toolstech-research/81255414 [https://perma.cc/S8L9-LX6H].

35. *See Genome Editing*, NAT'L HUM. GENOME RES. INST. (Aug. 3, 2017), https://www.genome.gov/27569222/genome-editing/ [https://perma.cc/CD2K-JKGC]. All other treatments to fight Layla's leukemia had failed, so a gene editing method called TALENs was employed to treat Layla. Researchers had to extract healthy T-cells, a type of immune cell, from a donor. These healthy cells were then introduced into Layla's system once the

employed by the U.K. scientists, but special permission did have to be obtained to edit Layla's genome and save her life.[36]

Germline[37] editing, even more so than somatic gene editing, is the source of much controversy.[38] This is because these genetic alterations are passed to future generations.[39] The genetic alterations of germline editing target genes in early stage embryos, eggs, or sperm, not human adults.[40] These changes to the genetic make-up affect all cells in the resulting individual and are therefore inheritable by that individual's offspring.[41] These inheritable gene edits would create "permanent changes to the human gene pool."[42] For researchers seeking to remove fatal genetic diseases from the genome, germline editing is optimal.[43] While it prevents scientists from having to repeat somatic gene therapy in each generation, the long-term effects of germline editing have not been determined.[44]

B. What Exactly is CRISPR?

As the "building blocks of life," DNA is stored in all cells of the body, other than red blood cells.[45] When viruses attack cells, they leave behind their

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TALEN enzyme had been used to modify Layla's "genes to protect the new cells from anticancer drugs . . . ." Sara Reardon, *Leukaemia Success Heralds Wave of Gene-Editing Therapies*, 527 NATURE 146, 146 (2015). For a description of TALENs, *see infra* note 73.

36. *See* NAT'L HUMAN GENOME RES. INST., *supra* note 35.

37. "Germ" in germline refers to egg and sperm cells that join together to form an embryo. Germline DNA is the source of DNA for all other cells in the body. *NCI Dictionary of Cancer Terms "germline DNA,"* NAT'L CANCER INST., https://www.cancer.gov/publications/dictionaries/cancer-terms/def/germline-dna [https://perma.cc/HS2U-3CW2].

38. *See* Karlin, *supra* note 17.

39. *See* CTR. FOR GENETICS & SOC'Y, *supra* note 30.

40. *See* ASS'N OF REPROD. HEALTH PROF'LS, HUMAN CLONING AND GENETIC MODIFICATION: THE BASIC SCIENCE YOU NEED TO KNOW 5, https://www.arhp.org/uploadDocs/cloning.pdf [https://perma.cc/B2WR-B8FN].

41. *Id.*

42. Nicholas Wade, *Scientists Seek Moratorium on Edits to Human Genome That Could be Inherited*, N.Y. TIMES (Dec. 3, 2015), https://www.nytimes.com/2015/12/04/science/crispr-cas9-human-genome-editing-moratorium.html?_r=0 [https://perma.cc/2FLZ-ANXE].

43. *See* Alice Park, *U.S. Scientists Use CRISPR to Fix Genetic Disease in Human Embryos for the First Time*, TIME (Aug. 2, 2017), http://time.com/4882855/crispr-gene-editing-human-embryo/ [https://perma.cc/UGP5-VBLU].

44. *See* NAT'L HUMAN GENOME RES. INST., *supra* note 35.

45. *See What is DNA?*, GENETICS HOME REFERENCE (May 22, 2018), https://ghr.nlm.nih.gov/primer/basics/dna [https://perma.cc/SV3Y-LZ2J]. Deoxyribonucleic acid, or DNA, is the storehouse for genetic material. There are four nucleic acid bases that make up the human genome, labeled A, T, G, and C. These bases pair up to form units. Repetitive elements are prevalent because each cell requires a duplicate of its DNA when it divides. Just as most cells in the human body have the same DNA, approximately ninety-nine percent of the three billion bases in the human body are the same in all people. *Id.*

DNA.[46] Researchers in 2005 found that certain kinds of bacteria contain the ability to create a record of all the viruses they have been exposed to by storing bits of viral DNA within clustered regularly interspersed short palindromic repeats ("CRISPRs").[47] In those bacteria, the CRISPR system is utilized as an immune system that destroys invading viruses.[48] This unique ability to remember which viruses it has been exposed to protects not only the infected cells, but their progeny as well.[49]

The CRISPR system contains a protein called Cas9 that can "cut" the DNA's double helix.[50] In the natural world, bacteria use CRISPR to cut up and fight off viruses.[51] Scientists have a different purpose in the lab, but the principle remains the same.[52] After being guided to the target DNA by guide RNA,[53] Cas9 binds to the targeted DNA.[54] Once Cas9 is bound to its target, that gene effectively shuts off when Cas9 cuts through the DNA.[55] This double-stranded DNA break created by the Cas9 protein must then be repaired. In the natural world, DNA breaks in cells are repaired by either piecing together the broken ends of the DNA with a slight change, or a new piece of

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46. *See* Jennifer Doudna, *How CRISPR Lets Us Edit Our DNA*, TED (Sept. 2015), https://www.ted.com/talks/jennifer_doudna_we_can_now_edit_our_dna_but_let_s_do_it_wisely [https://perma.cc/KR78-PV53].

47. Eileen M. Kane, *Human Genome Editing: An Evolving Regulator Climate*, 57 JURIMETRICS 301, 303-04 (2017). In combination with specific enzymes, CRISPRs can essentially remove DNA from viruses that attack the bacteria "in a process known as adaptive immunity" and serves as a defense system. *Id.* at 304.

48. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35.

49. *See* Doudna, *supra* note 46.

50. CRISPR and Cas9 have been anthropomorphized in many ways (find and replace in word processing, scissors, etc.), but the most common analogy likens the technology to a Swiss Army knife. This shows the cutting power of CRISPR-Cas9, but it does not produce a scalpel-precise cut. It also creates an image of varying instruments for varying tasks, all rolled into one neat package. *See* Rebecca Robbins, *The Best and Worst Analogies for CRISPR, Ranked*, STAT (Dec. 8, 2017), https://www.statnews.com/2017/12/08/crispr-analogies-ranked/ [https://perma.cc/9VX9-DPMC].

51. Robert Kolker, *This Gene-Editing Technology Will Change the World. But Who Gets the Credit?*, BLOOMBERG BUSINESSWEEK (June 29, 2016), https://www.bloomberg.com/features/2016-how-crispr-will-change-the-world/.

52. *Id.*

53. The job of ribonucleic acid ("RNA") is to transfer the genetic code needed for the creation of proteins from the nucleus to the ribosome. RNA is essential to the creation of proteins. *See What is RNA?*, RNA SOC'Y, https://www.rnasociety.org/about/what-is-rna/ (last visited Dec. 14, 2017). The Cas9 RNA combination can be programmed to detect certain DNA sequences, allowing precise breaks to be made at that site. *See* Kane, *supra* note 47, at 304. Only twenty letters of the guide RNA are used to target the desired DNA sequence. This makes designing the edits simple and inexpensive. *See* GENETICS HOME REFERENCE, *supra* note 45.

54. *See* BROAD INST., *supra* note 3.

55. *Id.*

DNA is integrated into that break.[56] With these planned breaks in a cell's DNA, scientists can introduce new DNA, as long as the two ends of it are homologous[57] to those around it. Biologist Ellen Jorgensen describes this new piece of DNA as a "Trojan horse" because it makes itself appear to belong.[58]

These capabilities lead to a powerful tool. Like using the find and replace function of a computer program, scientists can program the Cas9-bound RNA to seek out a specific sequence of DNA and change it.[59] Edits to the genome are not limited to insertions of new DNA. Deletions of unwanted sequences and alterations to existing DNA sequences can also be accomplished through use of the CRISPR-Cas9 system.[60] Research has shown that the CRISPR-Cas9 system also works as a genome editing method in eukaryotic cells.[61] Because human cells are eukaryotic cells,[62] controversy surrounds the use of this recently discovered targeting system.[63]

CRISPR-Cas9 has brought cost, speed, accuracy, and efficiency improvements to genome editing.[64] The CRISPR-Cas9 system can cleave DNA without being paired with additional enzymes.[65] This reduces costs because synthetic RNA sequences are less expensive to produce than the proteins needed for systems used prior to CRISPR.[66] Individual genes do not have to

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56. *See* ASS'N OF REPROD. HEALTH PROF'LS, *supra* note 40.

57. Homologous is defined as "having the same relative position, value, or structure". *Homologous*, MERRIAM-WEBSTER'S COLLEGIATE DICTIONARY (11th ed. 2003).

58. *See* Ellen Jorgensen, *What You Need to Know About CRISPR*, TED (June 2016), https://www.ted.com/talks/ellen_jorgensen_what_you_need_to_know_about_crispr [https://perma.cc/CB57-QSQZ]. Simply put, CRISPR-Cas9 can be used to add desirable traits and remove undesirable traits with precision. *See id.*

59. *See* Kolker, *supra* note 51.

60. *See* David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCIENCE 36 (2015).

61. *See* Kane, *supra* note 47 at 304. There are two basic types of cells: eukaryotic and prokaryotic. A eukaryotic cell possesses a clearly defined nucleus. A prokaryote, on the other hand, has no internal membranes and therefore lacks a distinct nucleus. The more-simple of the two, prokaryotic cells, have only one circular chromosome where all the cell's genetic information is contained. Bacteria are an example of prokaryotic cells. Eukaryotic cells have much larger DNA systems "contain[ed] in multiple linear chromosomes." Human cells are eukaryotic. *See* Kara Rogers & Robert J. Kadner, *Bacteria*, ENCYCLOPEDIA BRITANNICA, https://www.britannica.com/science/bacteria#ref463521 [https://perma.cc/PR5B-7HNW].

