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To Edit or Not to Edit?--Regulating CRISPR Transnationally

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To Edit or Not to Edit?—Regulating CRISPR Transnationally

ABSTRACT

After Chinese scientist Dr. He Jiankui's announcement that he had successfully edited the human genome using a new technology called CRISPR/Cas-9, Dr. He forced the world to address the ethical dilemmas introduced by gene-editing technologies. Born out of a historical tradition of human "improvement," gene-editing technologies like CRISPR/Cas-9 modify human genes down to DNA molecules. CRISPR can prevent and cure genetic diseases that have previously had no cure, but problems arise when CRISPR's use expands to enhancements or to modifications that would change the human genome permanently. Given CRISPR's potential profound impact, this Note analyzes how international bodies like the United Nations and countries like the United States, the United Kingdom, and Japan have attempted to regulate gene-editing technologies such that beneficial, individual modifications can flourish and rash, permanent modifications are avoided. This Note recommends the creation of the International Gene-Editing Ethics Commission, which would promulgate publicly approved ethical standards for gene editing while also providing member countries with access to publication in scientific journals, funding, and an international database.

TABLE OF CONTENTS

I. WHY WE NEED BETTER CRISPR REGULATIONS

In the fall of 2018, Chinese scientist Dr. He Jiankui announced that he edited the genes of human embryonic cells for the first time in history, and that the mother had given birth to the babies already.[1] Dr. He inserted CRISPR/Cas-9 (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9) into germline cells, in order to naturally immunize the babies to human immunodeficiency virus (HIV).[2] Once the embryonic cells received the vector, they were then placed in the mother via *in vitro* fertilization.[3] Nine months later, Dr. He announced his feat, propelling the global community into the germline-editing era without its permission. [4]

In 2015, before this groundbreaking announcement, the scientific communities of the United States, the United Kingdom, and China decided to meet for the first International Summit on Human Gene Editing in Washington, DC to hash out guiding principles for gene-editing technologies.[5] After several conferences and lengthy

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1. *See* David Cyranoski, *The CRISPR-Baby Scandal: What's Next for Human Gene-Editing*, NATURE (Feb. 26, 2019), https://www.nature.com/articles/d41586-019-00673-1 [https://perma.cc/AA4Q-AR9T] (archived Sept. 6, 2020).

2. *See* Jing-ru Li, Simon Walker, Jing-bao Nie & Xin-quing Zhang, *Experiments that Led to the First Gene-Edited Babies: The Ethical Failings and the Urgent Need for Better Governance*, 20 J. ZHEJIANG U. BIOMED. & BIOTECH. 32, 33 (2019).

3. *See* Cyranoski, *supra* note 1.

4. *See id.*

5. *See* David Baltimore, François Baylis, Paul Berg, George Daley, Jennifer Doudna, Paul Lander, Robin Lovell-Badge, Pilar Ossorio, Duanqing Pei, Adrian Thrasher, Ernst-Ludwig Winnacker & Qi Zhou, *On Human Gene Editing: International*

discussions among the lawyers, scientific leaders, and other international scholars, the Summit released its first statement on the issue of gene editing in clinical trials.[6] The Summit affirmed the need for meticulous preclinical research, approved clinical trials involving the editing of somatic cells under the existing regulatory framework, and firmly prohibited gene editing on germline cells until further notice.[7] The Committee emphasized that it was crucial to continue meeting to readdress the global scientific standards it had been charged with overseeing.[8]

The second International Summit met in Hong Kong in November of 2018 with quite a different tone.[9] At this summit, Dr. He announced his clinical trial and the birth of the twins.[10] While the Committee did not approve of Dr. He's experiment and he received three years in prison for it, the Committee understood that the gene editing of germline cells was a reality that needed to be addressed quickly and globally.[11]

By way of background, scientists divide gene editing into two broad categories: somatic cell editing and germline cell editing.[12] Somatic, literally meaning "of the body," refers to the living cells of humans, whereas germline cells are reproductive cells.[13] Modifying the somatic cells of a human corrects an inheritable gene in that person only; the modifications will not be inheritable because those cells will not be used in reproduction.[14] Germline cell modification, meaning

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Summit Statement, NAT'L ACAD. SCI., ENG'G, AND MED., (Dec. 3, 2015), http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a [https://perma.cc/GS6S-SZH4] (archived Sept. 6, 2020).