62. *See* Kane, *supra* note 47, at 304.

63. *See, e.g.*, Knoepfler *supra* note 14. The involvement of human DNA in biomedical research, thus leading to possible use in human subjects, elicits ethical concerns from scientists and the public alike. *Id.*

64. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35.

65. *Id.*

66. ZFN kits, sold by life science company Sigma-Aldrich, begin at $13,000 and can be customized at additional costs. *See* SIGMA-ALDRICH, https://www.sigmaaldrich.com/catalog/search?term=zfn&interface=All&N=0&mode=match%20partialmax&lang=en&region=US&focus=product [https://perma.cc/A95H-GDRS]. The popular Golden Gate TALEN

be targeted separately using CRISPR-Cas9, unlike its predecessors.[67] Multiple genes can be targeted simultaneously, reducing the amount of time needed to make the edit.[68] CRISPRs have the ability to be easily matched with guide RNA.[69] Libraries of tens of thousands of guide RNAs have been created on a genome-scale.[70] This creates an ease of use and availability that older gene-editing technologies could not harness.[71]

C. CRISPR's Lackluster Predecessors

Prior technologies, like Zinc-finger nucleases (ZFN)[72] and transcription activator-like effector nucleases (TALENs)[73] were complicated and fairly expensive.[74] The expansive process ZFN and TALENs required to construct new proteins was prone to error. CRISPR-Cas9, on the other hand, is simple and accurate.[75] Editing a gene requires only that a scientist give an "address" – a short string of letters that delineate a certain location on the gene – to a

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kit available from the nonprofit plasmid repository Addgene, costs $425, but is not a complete system and requires the purchase of additional components. *See Golden Gate TALEN and TAL Effector Kit 2.0*, ADDGENE, http://www.addgene.org/taleffector/goldengatev2/#kit-details [https://perma.cc/6SNC-6BBK]. The materials for CRISPR experiments, on the other hand, can be obtained for hundreds, not thousands of dollars. *See* Jorgensen, *supra* note 58. Outside the laboratory, gene therapy costs are far from affordable for the average American, with treatments ranging from $373,000 for more common diseases to $1,000,000 for diseases with fewer eligible patients. *See* Emily Mullin, *Tracking the Cost of Gene Therapy*, MIT TECH. REV. (Oct. 24, 2017), https://www.technologyreview.com/s/609197/tracking-the-cost-of-gene-therapy/ [https://perma.cc/CN9Z-VQVZ].

67. *See* BROAD INST., *supra* note 3.

68. *Id.* CRISPR-Cas9 is a more precise system than its predecessors, meaning that fewer trials are necessary to achieve the desired results. This reduces time and costs. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35.

69. *Id.*

70. Silvana Konermann et al., *Genome-Scale Transcriptional Activation by an Engineered CRISPR-Cas9 Complex*, 517 NATURE 583, 586 (2015). The National Cancer Institute is one research body that has created a library of small-guide RNAs (sgRNAs). These sgRNAs "guide the Cas9 enzyme" and allow scientists to quickly and efficiently conduct large-scale screening of cancer cells. CRISPR's precision accuracy allows total elimination of the target gene. *See* NAT'L CANCER INST., *infra* note 96.

71. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35.

72. ZFN were used by researchers in the 1990s in an attempt to improve the preciseness of gene editing. It is time-consuming and difficult to design and create successful ZFNs from naturally-occurring proteins. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35.

73. These proteins began to be used in genome editing in 2009. TALENs work similarly to ZFNs regarding efficiency of the genetic edits, but engineering TALENs is more simple than synthesizing ZFNs. *See id.*

74. *See* price discussion *infra* note 66.

75. *See* NAT'L HUM. GENOME RES. INST., *supra* note 35. One study showed that the CRISPR's accuracy for targeted gene mutations is six times more efficient than the results from ZFN or TALENs. *Id.*

strand of guide RNA.[76] One scientist claimed that a graduate student could master the process in an hour and an edited gene could be produced in a couple days.[77] Even reasonably priced do-it-yourself kits are available to the general public, who can conduct genetic experiments at home to insert jellyfish DNA into yeast to make it fluoresce.[78]

D. Current Uses of Gene Editing Technology

1. GMOs are in the News and on Our Tables

Genetically modified crops and the food derived from them have been on the market in the United States for years.[79] The first commercial crop altered using CRISPR-Cas9 technology, a "waxy" corn variety by DuPont Pioneer, will be on the market around 2020.[80] Scientists must no longer wait years for the desirable traits to be developed in productive plants.[81] The CRISPR-Cas9 system can quickly, and precisely, add or remove genetic traits in plants.[82] In the case of DuPont Pioneer's waxy corn variety, there was no need to introduce foreign DNA into the plant because CRISPR-Cas9 was used to partially knock out the gene that creates an undesirable enzyme.[83] Researchers continue to explore the use of CRISPR-Cas9 for commercial crop usage.[84] A team at North Carolina State University is investigating ways to use genome editing to increase oil production in canola.[85] One experiment involved placing a tomato gene into an oilseed plant.[86] In two years, not the

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76. *See* BROAD INST., *supra* note 3.

77. 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/GB7U-224N].

78. *See, e.g.*, *Genetic Engineering Kit: Genetically Engineer Any Brewing or Baking Yeast to Fluoresce*, ODIN, http://www.the-odin.com/ge-yeast/ [https://perma.cc/QX3H-H2ZM] (offering a starter CRISPR kit for $159 that allows users to insert a fluorescent gene from a jellyfish into yeast to make the yeast fluoresce).

79. In 1994, the FLAVR SAVR tomato, first genetically-modified food available in the United States, made its way into the marketplace. *See* Paul Enriquez, CRISPR GMOs, 18 N.C. J. L. & TECH. 432, 457 (2017).

80. Melody M. Bomgardner, *A New Toolbox for Better Crops*, CHEMICAL & ENGINEERING NEWS, June 12, 2017, at 30, 31.

81. *Id.* at 31-32. DuPont Pioneer's new waxy corn development began in 2015. This development to market time span is only five years, as compared to the usual eight years. *Id.*

82. *Id.* at 31.

83. *Id.*

84. *See, e.g.*, Leena Arora & Alka Narula, *Gene Editing and Crop Improvement Using CRISPR-Cas9 System*, FRONTIERS PLANT SCI., Nov. 2017, at 10. Corn is not the only commercial crop on which researchers are using the CRISPR-Cas9 system. Apples, oranges, mushrooms, and potatoes have also made the CRISPR research list. *Id.*

85. *See* Bomgardner, *supra* note 80, at 32.

86. *Id.*

usual ten-year turnaround with the older techniques, the yield doubled.[87] The team hopes to find and use genes native to the oilseed plant that will produce the same effect.[88]

2. *Porcine Organs Made Transplant Friendly*

CRISPR-Cas9 has been used by geneticists George Church and Luhan Yang at Harvard University to create gene-edited piglets with organs that are transplant-friendly to humans.[89] Without modification, pig organs are suited for transplant into humans because of their relative size similarity to human organs.[90] The idea that transplants could eventually be done using pig organs came about in the 1990s, but it was not until the advent of CRISPR-Cas9 that such a dream became reality.[91]

The need for gene editing arises because the pig genome contains fragments of porcine endogenous retroviruses, known by the acronym PERV, which could later infect a human transplant recipient.[92] To ensure the human body would not reject the pig organs, it was necessary to remove all traces of PERV genes from the pig genome.[93] In 2016, there were 116,800 patients on organ transplant waiting lists.[94] The availability of porcine organs for transplant could save thousands of lives.[95]

3. *Cancer Research*

CRISPR technology is being used by the National Cancer Institute's Laboratory of Cancer and Biology and Genetics to study cancer cells and how those "mutated genes form abnormal regulatory networks within the cells."[96] These regulatory networks can serve as targets for new cancer drugs.

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87. *Id.*

88. *Id.*

89. *See* Kelly Servick, *CRISPR Slices Virus Genes Out of Pigs, But Will It Make Organ Transplants to Humans Safer?*, SCI. MAG. (Aug. 10, 2017, 2:00 PM), http://www.sciencemag.org/news/2017/08/crispr-slices-virus-genes-out-pigs-will-it-make-organ-transplants-humans-safer [https://perma.cc/X7BT-QE24].

90. *Id.*

91. *See* Gina Kolata, *Gene Editing Spurs Hope for Transplanting Pig Organs into Humans*, N.Y. TIMES (Aug. 11, 2017), https://www.nytimes.com/2017/08/10/health/gene-editing-pigs-organ-transplants.html [https://perma.cc/D5J7-69RH].

92. *See* Servick, *supra* note 89.

93. *Id.*

94. *See* Kolata, *supra* note 91.

95. Porcine organs could be used to close the large gap between the available number of human organs and the need. *See generally id.*

96. *CRISPR: Genome Editing Comes of Age*, NAT'L CANCER INST. (Sept. 23, 2015), https://www.cancer.gov/about-cancer/causes-prevention/research/crispr [perma.cc/5NNC-QBM9].