6. *See id.*

7. *See id.*

8. *See id.*; *see generally* NAT'L ACADS. OF SCIS., ENG'G, AND MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE (2017) (serving as the definitive report following the International Summit's statement).

9. *See* David Baltimore, Alta Charo, George Daley, Jennifer Doudna, Kazuto Kato, Jin-Soo Kim, Robin Lovell-Badge, Jennifer Merchant, Indira Nath, Duanqing Pei, Matthew Porteus, John Skehel, Patrick Tam & Xiaomei Zhai, *On Human Gene Editing II: International Summit Statement*, NAT'L ACAD. SCI., ENG'G, AND MED. (Nov. 28, 2018), https://www.nationalacademies.org/news/2018/11/statement-by-the-organizing-committee-of-the-second-international-summit-on-human-genome-editing [https://perma.cc/KNS3-RJF4] (archived Sept. 6, 2020); Sui-Lee Wee, *Chinese Scientist Who Genetically Edited Babies Gets 3 Years in Prison*, N.Y. TIMES (Dec. 30, 2019), https://www.nytimes.com/2019/12/30/business/china-scientist-genetic-baby-prison.html [https://perma.cc/EYA6-93UX] (archived Nov. 10, 2020).

10. *See id.*

11. *See id.*

12. *See id.*

13. *See Somatic*, MERRIAM-WEBSTER DICTIONARY (2019); Giulia Cavaliere, *Background Paper: The Ethics of Human Genome Editing*, WORLD HEALTH ORG. 1 (Mar. 18, 2019), https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Ethics-paper-March19.pdf [https://perma.cc/NUB5-U3GC] (archived Sept. 6, 2020).

14. *See* Cavaliere, *supra* note 13, at 2.

modifications of the cells used to reproduce, will affect the human genome permanently because changes in those cells are inheritable.[15]

Different ethical issues arise with each type of gene editing. Ethical questions arise in the somatic cell editing context when deciding which purposes are acceptable for justifying its use. Germline cell editing can raise questions about designer babies and consent.[16] Yet some bioethical concerns underpin both types of editing—those questions such as accessibility, regulation, and scientific responsibility.[17] This Note will primarily focus on questions surrounding the regulation of clinical somatic cell editing, though much of its discussion could apply to germline editing in the future. Because CRISPR's minimal off-target effects, cheaper use, and precision distinguish it from other gene-editing technologies, like zinc-finger nucleases and TALENs (transcriptor activator-like effector nucleases), gene editing is more accessible than ever before.[18] Additionally, considering the existing global and national frameworks failed to prevent a scientist from using CRISPR to permanently alter the human genome, the need for an international legal solution is clear.

Beyond the international summits discussed above, international legal communities are working together to begin addressing the issues surrounding gene editing. Because the scientific community is truly a global one, international legal communities aim to harmonize regulation of technological advancement.[19] In 1998, the United Nations published the Universal Declaration of the Human Genome and Human Rights. Among other things, it emphasized the dignity of the human genome; the rights of patients; the goals of promoting respectful, cooperative, and innovative research; the need for national regulations of gene-editing technologies; and the need for international solidarity on each of these topics.[20] In 2015, the International Summit on Human Gene Editing, referenced above, prompted a conversation between the world's scientific scholars and bioethicists concerning the

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15. *See id.*

16. For example, parents who decide to use gene-editing technology to ensure their baby has blue eyes cannot obtain the consent of the baby. *See* Tara R. Melillo, Note, *Gene Editing and the Rise of Designer Babies*, VAND. J. TRANSNAT'L. L. 757, 771 (2017).