CRISPR's precision allows the insertion of specific mutations so scientists can determine what number and order of mutations are necessary to change a normal cell into a cancer cell.[97] These CRISPR-aided studies, currently limited to the laboratory, help scientists understand the evolution of various cancers and can lead to possible treatment approaches.[98]

4. Three-Parent Children

The greatest controversy with CRISPR involves using this biotechnology to modify human embryos.[99] CRISPR-Cas9 technology was not harnessed until 2012,[100] but germline genetic modification was successful in human reproduction in 1997.[101] Emma Ott, now a thriving 20-year-old, was born after use of a controversial in vitro fertilization technique called cytoplasmic transfer.[102] This technique mixes genes belonging to three people, thus leaving the resulting children with inherited DNA from three sources.[103] Effectually, cytoplasmic transfer resulted in germline modification because the DNA from both female donors is inheritable through the maternal line.[104] While Emma is still young, there have been no recorded complications from this sort of genetic editing.[105]

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97. *Id.*
98. *Id.*
99. *See* Knoepfler, *supra* note 14.
100. *See* Kolker, *supra* note 51.
101. Steve Connor, *Three-Parent Babies: 'As Long as She's Healthy, I Don't Care,' Says Mother of IVF Child*, INDEPENDENT (Aug. 25, 2014, 8:07 PM), http://www.independent.co.uk/news/science/three-child-babies-the-mothers-view-as-long-as-she-s-healthy-i-don-t-care-9690059.html [https://perma.cc/7ALB-YWJE].
102. *Id.* Cytoplasmic transfer involves taking "a small quantity of cytoplasm – the jelly-like material outside the cell nucleus – from a healthy donor egg [and] inject[ing] [it] into an egg cell of [Emma's] mother before being fertilized in vitro with [Emma's father's] sperm." This type of transfer was used "as a way of boosting the chances of a successful IVF cycle." The resulting embryo inherited mitochondrial DNA of the cytoplasm donor, mitochondrial DNA and nuclear DNA from the mother, and nuclear DNA from the father. Emma was one of seventeen babies born after successful cytoplasmic transfer. *Id.*
103. Sara Reardon, *Baby's DNA Mix Revealed*, 544 NATURE 17, 17 (2017) (discussing a more recent cytoplasmic transfer at a U.S. fertility clinic.).
104. Connor, *supra* note 101. The IVF laboratory where the cytoplasmic transfer took place was in Britain, where it was illegal to perform human germline modifications. In 2014, seventeen years after Emma's birth, the Department of Health in Great Britain ruled that mitochondrial donation does not qualify as genetic modification, even though this germline therapy has inheritable consequences. *Id.*
105. *Id.*

5. *Non-Viable Genome Edits Abroad and at Home*

In 2015, scientists in China were the first to edit human embryo genomes.[106] The CRISPR-Cas9 technology was used on 'non-viable' embryos[107] from nearby fertility clinics. These embryos were fertilized, but had an extra set of chromosomes that prevented development beyond the first stages.[108] The focus of the genome edits was the gene responsible for an often-fatal blood disorder, β-thalassemia.[109] Forty-eight hours after injecting eighty-six embryos with the CRISPR-Cas9 complex, seventy-one survived the procedure and fifty-four were subject to genetic testing.[110] The target for successful slicing of replacement genetic material was close to 100%, but this experiment yielded a mere fraction of that.[111] This led to a suspension of the research because scientists concluded the technique was "too immature."[112]

The following year, another China-based research team reported using CRISPR-Cas9 editing to edit human embryos in an attempt to make them HIV-resistant.[113] A mutation that alters the CCR5 protein[114] was introduced into the non-viable embryos.[115] Approximately fifteen percent of the embryos were modified successfully.[116] This emphasizes the fact that technical difficulties still plague these experiments.[117]

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106. David Cyranoski & Sara Reardon, *Chinese Scientists Genetically Modify Human Embryos*, NATURE (Apr. 22, 2015), https://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378 [https://perma.cc/LN45-S97Z].

107. Non-viable embryos cannot result in a live birth. *Id.*

108. *Id.*

109. *Id.*

110. *Id.*

111. David Cyranoski & Sara Reardon, *Chinese Scientists Genetically Modify Human Embryos*, NATURE (Apr. 22, 2015), https://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378 [https://perma.cc/LN45-S97Z]. Only fifty-two percent of the embryos were efficiently cleaved using CRISPR-Cas9 and of those, only 14.3% were clearly edited in the manner the scientists intended. *See* Puping Liang, et al., *CRISPR/Cas9-Mediated Gene Editing in Human Tripronuclear Zygotes*, 6 PROTEIN & CELL 363, 366 (2015).

112. Cyranoski & Reardon, *supra* note 106.

113. Ewen Callaway, *Second Chinese Team Reports Gene Editing in Human Embryos*, NATURE (Apr. 8, 2016), https://www.nature.com/news/second-chinese-team-reports-gene-editing-in-human-embryos-1.19718 [https://perma.cc/RCN9-ZH8Y].

114. This mutation (known as CCR5Δ32) is carried naturally by some humans. These people are resistant to the HIV virus because the mutation prevents the HIV virus from infecting the host's T cells through an alteration of the CCR5 protein. *Id.*

115. *Id.*

116. *Id.*

117. Such low percentages of successful genetic modifications on human embryos are far from the desired 100% target. *See* Cyranoski & Reardon, *supra* note 106.

China is not the only nation to edit the genes of human embryos. An international team of scientists at Oregon Health & Science University confirmed, at the end of July 2017, that they used non-viable embryos to target a gene mutation that causes hypertrophic cardiomyopathy.[118] This dominant mutation, in a gene referred to as *MYBPC3*, only requires one copy of the mutated gene to be inherited for a child to be effected.[119] The targeting efficiency in this study was much higher than the Chinese experiments with 72.2% efficiency.[120] There were fewer undesirable off-target gene mutations in this study,[121] which had been a major concern in previous studies.[122]

E. Public Reactions to Advances in Biotechnology

There have been mixed reactions to the wide-spread use of CRISPR-Cas9 technology to edit genes.[123] While minimal research has been done to ascertain the general public's attitude toward genetic editing, a STAT-Harvard survey conducted in 2016 intimated that only thirty-five percent of citizens in the United States would support therapeutic genetic treatment for unborn human babies.[124] A more systematic study was done later that year that contradicted the findings of the previous study.[125] Gene therapies, both somatic and germline, were seen as acceptable by approximately two-thirds of respondents, with over half of them expressing support for treating medical conditions with genetic editing.[126] Genetic enhancements did not fare as well, with fifty-one percent of participants finding germline enhancements unacceptable and thirty-five percent deeming somatic enhancements

118. Heidi Ledford, *CRISPR Fixes Disease Gene in Viable Human Embryos*, 548 NATURE 13 (Oct. 3 2017), https://www.nature.com/news/crispr-fixes-disease-gene-in-viable-human-embryos-1.22382 [https://perma.cc/5YDS-A2HA]. Hypertrophic cardiomyopathy involves the thickening of the heart muscle and is "the leading cause of sudden death in young athletes." *Id.* It is notable that this study was privately funded and thus escaped the funding compliance dilemma that plagues federally funded institutions. *See* funding discussion *infra* pp. 25-26.

119. *Id.*

120. Hong Ma, et al., *Correction of a Pathogenic Gene Mutation in Human Embryos*, 548 NATURE 413, 415 (2017).

121. *Id.* at 416-17.

122. *See* Cyranoski & Reardon, *supra* note 106, *see also* Callaway, *supra* note 113.

123. *See, e.g.*, Knoepfler *supra* note 14 (advocating for a complete ban on human genetic modification). *But see* STEVE OLSON & COMMITTEE ON SCIENCE, TECHNOLOGY, AND LAW POLICY AND GLOBAL AFFAIRS, INTERNATIONAL SUMMIT ON HUMAN GENE EDITING: A GLOBAL DISCUSSION 7 (2015) [hereinafter SUMMIT] (calling for regular review of advances in clinical germline editing to determine when it should proceed under regulatory oversight).

124. *See* Dietram A. Scheufele, et al., *U.S. Attitudes on Human Genome Editing*, 357 SCIENCE 553, 553 (2017). The survey did not differentiate between somatic and germline edits. *Id.*

125. *Id.*

126. *Id.*

unacceptable.[127] The distinction between genome editing for enhancement and treatment carried more weight than the distinction between somatic and germline modifications.[128] Finally, an online survey of 2,493 subjects, the results of which were published in May 2016, showed there was relative support for furthering this type of biotechnology and research, even when the potential risks were disclosed.[129]

III. SCIENTIFIC AND LEGAL REGULATIONS TO DATE

A. Bioethics

The discovery and use of CRISPR has sparked debate throughout the scientific community regarding the ethical considerations of forever changing not only one person's genome, but the genetic make-up of all their offspring.[130] Long-term effects of human germline modification have yet to be discovered and many scientists have called for a complete moratorium[131]–some call it a "pause"[132]–on clinical applications of CRISPR technology.[133] This "pause" is akin to the 1970s moratorium on molecular cloning.[134]

1. The Birth of Bioethics in the United States

Prior to the 1970s, science as a profession was fairly self-governing in determining hierarchical authority and recognition of accomplishments.[135] While other professions addressed the changes in the so-called "social contract" between their work and society as the decades have passed, the scientific profession lagged.[136] Science has always separated itself from society.[137]

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127. *Id.* at 553-54.

128. Dietram A. Scheufele, et al., *U.S. Attitudes on Human Genome Editing*, 357 SCIENCE 553, 553 (2017). Religion appears to play a role in the support and/or disapproval of genome editing and embryonic research. *Id.* at 554. Much of this discussion about religious implications is outside the scope of this Comment.

129. Steven M. Weisberg, Daniel Badgio, & Anjan Chatterjee, *A CRISPR New World: Attitudes in the Public Toward Innovations in Human Genetic Modification*, 5 FRONTIERS PUB. HEALTH 1, 7 (May 22, 2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5439143/pdf/fpubh-05-00117.pdf. [https://perma.cc/3XSD-E2Q4].

130. *See* Knoepfler, *supra* note 14.

131. *See* Baltimore et al., *supra* note 60, at 37.

132. *See* Doudna, *supra* note 46.

133. *See* Baltimore et al., *supra* note 60, at 37.

134. *See* Doudna, *supra* note 46.

135. *See* JUNE GOODFIELD, PLAYING GOD 77-79 (1977).

136. *Id.* at 79.

137. *Id.* at 86-87. History had not been kind to scientists who focused solely on facts and the results of investigations. The technological advances of the Twentieth Century

This separation and superiority complex was widespread in the eugenics[138] research done at Cold Spring Harbor Eugenics Record Office, funded in part by the renowned Carnegie Institute and the Rockefeller family.[139] While eugenics was considered a legitimate science at the time, public sentiment rightly turned against such research, and discomfort grew with conducting human scientific research.[140]

Senator Walter Mondale initiated Senate hearings in the late 1960s regarding the new life science technologies and what mechanisms the government should put in place.[141] This was prior to the public disclosure of the Tuskegee Syphilis Study,[142] which, when revealed, led to the creation of the first bioethics commission.[143] The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) was created in 1974.[144] The most well-known product of this commission is the *Belmont Report*,[145] which paved the way for federal regulations regarding human subjects in research.[146] The framework devised by the

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intertwined science and society to a point where governments and the public could no longer allow science to proceed unchecked. *Id.*

138. *See Eugenics, supra* note 6.

139. *See* Joshua A. Krisch, *When Racism was a Science*, N.Y. TIMES (Oct. 13, 2014), https://www.nytimes.com/2014/10/14/science/haunted-files-the-eugenics-record-office-recreates-a-dark-time-in-a-laboratorys-past.html [https://perma.cc/GT4E-GB4U].

140. *Id.* The ethical concerns brought forward by the Human Genome Project encouraged the creation of an online archive of the Eugenics Records Office files in 2000. Transparency of American scientists improperly using science as a method to hide racist research is thought to serve as a warning to today's society. *Id.*

141. Jenny Dyck Brian & Robert Cook-Deegan, *What's the Use? Disparate Purposes of U.S. Federal Bioethics Commissions*, 47 HASTINGS CTR. REP. S14, S14-16 (2017).

142. For 40 years, researchers, backed by funding from the United States government, conducted a medical study on economically disadvantaged African American men. They lied about the purpose of this medical study and denied the participants access to standard treatments for their disease. This non-therapeutic study made no headway to disease cures or prevention in an area that had already been documented by the medical community. *See* Ruqaiijah Yearby, *Exploitation in Medical Research: The Enduring Legacy of the Tuskegee Syphilis Study*, 67 CASE W. RES. L. REV. 1171, 1172-73 (2017).

143. *See* Dyck Brian & Cook-Deegan, *supra* note 141, at S14.

144. *Id.*

145. NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1978). The Commission was tasked with identifying ethical principles and developing guidelines for the use of human subjects in biomedical and behavioral research. *Id.* at 1. The basic ethical principles focused on by the Belmont Report included: (1) respect for persons; (2) beneficence, the consideration of a human subject's well-being, broken down into doing no harm and "maximize possible benefits and minimize possible harms"; and (3) justice. *Id.* at 4-6.

146. *See, e.g.*, Protection of Human Subjects, 45 C.F.R. §§ 46.101-46.505 (2010).

National Commission in the 1970s is part of the current debate surrounding U.S. research policy.[147]

The first report regarding the prospect of genetic engineering in human beings, *Splicing Life*,[148] came about in 1982 not as part of a legislative mandate, but in response to concerns from Jewish, Catholic, and Protestant councils about the use of recombinant DNA in gene therapy.[149] Prior to this report, no one federal agency was tasked with oversight or control of genetic engineering techniques.[150] The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research found that, although genetic engineering technology was advancing rapidly, the public concern about "rema[d]e human beings" was exaggerated.[151] The Commission called for thoughtful, close scrutiny for any procedures that might create germline genetic changes and for those whose aim was to "enhanc[e] normal people, as opposed to remedying recognized genetic defects."[152]

This report also got to the heart of the public uneasiness that is still a concern today. It is often referred to as the "Frankenstein factor" because the public fears change to the nature of human beings.[153] With the invention of complicated biotechnology that few members of society understand, the high level of anxiety surrounding such experimentation is understandable.[154] People worry that incurable diseases, even biological weapons, may be created in laboratories.[155]

2. *Scientists Confer on CRISPR Technology*

While some scientists in the 1970s were unsettled by removing genes from one genome and inserting them into another,[156] an international group of scientists in late 2015 called for a moratorium on making human germline

147. *See* Dyck Brian & Cook-Deegan, *supra* note 141, at S14.

148. PRESIDENT'S COMM'N FOR THE STUDY OF ETHICAL PROBLEMS IN MED. & BIOMEDICAL & BEHAVIORAL RESEARCH, SPLICING LIFE: A REPORT ON THE SOCIAL AND ETHICAL ISSUES OF GENETIC ENGINEERING IN HUMAN BEINGS (1982) [hereinafter President's Commission].

149. *See* Dyck Brian & Cook-Deegan, *supra* note 141, at S15.

150. *See* President's Commission, *supra* note 148, at 2.

151. *Id.*

152. *Id.* at 3.

153. *Id.* at 14.

154. *See* Transcript of Oral Argument, *supra* note 22. Notwithstanding the Justices' confusion regarding how CRISPR works, one can see how the general public would be wary of such a complicated addition to the metaphorical technological arsenal.

155. *See* Eric Niiler, *The Pentagon Ponders the Threat of Synthetic Bioweapons*, WIRED (July 10, 2017, 7:00 AM), https://www.wired.com/story/the-pentagon-ponders-the-threat-of-synthetic-bioweapons/ [https://perma.cc/UY4E-HL2E] (discussing the U.S. military's response to a hypothetical bio-engineered virus).

156. *See* President's Commission, *supra* note 148, at 14.

modifications.[157] This international summit addressed the deficiencies in CRISPR-Cas9 as well as its possible applications.[158]

Caution was encouraged to be exercised in abundance by many researchers attending the summit.[159] One scientist extoled the goal of society as "promot[ing] a better life for all, and . . . ensur[ing] that everybody can live a life in dignity and freedom."[160] The lack of data on future germline editing implications is a major sticking point.[161] More than one scientist at the summit was reluctant to endorse germline editing due to the unpredictable risks to future generations.[162] With the prediction that the benefits of germline editing may be outweighed by the unknown long-term harms, there was a morality call for not only researchers but future parents to take the status of a human embryo, lacking the capability to make decisions for its own future, into account.[163]

The wide-spread introduction of CRISPR-Cas9 technology for editing the human germline prompted scientists to self-regulate regarding the appropriateness of proceeding with making permanent changes to the human genome.[164] As with most issues, the scientific community is still divided on whether science should be vigorously pursued or if a pause is necessary to fully comprehend and address the implications of permanently altering the human genome.[165] The end of the International Summit on Human Gene Editing brought the following conclusions: (1) basic and preclinical research should proceed, but no pregnancies should be established using modified cells and all research is subject to legal and ethical rules; (2) somatic gene editing may proceed within current and evolving regulations; (3) proceeding with germline editing would be "irresponsible" due to unresolved safety issues, lack of societal consensus, and wide-spread regulatory or legislative bans; and (4) continuation of an international forum to establish norms and discourage inappropriate activities.[166] While these conclusions provide an excellent base for scientists to self-regulate, the Summit's third conclusion, that

157. *See* Doudna, *supra* note 46.
158. *See* SUMMIT, *supra* note 123, at 1-2.
159. *Id.* at 3.
160. *Id.* at 4.
161. *Id.*
162. *Id.*
163. STEVE OLSON & COMMITTEE ON SCIENCE, TECHNOLOGY, AND LAW POLICY AND GLOBAL AFFAIRS, INTERNATIONAL SUMMIT ON HUMAN GENE EDITING: A GLOBAL DISCUSSION 4 (2015).
164. The academies that convened to seek the moratorium lack regulatory power, but such a strong declaration of moral authority was likely to be widely accepted by scientists across the globe. *See* Doudna, *supra* note 46.
165. *See generally* Wade, *supra* note 42.
166. *See* SUMMIT, *supra* note 123, at 6-7.

proceeding with germline editing would be irresponsible, is too narrow and focuses only on the fear of failure instead of the promise of success.

B. Federal Regulations

Legislators have grown more aware of the need to regulate emerging biotechnologies.[167] Yet, regulations have always served as the tortoise pitted against science's hare with the finish line far in the distance. Relevant regulations are sorely lacking while prohibitions on federal funding for research involving human embryos is overly strict.[168] In order to determine how current regulations should look, one must examine those currently in place and how they are currently ineffectual.

1. GMOs and CRISPR-Cas9

Genetically modified organisms (GMOs) have been regulated in the United States since 1986.[169] The Food and Drug Administration regulates human and animal food that is a product of genetically engineered plants.[170] Currently, gene-edited crops are not regulated in the same way genetically engineered crops are.[171] Companies that create gene-edited plants and wish to market them to consumers can ask the USDA whether regulatory review is required for that product. To date, gene-edited plants lacking foreign DNA

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167. *See infra* notes 169, 177-81 and accompanying text. Possible challenges faced by regulatory agencies, such as jurisdiction and protecting consumers using risk-analysis tools, were acknowledged in NAT'L ACADS. OF SCI., ENGINEERING, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 11 (2017).

168. *See* discussion *infra* Part II, Section B(5) and notes 196-208.

169. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,3302 (June 26, 1986) [hereinafter Coordinated Framework]. Agency jurisdiction over new biotechnologies is determined by the use of the product. *Id.* at 23,304. *See also* Luis Acosta, *Restrictions on Genetically Modified Organisms: United States*, LIBR. CONGRESS (Mar. 2014), https://www.loc.gov/law/help/restrictions-on-gmos/usa.php [https://perma.cc/2TU9-4WRL] (describing GMOs in terms of the structure of agencies tasked with regulating them and the restrictions placed upon research, production, and marketing).

170. *See* Federal Food, Drug, and Cosmetics Act, 21 U.S.C. §§ 16-2252; *see also* National Bioengineered Food Disclosure Standard, 7 U.S.C. § 1639 (2016); *see also Food from Genetically Engineered Plants*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/Food/IngredientsPackagingLabeling/GEPlants/default.htm [https://perma.cc/PQZ5-5UF7] (providing a brief history of the FDA's biotechnology policies).

171. *See* Bomgardner, *supra* note 80, at 32. PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY concluded that as the rate of biotechnology is growing, societal factors will remain important in the debate regarding the uses of biotechnology products. *See* NAT'L ACADS. OF SCI., ENGINEERING, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 172-74 (2017).

are not under the USDA's regulatory authority.[172] Many researchers agree that the regulatory focus should be on the foreseeable risks posed by added or altered traits instead of the process used to insert the trait into the plant.[173]

Using CRISPR-Cas9, Penn State professor Yinong Yang removed a specific browning enzyme from a mushroom's DNA in 2016.[174] The USDA later confirmed that this mushroom would not require USDA approval or regulatory review.[175] This mushroom differs from most GMO crops because no foreign DNA was ever introduced; only naturally occurring enzyme production was removed.[176]

2. *Early Regulatory Framework for Genetically Altered Goods*

With concerns about "whether the regulatory framework that pertained to products developed by traditional genetic manipulation techniques was adequate for products obtained with [then] new techniques,"[177] a comprehensive Federal regulatory policy was published in 1986.[178] Setting forth the system for evaluating modern biotechnology products was based upon laws that were designed to protect public health and the environment.[179]

Human genetics research was not addressed until 2004 when the President's Council on Bioethics[180] proposed modifications to legislation

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172. *See* Bomgardner, *supra* note 80 at 34.

173. *Id.* One example of a foreseeable risk given by the director of the Center for Science in Public Interest, Gregory Jaffe, would be the possibility of allergic reactions if a Brazil nut gene that improved resistance to disease were inserted into another plant. *Id.*

174. *See* Chuck Gill, *Gene-Edited Mushroom Created by Penn State Researcher is Changing GMO Dialogue*, PENN ST. NEWS (Apr. 19, 2016), http://news.psu.edu/story/405406/2016/04/19/research/gene-edited-mushroom-created-penn-state-researcher-changing-gmo [https://perma.cc/3M66-JZDF].

175. *Id.*

176. *Id.*

177. Coordinated Framework, *supra* note 169, at 23,302.

178. *See id.* This framework laid out which agencies oversee biotechnology products—mainly the EPA, FDA, and USDA—and was later updated to include descriptions for "proper basis for agencies' exercise of oversight authority within the scope of discretion afforded by statute." EMERGING TECHNOLOGIES INTERAGENCY POLICY COORDINATION COMM.'S BIOTECHNOLOGY WORKING GRP., NATIONAL STRATEGY FOR MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS (2016), https://www.epa.gov/sites/production/files/2016-12/documents/biotech_national_strategy_final.pdf [https://perma.cc/67V9-6534] [hereinafter STRATEGY].

179. *See* STRATEGY, *supra* note 178. Precisely editing the human genome was still in the future when this framework was adopted, so it focused only on enhanced or manufactured foods, waste disposal, medicines, and pesticides. *See id.*

180. Formed by an executive order in 2001 and formed to advise the President on emerging bioethical issues, the President's Council on Bioethics was tasked with five functions:

targeting possibly unethical practices in human reproduction.[181] Members of the Council were acutely aware that public policy as well as public understanding were far behind biotechnical developments. Somatic gene therapy was addressed at length by the Council, but it was only hypothetical at the time.[182] No products for gene-therapy have been approved for general use by the FDA and any such products require the "submission of an investigational new drug (IND) application to the FDA."[183]

3. *Updated Framework Restricts Progress*

Biotechnology advancements, such as CRISPR-Cas9, led to an attempt to modernize regulations for products created using such technology.[184] The 1986 framework set up the regulatory structure, but it was overly complicated and burdensome for researchers seeking funding and left uncertainty about each agency's jurisdiction.[185] In acknowledging the rapid advancements in the biotechnology field, the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology stresses the safety of biotechnology products, aims to increase public confidence, and strives to remove barriers to innovation.[186] While this update may increase public confidence by simplifying and breaking out what each agency's roles, responsibilities, and goals are,[187] "unnecessary barriers to future innovation and competitiveness"[188] remain. The complete ban on germline therapy, as discussed below, is a restriction on innovation.[189]

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(1) to undertake fundamental inquiry into the human and moral significance of developments in biomedical and behavioral science and technology;
(2) to explore specific ethical and policy questions related to these developments;
(3) to provide a forum for a national discussion of bioethical issues;
(4) to facilitate a greater understanding of bioethical issues; and
(5) to explore possibilities for useful international collaboration on bioethical issues.
Exec. Order No. 13,237, 66 Fed. Reg. 59,851 (Nov. 30, 2001).

181. PRESIDENT'S COUNCIL ON BIOETHICS, REPRODUCTION & RESPONSIBILITY: THE REGULATION OF NEW BIOTECHNOLOGIES xviii (2004) https://repository.library.georgetown.edu/bitstream/handle/10822/559381/_pcbe_final_reproduction_and_responsibility.pdf?sequence=1&isAllowed= [https://perma.cc/AW5B-EB7E] [hereinafter REPRODUCTION & RESPONSIBILITY].

182. *Id.* at 105-10

183. *Id.* at 111.

184. See Cyranoski & Reardon, *supra* note 106.

185. EPA, MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS: FINAL VERSION OF THE 2017 UPDATE TO THE COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY 5 (2017), https://www.epa.gov/sites/production/files/201701/documents/2017_coordinated_framework_update.pdf. [https://perma.cc/YYX3-SXR3] [hereinafter FINAL VERSION].

186. *Id.* at 1.

187. *See, e.g.*, *id.* at 8-35.

188. *Id.* at 1.

189. *See* discussion *infra* Part III, Section B(5)-(7).

4. *The Common Rule Would Apply if Germline Editing Was Allowed*

Research on human subjects is heavily regulated in the United States.[190] Federal Policy for the Protection of Human Subjects, referred to as the "Common Rule" was adopted in 1991.[191] These protections were codified by fifteen federal agencies and departments in separate regulations, with the regulations of the Department of Health and Human Services being most applicable to CRISPR-Cas9.[192] Under this policy, any research institutions supported by the funding from the federal government must comply with all requirements.[193] The Common Rule applies, with a few exceptions, to all research that involves human subjects.[194] It outlines the requirements for informed consent, institutional review board involvement and functions, assurances required for the protection of the rights and welfare of the human subjects, certification requirements, and research approval requirements.[195]

5. *Lack of Federal Funding Stymies CRISPR-Cas9 Innovation*

Research into human germline modification only partially falls under the Common Rule.[196] While any research done involving human subjects

190. Protection of Human Subjects, 45 C.F.R. §§ 46.101-46.505 (2009); *see infra* note 194.

191. *Id.*

192. Basic HHS Policy for Protection of Human Research Subjects, 45 C.F.R. §§ 46.101-46.124 (2009).

193. Assuring Compliance with This Policy – Research Conducted or Supported By Any Federal Department or Agency, 45 C.F.R. § 46.103 (2009). The revised final rule declined to extend the Common Rule to privately-funded clinical trials. Federal Policy for the Protection of Human Subjects, 82 Fed. Ref. 7149, 7150 (Jan. 19, 2017). Originally set to become effective January 19, 2018, the effective date of the revised Common Rule was extended to July 19, 2018. *HHS and 15 Other Federal Departments and Agencies Announce an Interim Final Rule that Delays Both the Effective Date and the General Compliance Date of the Revisions to the Federal Policy for the Protection of Human Subjects to July 19, 2018,* U.S. DEP'T. HEALTH & HUM. SERVS. (Jan. 17, 2018), https://www.hhs.gov/ohrp/interim-final-rule-common-rule.html [https://perma.cc/29MZ-BAEA].

194. 45 C.F.R. §46.102(f) (2009) defines "human subject" as "a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interactions with the individual, or (2) identifiable private information." The regulation provides additional protections for pregnant women, fetuses, and newborns. 45 C.F.R. §§ 46.201-46.207 (2009). Prisoners are provided additional protections under 45 C.F.R. §§ 46.301-46.306 (2009). There are additional requirements for using children as research subjects. 45 C.F.R. §§ 46.401-46.409 (2009).