17. *See, e.g.*, Siddhartha Mukherjee, *Ethical Challenges Accompany Genetic 'Fixes'*, VAND. CHANCELLOR'S LECTURE SERIES (Nov. 2, 2018), https://news.vanderbilt.edu/2018/11/02/chancellors-lecturer-ethical-challenges-accomp any-genetic-fixes/ [https://perma.cc/8EQ4-GB3L] (archived Sept. 6, 2020) (noting that with technologies that can sequence the human genome and even alter it, companies like 23andMe now have access to millions of people's genetic data with very little guidance on how to treat this information).

18. *See id.*; Cavaliere, *supra* note 13, at 1.

19. *See* R. Alta Charo, *The Legal and Regulatory Context for Human Gene Editing*, 32 no. 3 ISSUES IN SCI. & TECH. (2016), https://issues.org/the-legal-and-regulatory-context-for-human-gene-editing/ [https://perma.cc/QDN5-57NS] (archived Sept. 6, 2020).

20. *See* G.A. Res. 53/152, Declaration on the Human Genome and Human Rights (Dec. 9, 1998).

use of gene editing in clinical trials.[21] The World Health Organization's Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing met for the first time in 2019 to discuss plans for the next twelve to eighteen months.[22] But Dr. He's permanent alteration of the human genome calls the practicality and effectiveness of such vague international guidance into question.[23]

On a national scale, countries like the United States, the United Kingdom, and Japan have hashed out the details of regulating clinical somatic cell editing in their respective countries.[24] Each of these countries attempt to balance retaining pre- and post-market control of gene-editing technologies with too strict regulations that may stifle scientific innovation altogether.[25] The United States established a complex regulatory framework for policing mainly pre-market gene-editing technologies via guidelines for research funding.[26] While this has appeared to effectively control research and pre-market practices, these regulations are relatively weak once an item is in the market. The regulations fail to control who can use the technology, in what conditions they can use the technology, and how often they may use the technology.[27] The United Kingdom regulates both the pre-market and post-market research and treatment of gene-editing technologies at length, while still complying with the European Union's framework.[28] Finally, in Japan, the regulations of gene editing classify each product by degree of risk and apply a regulatory process based on that determination.[29] Though Japan's science, technology, and

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21. *See* Baltimore, Baylis, Berg, Daley, Doudna, Lander, Lovell-Badge, Ossorio, Pei, Thrasher, Winnacker & Zhou, *supra* note 5.

22. *See* World Health Organization [WHO], *Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing*, WORLD HEALTH ORG. (2019), https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Ethics-paper-March19.pdf [https://perma.cc/ZQ57-GPWF] (archived Sept. 6, 2020).

23. *See* Tsung-Ling Lee, *Two Minutes to Midnight—What International Law Can Do About Genome Editing*, 14 ASIAN J. WTO & INT'L HEALTH L. & POL'Y 227, 244–48 (2019). *See generally* Li, Walker, Nie & Zhang, *supra* note 2.

24. *See* Charo, *supra* note 19.

25. *See id.*

26. *See id.*; Evita V. Grant, *FDA Regulation of Clinical Applications of CRISPR-CAS Gene-Editing Technology*, 71 FOOD & DRUG L.J. 608, 614–16 (2016). *But see* National Institute of Health Office of Science Policy, *Recombinant DNA Advisory Committee Archives*, NAT'L INST. OF HEALTH (2019), https://osp.od.nih.gov/biotechnology/recombinant-dna-advisory-committee/ [https://perma.cc/H858-BN7L] (archived Sept. 6, 2020) (noting that the Recombinant DNA Advisory Committee has taken a broader focus on recombinant or synthetic nucleic acid research and renamed itself the Novel and Exception Technology and Research Advisory Committee, or NExTRAC).

27. *See* Charo, *supra* note 19.

28. *See id.*; James Lawford Davies, *The Regulation of Gene Editing in the United Kingdom*, 13 SCITECH LAW. 14, 16 (2016).