195. *See generally* 45 C.F.R. § 46 (2009).

must adhere to the requirements of the Common Rule,[197] currently, federal funding for such research is prohibited.[198] This prohibition is a result of the Dickey-Wicker amendment (D-W), which bars the NIH from providing federal funding for the creation of human embryos for research purposes as well as the destruction, discard, or subjecting human embryos "to risk of injury or death greater than that allowed for research on fetuses in utero."[199] Each year since 1996, the D-W has been added to Labor, Health and Human Services, and Education appropriations legislation.[200] After President Obama issued an executive order in 2009,[201] authorizing the NIH to fund and conduct embryonic stem cell research, the United States Court of Appeals for the District of Columbia affirmed in *Sherley v. Sebelius*[202] that D-W was not violated because the present tense text addressing research is ambiguous and that NIH's interpretation of D-W is reasonable.[203]

Funding has continued to be an issue for researchers seeking federal funding for germline modification studies.[204] Section 749 of the

196. *See* Rebecca Dresser, *Genetic Modification of Preimplantation Embryos: Toward Adequate Human Research Policies*, 82 MILBANK Q. 195 (2004) (discussing shortcomings of regulations for genetically modified embryos).

197. *Id.*

198. *See, With Stringent Oversight, Heritable Germline Editing Clinical Trials Could One Day be Permitted for Serious Conditions; Non-Heritable Clinical Trials Should be Limited to Treating or Preventing Disease or Disability at this Time*, NAT'L ACAD. MED. (Feb. 14, 2017), https://nam.edu/with-stringent-oversight-heritable-germline-editing-clinical-trials-could-one-day-be-permitted-for-serious-conditions-non-heritable-clinical-trials-should-be-limited-to-treating-or-preventing-diseas/ [https://perma.cc/P446-CX5P].

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

200. 156 CONG. REC. S7036 (daily ed. Sept. 13, 2010) (statement of Sen. Specter).

201. Exec. Order. No. 13,505, 74 Fed. Reg. 10,667 (Mar. 11, 2009) (lifting human embryonic stem cell research funding restrictions instituted in the Bush administration).

202. Sherley v. Sebelius, 644 F.3d 388, 394-96 (2011); *see* Chelsea L. Gulinson, *Embryonic Stem Cell Tourism*, 58 JURIMETRICS 17 (2017) (arguing that restricting stem cell research funding not only impedes scientific progress, but promotes risky procedures conducted abroad).

203. *Sherley v. Sebelius* bounced from the District Court to the Court of Appeals multiple times for standing related issues. The final decision rested on the fact that NIH was not funding research projects that obtained embryonic stem cells by destroying embryos, but provided funding for projects in which embryonic stem cells would be used. *Sherley*, 644 F.3d. at 390. Unfortunately, D-W still applies to germline modifications to human embryos due to the high death/destruction rate of the embryos.

204. When government funds are not available to institutions that rely on federal grants for most of their research funding, private funding must be obtained. *See* Tanya Lewis, *Congress Just Put a Massive Roadblock in the Way of Genetically Editing Human Embryos*, BUS. INSIDER (Dec. 16, 2015, 2:45 PM) http://www.businessinsider.com/congress-bans-funding-for-embryo-gene-editing-2015-12 [https://perma.cc/BZ72-PRHF] (discussing the funding limitations of the Consolidated Appropriations Act of 2016, Pub. L. No. 114-113, § 749, 129 Stat. 2242, 2283 (2015)).

appropriations bill for fiscal year ending September 30, 2016, states "None of the funds made available by this Act may be used . . . in research in which a human embryo is intentionally created or modified to include a heritable genetic modification."[205] This rider was renewed again for fiscal year 2017.[206] This rider essentially continues the ban of therapeutic germline modifications and creates a roadblock for any corporate entity that seeks to gain FDA approval for clinical trials.[207] Limiting funding for human germline editing to privately funded institutions creates a lack of transparency that is required for publicly funded institutions. Withholding funding simply encourages back-alley deals and research. As of the writing of this Comment, a consolidated appropriations bill has not been passed for fiscal year 2018.[208]

6. *Purporting Advancement of Biomedical Research, the 21st Century Cures Act Falls Flat*

The end of 2016 brought passage of the 21st Century Cures Act[209] ("Cures Act"), legislation designed to accelerate development of biomedical products and availability of advances to needy patients.[210] The Precision Medicine Initiative outlined in the Cures Act provides funding for disease prevention as well as diagnosis and treatment.[211] Yet, nowhere in this statute is genetic editing authorized. Precision is one of the advantages touted by CRISPR supporters,[212] but it does not seem to be precise enough to be included in the Precision Medicine Initiative. There is authorization for use of "targeted drugs for rare diseases,"[213] but the qualifications for incorporating

205. Consolidated Appropriations Act of 2016, Pub. L. No. 114-113, § 749, 129 Stat. 2242, 2283 (2015).

206. Consolidated Appropriations Act of 2017, Pub. L. No. 115-31, § 736, 131 Stat. 135, 173 (2017).

207. I. Glenn Cohen & Eli Y. Adashi, *The FDA is Prohibited from Going Germline*, 353 SCIENCE 545, 546 (2016).

208. Press Release, U.S. House of Representatives Committee on Appropriations, House Approves Budget and Emergency Supplemental Agreement (Feb. 9, 2018), https://appropriations.house.gov/news/documentsingle.aspx?DocumentID=395097 [https://perma.cc/7JGE-87HK] (approving funding for government operations until March 23, 2018).

209. 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016) [hereinafter Cures Act]. In addition to promoting medical product development and granting new authority to the FDA for training and retention of experts, major funding was authorized for NIH Innovation Projects, the Precision Medicine Initiative, the "BRAIN Initiative," adult stem cell research, FDA Innovation Projects, and Opioid Abuse Crisis funding for the States. *See id.*

210. *See id.*

211. 21st Century Cures Act, Pub. L. No. 114-255, § 498E(a), 130 Stat. 1033, 1048 (2016).

212. *See* Kolker, *supra* note 51.

213. 21st Century Cures Act, Pub. L. No. 114-255, § 529A, 130 Stat. 1033, 1091 (2016).

genetically targeted technology – much like what CRISPR-Cas9 technology can offer – are limited to non-replicating nucleic acid and analogous compounds,[214] which are not included in the type of gene therapy CRISPR-Cas9 can provide.[215] In fact, the word "germline" is not to be found in the entirety of the Cures Act.

7. *Scientific Community Proposes Balance*

In February 2017, a committee from the National Academy of Sciences, Engineering and Medicine endorsed the modification of human embryos with the limitation that it only be done to correct mutations causing "serious disease or condition" when no other "reasonable alternatives" are available.[216] This caveat is reasonable considering the current practical applications of this biotechnology and lack of knowledge regarding long-term consequences of human germline modifications.[217]

The most applicable document to human germline editing using the CRISPR-Cas9 system is a position statement issued by the American Society of Human Genetics (ASHG).[218] A myriad of professional science organizations from six continents reviewed and endorsed this statement,[219] which discussed and offered solutions for the ethical issues raised by CRISPR-Cas9 germline gene editing.[220] ASHG's position is:

> (1) At this time, given the nature and number of unanswered scientific, ethical, and policy questions, it is inappropriate to perform germline editing that culminates in a human pregnancy. . . .
>
> (2) Currently, there is no reason to prohibit in vitro germline genome editing on human embryos and gametes, with appropriate oversight and consent from donors, to facilitate research on the possible future clinical applications of gene

214. DNA replication is necessary for cell division and organisms cannot grow without it. *See* Richard J. Roberts, *Nucleic Acid*, ENCYCLOPEDIA BRITANNICA, https://www.britannica.com/science/nucleic-acid/Nucleic-acid-metabolism [https://perma.cc/C2C8-7JD5] (last visited Feb. 4, 2018).

215. 21st Century Cures Act, Pub. L. No. 114-255, §3012, 130 Stat. 1033, 1091 (2016).

216. Pam Belluck, *In Breakthrough, Scientists Edit a Dangerous Mutation from Genes in Human Embryos*, N.Y. TIMES (Aug. 2, 2017), https://www.nytimes.com/2017/08/02/science/gene-editing-human-embryos.html [https://perma.cc/2HHX-MZ2P].

217. *See* Doudna, *supra* note 46.

218. *See* ASHG Statement, *supra* note 24.

219. *Id.* at 167.

220. *Id.* at 169-74.

> editing. There should be no prohibition on making public funds available to support this research. . . .
>
> (3) Future clinical application of human germline genome editing should not proceed unless, at a minimum, there is (a) a compelling medical rationale, (b) evidence base that supports its clinical use, (c) an ethical justification, and (d) a transparent public process to solicit and incorporate stakeholder input.[221]

This stance is not only rational, but within reach. The ASHG Statement has mountainous support from highly respected and knowledgeable geneticists around the world.[222] Researchers, not limited to private funding, are encouraged by the ASHG Statement to proceed with germline gene editing on non-viable human embryos that is limited by oversight and consent from donors.[223]

IV. NEED TO EVOLVE

The ASHG Statement advocates for waiting on answers to ethical, scientific, and policy questions before editing the germline of viable human embryos; providing public funding for researchers who meet the appropriate guidelines; and proceeding with human germline editing in future clinical applications when there is a compelling, evidence-based medical rationale, it is ethically justified, and the public is aware of the process.[224] This statement should be adopted in full. The following sections discuss how the three suggestions of the ASHG are necessary for United States policy makers to consider.

A. Ethical Considerations Cannot Justify Lack of Forward Movement

The breakneck pace of science cannot be matched by the slow and steady regulatory system. While scientists and researchers can have multiple experiments and trials running at the same time for the same principles,

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221. *Id.* at 172-73.

222. *Id.* at 167. Among those organizations that approved the position statement are the Association of Genetic Nurses and Counselors, Canadian Association of Genetic Counsellors, International Genetic Epidemiology Society, American Society for Reproductive Medicine, Asia Pacific Society of Human Genetics, British Society for Genetic Medicine, Human Genetics Society of Australasia, Professional Society of Genetic Counselors in Asia, and Southern African Society for Human Genetics. Kelly Ormond, et al., *Human Germline Genome Editing*, 101 AM. J. HUM. GENETICS 167 (2017).