29. *See* Charo, *supra* note 19.

biotechnology market ranks second-most advanced in the world, the bureaucratic process through which scientists must venture in order to receive funding for gene therapy research and clinical trials has substantially slowed growth in that area.[30]

Even assuming domestic governments are in the best position to regulate scientific technology, an issue as fundamental and global as the future of the human genome requires an international, legally binding solution.[31] Part II details the history of gene editing with CRISPR and its journey to becoming an accepted tool in somatic cell clinical trials. Part III will analyze the existing international and national frameworks regulating clinical trials of somatic cell gene editing in the United States, the United Kingdom, and Japan, with an eye towards the possibility of germline editing. Finally, Part IV of this Note will propose the International Gene-Editing Ethics Commission to create and enforce a binding whistle-blower framework in the global scientific community. This whistle-blower framework would provide qualifications to become a member of the commission and standards for clinical trial approval that emphasize transparency and consensus. It would then provide a way for scientists to blow the whistle on questionable experiments, and issue penalties for those who violate standards.

II. WHAT IS CRISPR AND WHY SHOULD WE REGULATE IT?

Ideas about changing the human race biologically dramatically pre-date gene-editing technology itself.[32] This Part briefly outlines the historical origins of the ideas that underpin gene editing, explains what CRISPR actually does, and highlights bioethical concerns implicated by CRISPR that affect its governance.

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30. *See* Sunyoung Kim, Zhaohui Peng & Yasufumi Kaneda, *Current Status of Gene Therapy in Asia*, 16 MOLECULAR THERAPY 237, 239–40 (2008).

31. *See* NAT'L ACADS. OF SCIS., ENG'G., AND MED., *supra* note 8, at 57 ("As noted by former FDA Commissioner Robert Califf, '[s]cientific advances do not adhere to national boundaries and therefore it is critical that we understand the evolving views of our international counterparts.'").

32. *See* PHILLIPA LEVINE, EUGENICS: A VERY SHORT INTRODUCTION 4 (2017) (discussing eugenics as a part of gene editing history).

A. *Origins of Gene Editing Indicate the Need for Regulation*

Gene editing originated, at least partially, in eugenics.[33] The definition of eugenics is subjective—generally, it is the idea that one can control reproduction in a way that "improves" future generations. The danger of eugenic thought lies in the decision of what "improves" a future generation. Gene-editing technologies are inherently eugenic because a current generation decides what would genetically improve the next generation. Given this intertwining of gene editing and eugenics, the following chronological history of gene editing and eugenics exemplifies the gravity of the need for regulation of gene-editing technologies. Gregor Mendel's discovery of inheritable traits that could not be changed throughout life laid a foundational concept in the minds of scientists when it was translated in the early twentieth century: our genes cannot be changed by behavior or environment.[34]

Francis Galton aimed to apply Mendel's findings to human reproduction, and the eugenics movement caught momentum in the United States.[35] Even influential leaders like Theodore Roosevelt, Francis Crick, and Oliver Wendell Holmes supported the eugenics movement.[36] Left unchecked, this kind of eugenic thought pervaded legislation during the early half of the twentieth century. For example, the Eugenics Records Office championed the passage of The Immigration Restriction Act of 1924, hoping to keep bloodlines "pure" by controlling who could live in America.[37] Midcentury, the eugenic

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33. English statistician and father of eugenics Francis Galton built on Mendel's foundation by collecting statistical information on rabbits' intelligence and physical capabilities in the hopes of someday improving human reproduction. Galton defined eugenics as the idea of "improving stock . . . to give to the more suitable races or strains of blood a better chance of prevailing speedily over the less suitable . . .." Galton's work inspired and combined with that of his cousin, Charles Darwin, to become so powerful it influenced governmental policies around the turn of the twentieth century through an ideology known as Social Darwinism. FRANCIS GALTON, INQUIRIES INTO HUMAN FACULTY AND ITS DEVELOPMENT 17 n.1 (Gavan Tredoux ed., 2d ed. 1907); *see* LEVINE, *supra* note 32, at 3.