223. *See* ASHG Statement, *supra* note 24, at 167.

224. *Id.* at 172-74.

legislators and regulatory agencies do not have that luxury.[225] This does not excuse the lack of proper regulations and funding for human germline editing. Just as the ASHG proposed, human germline editing research can be conducted in an ethical manner while complying with all pertinent laws and policies.[226] The benefits of such research and the possibility of medical breakthroughs for those people struggling with devastating genetic diseases far outweigh the ethical concerns that have been addressed for decades.[227] This is not a call to immediately begin germline editing on viable human embryos. As the ASHG Statement suggests, there are certain questions that must be answered prior to taking that step.[228]

Gone are the days of thinking hypothetically about genetic modifications in humans.[229] The Frankenstein factor[230] has been brought from the shadows into the limelight. The hype around the evils of genetic editing goes back to when evil was trying to conduct gene editing based on bigotry.[231] The here and now reality is that editing the human germline is possible, but scientists are incredibly concerned with the ethical implications of such biotechnical advances.[232] Some opponents argue that editing the human germline is like "playing God" and should never be allowed.[233] This philosophical argument does not withstand practicality. Modern medicine intervenes on a daily basis with life-saving surgeries and prescription medicines. "Do not resuscitate" orders are the exception, not the standard.[234] The possibility that CRISPR-Cas9 can be used to treat cancer patients and eradicate debilitating genetic diseases by modifying the human germline outweighs any abstract reasoning against the process because, as the ASHG statement proposes, all clinical applications of this technology must meet stringent standards.[235]

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225. While there are multiple committees in the House and Senate, with each reviewing multiple bills, all those committees must come together to debate, amend, and vote on each bill. This can be a time-consuming process with many legislators involved. *See The Legislative Process*, U.S. HOUSE REPRESENTATIVES, https://www.house.gov/the-house-explained/the-legislative-process [https://perma.cc/3CKF-3CA2].

226. *See* ASHG Statement, *supra* note 24.

227. *See* Glenn McGee, *Genetic Imagination: Ethics and 21 Century Genetics*, 3 J. L. & SOC. CHALLENGES 139 (1999) (discussing the history, weaknesses, and proposed reform for genetic science).

228. *See* ASHG Statement, *supra* note 24, at 172-73.

229. *See* REPRODUCTION & RESPONSIBILITY, *supra* note 181, at 107.

230. *See* President's Commission, *supra* note 148.

231. *See* Steven A. Farber, *U.S. Scientists' Role in the Eugenics Movement (1907-1939): A Contemporary Biologist's Perspective*, 5 ZEBRAFISH 243, 243-44 (2008).

232. *See* Doudna, *supra* note 46.

233. *See generally* GOODFIELD, *supra* note 135.

234. Codification of this rule varies by state. In Illinois, health care providers are to provide life-sustaining treatment unless directed otherwise by a do not resuscitate order. 755 ILL. COMP. STAT. 40/65 (2017).

235. ASHG Statement, *supra* note 24, at 173.

B. With Great Power Comes Great Responsibility

Ethical issues arise with each new technology.[236] The real ethical assessment falls into two categories: (1) issues that arise through human germline editing success and (2) issues that arise through its failure. A prudent step toward proper regulation of biotechnologies, such as CRISPR-Cas9, can address all these issues. Regulating this technology now, when the technology is not yet advanced enough to create viable embryos, could prevent unethical exploration of non-therapeutic use.

Success in experimentation is usually the goal of each scientist conducting an experiment. There is always trial and error, but repetitive successes are what lead to medical innovations that benefit society as a whole. Even the "most famous failed experiment[]" contributed to the greater good.[237] A successful germline experiment could take many forms, but opponents of germline editing focus on the "Frankenstein factor"[238] as opposed to the good that comes from embryonic deletion of the expanded portion of the inheritable gene that causes Huntington's Disease.[239]

The benefits of the proposed gene therapy outweigh the possible embryo loss and risks by offering generations without debilitating genetic diseases.[240] Eradicating such a devastating inheritable genetic disease, such as Huntington's Disease, is a compelling medical rationale that should not be overlooked. The severity of the condition and lack of other options for treatment meet the standard laid out in the ASHG Statement.[241] As CRISPR-Cas9 becomes more widely available, lack of regulation and guidance regarding

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236. *See, e.g.*, William S. Singer, *Exploring New Terrain: Assisted Reproductive Technology (ART), The Law and Ethics*, 8 RUTGERS J. L. & PUB. POL'Y 918 (2010) (discussing the ethical issues attorneys face when dealing with assisted reproductive technology).

237. The Michelson-Morley experiments focused on the speed of light in a vacuum. The results of this failed experiment would later support Albert Einstein's theories of special relativity. *See* Sarah Wells, *The Most Famous Failed Experiment*, STEMVISISONS BLOG (Nov. 15, 2016), https://ssec.si.edu/stemvisions-blog/most-famous-failed-experiment [https://perma.cc/QZV9-YEJV].

238. *See* President's Commission, *supra* note 148.

239. *What is Huntington's Disease?*, HUNTINGTON'S DISEASE SOC'Y AM., http://hdsa.org/what-is-hd/ [https://perma.cc/QD2H-CKEQ] [hereinafter *Huntington's*]. Huntington's Disease, a fatal genetic disorder, is inheritable. "Every child of a parent with HD has a 50/50 chance of inheriting the expanded gene that causes the disease." This incurable disease causes nerve cells in the brain to progressively breakdown until the ability to walk and speak ceases. *See id.*

240. *See* discussion, *infra* Part IV, Section C.

241. *See* ASHG Statement, *supra* note 24, at 173. Suggestions for qualifying rationales include looking at the quality of life and level of impairment by considering the treatability, medical severity, available treatments, and the risk of occurrence of the condition. *Id.*

this biotechnology promotes unregulated labs to forego proper formal review and approval before implementing these techniques.[242]

Opponents of CRISPR-Cas9 modifications point to the high percentage of off-target mutations that researchers assume are introduced by CRISPR-Cas9.[243] The failure rate of the first non-viable embryo CRISPR-Cas9 experiments in China was astounding.[244] Only a fraction of the embryos were successfully modified, leading one stem biologist to say, "Their study should be a stern warning to any practitioner who thinks the technology is ready for testing to eradicate disease genes."[245] While these initial studies seem concerning, no new biomedical technology is 100% safe and reliable. Oftentimes, it is a matter of determining if the benefits outweigh the risks. The need to continue to refine the CRISPR-Cas9 process is part of why scientists continue to conduct studies on non-viable embryos, just as the ASHG Statement proposes.[246] Scientists are not proposing to create designer babies in the near future.[247] Regulating now, with a prohibition on such genetic enhancements, could assuage the ethical concerns of some CRISPR and germline modification opponents and further the ASHG's position by requiring a compelling medical rationale with an evidence base.[248] Placing limits on the use of CRISPR-Cas9 will not harm the refinement process, but allows for eventual correction of well-known diseases.

C. Correction of Well-Known Fatal Genetic Diseases

Embracing CRISPR-Cas9 for disease correction only is a step in the right direction for regulators. Some critics argue that curing deadly genetic diseases is unnatural because, in the whole of human history, it is normal for the human population to be reduced by epidemics.[249] The benefits of human germline editing on such diseases outweigh the risks because correcting or possibly eradicating genetic diseases benefits humanity's goal of a healthier human race and can be accomplished by adopting the ASHG suggestions moving forward. Fatal genetic diseases such as Huntington's Disease and

242. *See id.*
243. *See* Cyranoski & Reardon, *supra* note 106.
244. *Id.*
245. *Id.*
246. ASHG Statement, *supra* note 24, at 172.
247. *See* Knoepfler, *supra* note 14.
248. *See id.* While Knoepfler calls for a flat-out moratorium on CRISPR use in reproduction, there are consequences to not acting as well. Allowing children to be born with debilitating diseases like Huntington's, when the technology exists to eradicate it, is irresponsible.
249. *See* Juan Enriquez, *Future Consequences*, TED RADIO HOUR (Sept. 14, 2017), https://www.npr.org/programs/ted-radio-hour/547886174/future-consequences [https://perma.cc/35W2-KZHC].

amyotrophic lateral sclerosis (ALS)[250] can only benefit from such emerging biotechnologies as CRISPR-Cas9. Not all fatal inheritable genetic diseases have high chances to be passed in the familial form.[251] While the children of a parent with Huntington's Disease have a 50/50 chance of inheriting the disease,[252] only five to ten percent of all ALS cases are inherited from a parent.[253] Allowing researchers the freedom and funding to conduct studies where CRISPR-Cas9 is used to correct or potentially eradicate such devastating diseases at the source, DNA, is the path regulators should take.

This type of germline editing falls under the ASHG suggestion that "[f]uture clinical application of human germline genome editing should not proceed unless . . . there is (a) a compelling medical rationale, (b) an evidence base . . . (c) an ethical justification, and (d) a transparent public process . . . ."[254] The treatment of such diseases is compelling, with an evidence base to support a clinical use of germline editing, and is compassionate and ethically sound. Such a framework of requirements prompts scientists to do what is in the best interest of the patient, while the transparency requirement holds the researchers accountable to not just the government, but to society.

In addition to the required compelling medical rationale, evidentiary basis, ethical justification, and a transparent public process, enforcement may be accomplished through an oversight committee. An active committee review for individual projects, similar to the committees formed when in vitro fertilization was a relatively young technology,[255] can be included to ensure the study falls under the auspices of the framework. Researchers would also have to comply with the informed consent guidelines as outlined in the Common Rule.[256] This Comment leaves medical rationale and ethical

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250. ALS is also known as Lou Gehrig's Disease. This incurable progressive neurological disease affects the neurons "responsible for controlling voluntary muscle movement" like walking and talking. *Amyotrophic Lateral Sclerosis (ALS) Fact Sheet*, NAT'L INST. NEUROLOGICAL DISORDERS & STROKE, https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet [https://perma.cc/4NY5-ANQF] [hereinafter *ALS*].

251. For example, sickle cell anemia, a heritable disease that leads to a lower than normal number of red blood cells, has a one in four chance that a child born to parents who both carry the sickle cell trait will inherit the condition. *Sickle Cell Anemia*, NAT'L INSTS. HEALTH, https://rarediseases.info.nih.gov/diseases/8614/sickle-cell-anemia [https://perma.cc/9L5G-U6SW].

252. *See Huntington's*, *supra* note 239.

253. *See ALS*, *supra* note 250.

254. *See* ASHG Statement, *supra* note 24, at 173.

255. *See generally* SUZANNE WYMELENBERG & INST. OF MEDICINE, SCIENCE AND BABIES: PRIVATE DECISION, PUBLIC DILEMMAS 153-56 (1990). Without active oversight and ethics review committees, the transparency of these technologies lessens and the public mechanism for acknowledging and addressing social and ethical concerns vanishes. *Id.* at 156.

256. 45 C.F.R. § 46 (2009).

justifications to the medical community, but goes on to discuss the remaining issues of transparency and the need for cooperation.

D. Transparency

Transparency is created when public funding is available. Limiting this biotechnology to private institutions and private funding provides little oversight. As clinical trials move forward, baselines are created for new medications and procedures. It is that new data that provides insight for not only scientists, but regulators, such as the FDA. As previously discussed, allowing disease prevention at the source, DNA, has both an evidence base and an ethical justification.[257] Transparency can also be created through publicly funding such clinical trials because, often to the disdain of researchers, a great deal of reporting must be done.[258]

When scientists openly share information in a manner that is accessible to patients, their families, and other researchers, while respecting the privacy of the patients, everyone wins.[259] There is currently little collaboration in biomedical research, where competition is encouraged and rewarded.[260] It is often a race to publish instead of a race to alleviate the suffering of those who depend on biomedical and biotechnical research.[261] This needs to change. Advances in disease identification and treatment should not be withheld from the masses simply because the federal government cannot move quickly with enough foresight and confidence in the medical community to properly fund such research.[262] Legislators need to address the lack of proper regulations and funding by adopting the ASHG's second suggestion and facilitate research of human germline editing by providing such funds to researchers and institutions.[263] Transparency leads to holding members of the government and regulatory agencies accountable to the public.[264]

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257. *See* discussion *supra* Part IV, Section C.

258. *See generally* Cures Act, *supra* note 209.

259. *See* Sharon Terry, *Citizen Science*, TED RADIO HOUR (Sept. 28, 2017), https://www.npr.org/programs/ted-radio-hour/551030943/citizen-science?showDate=2017-09-29 [https://perma.cc/M25J-MFF5] (discussing researchers' response to a mother's plea that they obtain her children's blood samples from a team of researchers that had drawn some two days earlier).

260. *Id.*

261. *Id.*

262. *See* discussion *supra* Section III, Part B(3)-(6).

263. ASHG Statement, *supra* note 24, at 173.

264. *See* Elena Kagan, *Presidential Administration*, 114 HARV. L. REV. 2245 (2001) (examining President Clinton's enhanced presidential control and advocating that this type of presidential administration creates a more transparent government).

Federal grants fund much of the research taking place in universities, hospitals, medical centers, national labs, and other research facilities.[265] Drastic cuts have been made to funding allocations from the federal government since fiscal year 2011.[266] With the NIH providing the largest amount of funding for biomedical research, change should originate here.[267] While the Cures Act does provide funding for many areas of biomedical research, the funding for human germline editing remains woeful.[268] It could easily be classified as precision medicine, but legislators and regulators refuse to do so. If they were to qualify the CRISPR-Cas9 system as it actually is, a biotechnical advancement capable of precisely editing the human germline in a manner that benefits families dealing with fatal genetic diseases, and regulate it, funding could be available. Simply providing funding for the development of transplantable porcine organs[269] could help prevent trade in black market organs for transplant.[270]

In addition to lack of funding from NIH, the longevity of funding restraints such as D-W is a concern. The renewal of the appropriations rider prohibiting funding for human embryos that have been modified at the germline level is another concern.[271] The continuation of such restrictions should not be condoned simply because it has always been that way.[272] Legislators should do what is right for their constituents and the greater good should take precedent over precedent. The transparency created by the provision of public funding for human germline editing research gives the opportunity for a vocal response from the greatest stakeholders, the American public.

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265. *See generally Federal Funding for Biomedical and Related Life Sciences Research: FY 2018*, FED'N AM. SOC'YS FOR EXPERIMENTAL BIOLOGY (2017), http://faseb.org/Portals/2/PDFs/opa/2017/Federal%20Funding%20Report%20FY%202018.pdf [https://perma.cc/4EDJ-AESP].

266. *Id.* at 1. In the United States, there was a thirteen percent federal funding reduction for medical research from fiscal year 2011 to fiscal year 2015. In South, East, and Southeast Asia, funding in this area "grew from 27 to 40 percent." *Id.* For the United States to remain competitive, federal funding should increase and remain stable.

267. *See id.* at 3. "NIH's focus on investigator-initiated research identified the underlying causes of many diseases and fostered the translation of scientific discoveries into effective clinical interventions" is just further proof that NIH-funded scientists are essential to furthering research in human germline editing. *Id.*

268. *See* funding discussion *supra* Part II, Section B.

269. *See* Kolata, *supra* note 91; *see also* discussion *supra* Part I, Section D(2).

270. *See* Kristin Houser, *Black Market Bodies: How Legalizing the Sale of Human Organs Could Save Lives*, FUTURISM (Nov. 6, 2017), https://futurism.com/sale-human-organ/ [https://perma.cc/A7TG-A9DH]. While not advocating for the sale of human organs, transplantable organs produced using CRISPR-Cas9 can serve the same purpose.

271. *See* Consolidated Appropriations Act of 2017, *supra* note 206.

272. Legislators may want to remember when their mothers asked, "just because your friend jumped off a bridge, does that mean you should too?" Keeping up with the status quo is not a rational reason for denying funding for germline modification research.

E. International Cooperation

Countries tend to govern as they see fit for their own country.[273] That is a logical and practical way to embrace the needs of the members of its society. Great Britain has decided that genetic editing, within certain boundaries, serves the greater good.[274] If scientists could gather at the International Summit on Human Gene Editing in 2015,[275] they can continue to collaborate and share their successes and failures so that mankind may benefit. The ASHG Statement is proof that science breaks language barriers and the vast majority of researchers and scientists have the best interests of society in mind.[276]

While this Comment does not advocate for all countries to assume the position of the ASHG, it does address the American legal and scientific landscape. This biotechnology is projected to be worth $25,000,000,000 by 2030 and yet, the American regulatory system has not laid a proper groundwork for this biotechnology to advance medical research while remaining ethical and transparent.[277] Now is the time for American legislators to address human germline editing and adopt the ASHG's position statement in full.

V. CONCLUSION

It takes time for something new, be it regulatory, political, or scientific, to become accepted. As the authors of the initial genome sequencing paper wrote, "[T]he science is only part of the challenge. We must also involve society at large in the work ahead."[278] Because science moves so quickly, scientists and regulatory agencies need to consider how best to regulate germline editing technology such as CRISPR-Cas9 while involving the

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273. *See, e.g.*, Jonathan Masters, *How Do U.S. Gun Laws Compare to Other Countries?*, PBS NEWS HOUR (June 13, 2016, 12:59 PM), https://www.pbs.org/newshour/nation/how-do-u-s-gun-laws-compare-to-other-countries (comparing gun ownership laws in the United States to those of Canada, where all weapons must be registered; Australia, where licensing, registration, and firearm safety courses are mandated; and Japan, where most guns are illegal).

274. *See* Ewen Callaway, *Embryo Editing Gets Green Light*, 530 NATURE 18 (2016), https://www.nature.com/polopoly_fs/1.19270!/menu/main/topColumns/topLeftColumn/pdf/nature.2016.19270.pdf [https://perma.cc/GV6W-QZLD]. CRISPR-Cas9 was approved as a technique to alter genes in human embryos as long as the embryos were destroyed and non-viable. *Id.*

275. *See* SUMMIT, *supra* note 123.

276. *See* ASHG Statement, *supra* note 24.

277. Reenita Das, *Gene Editing with CRISPR-Cas9: The Next Step in Human Evolution will be Worth $25 Billion by 2030*, FORBES (Dec. 14, 2017, 8:34 AM), https://www.forbes.com/sites/reenitadas/2017/12/14/gene-editing-with-crispr-cas9-the-next-step-in-human-evolution-to-be-worth-25-billion-by-2030/#713c12e4449f [https://perma.cc/HR7S-23YB] (discussing the potential revenues of CRISPR-Cas9 in research, agriculture, human therapeutics, and animal biotech).

278. Initial Sequencing, *supra* note 28, at 914.

greatest stakeholders, society. They should do this not only for their constituents, but for all those children who may be born with debilitating or fatal genetic diseases. They should create regulations for mothers who face only two choices: sick child or no child. Placing a complete ban on human germline editing because of what some view as the possible Frankenstein-esque outcomes is not only irresponsible but unethical. Change needs to occur and it needs to occur now.