34. *See* LEVINE, *supra* note 32, at 4 (describing Mendel's pea plant experiments as the birth of gene editing and eugenics). Also note that genes can manifest differently based on environment, but they cannot be fundamentally changed. *But see* Danielle Simmons, *Epigenetic Influences and Disease*, NATURE (2008), https://www.nature.com/scitable/topicpage/epigenetic-influences-and-disease-895/ [https://perma.cc/U6KS-GUFD] (archived Sept. 16, 2020) (explaining that while our fundamental genes cannot be altered, their expression can change depending on environmental factors; for example, malnutrition before puberty causing cardiovascular disease in children who were not especially genetically susceptible to that disease).

35. *See* Seema Mohapatra, *Politically Correct Eugenics*, 12 FIU L. REV. 51, 53–54 (2016); LEVINE, *supra* note 32, at 18 (describing "Fitter Family" awards given to families who entered and won eugenics contests in interwar America); Melillo, *supra* note 16, at 768–69. *See also* Buck v. Bell, 274 U.S. 200, 208 (1927) (Justice Holmes upheld state-forced sterilization of "unfit" people).

36. *See* Mohapatra, *supra* note 35, at 53.

37. *See id.*

movement reached its most horrifying, unspeakably tragic iteration in Hitler's Nazism that led to the death of millions of Jewish people in the Holocaust.[38]

A far less extreme version of eugenic thought appeared around the 1970s, when scientists created *in vitro* fertilization (IVF) as a way of alternative reproduction. [39] Scientists could examine the fertilized embryos for chromosomal or genetic flaws before even implanting the embryo into the mother. Prenatal technology also advanced such that parents could detect genetic mutations before birth[40]

Today, with technologies like CRISPR/Cas-9, the benefit of improving human genes can potentially be available not only to future generations, but to the consumers themselves.[41] For example, a research group created a nanocapsule that effectively and accurately delivers a largely customizable CRISPR Cas-9 protein into target cells, which can be stored in a frozen powder and easily administered in different dosages.[42] While CRISPR has the potential to help many people, eugenic history illustrates how dangerous gene-editing technology can be. Considering both the potential benefits and dangers of gene editing, the force of CRISPR/Cas-9 is limitless and must be regulated.[43]

B. *The Discovery of CRISPR*

The nature of CRISPR's discovery helps to explain its mechanisms, and it also demonstrates the truly global character of

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38. *See* Daniel J. Kevles, *The History of Eugenics*, 32 no. 3 ISSUES IN SCI. & TECH (2016), https://issues.org/the-history-of-eugenics/ [https://perma.cc/D7WC-RVWE] (archived Sept. 6, 2020) (describing how Hitler manipulated eugenic thinking to incite Aryan supremacy and anti-Semitism in the Nazi party to tragically kill millions of Jewish people); Melillo, *supra* note 16, at 769–70 (connecting the American eugenic movement to the Holocaust in Germany).

39. *See* Kevles, *supra* note 38 (demonstrating that even the advent of IVF brought about bioethical criticism about consent and eugenics); Melillo, *supra* note 16, at 771 (noting that the clinical and scientific communities worry that gene editing could overstep ethical boundaries, exemplified in "designer babies" whose traits have been selected before birth).

40. *See* Kevles, *supra* note 38.

41. *See id.*

42. *See* Guojun Chen, Amr Abdeen, Yuyuan Wang, Pawan Shahi, Samantha Robertson, Ruosen Xie, Masatoshi Suzuki, Bikash Pattnaik, Krishanu Saha & Shaoqin Gong, *A Biodegradable Nanocapsule Delivers a Cas9 Ribonucleoprotein Complex for in Vivo Genome Editing*, 14 NATURE NANOTECHNOLOGY 974, 974–79 (2019) (explaining mechanics and methods used for developing and testing the nanocapsule); *see also* Francis Collins, *Nano-Sized Solution for Efficient and Versatile CRISPR Gene Editing*, NAT'L INSTS. HEALTH, https://directorsblog.nih.gov/2019/09/17/nano-sized-solution-for-efficient-and-versatile-crispr-gene-editing/ (last visited Jan. 17, 2020) [https://perma.cc/MCV6-VNTL] (archived Sept. 6, 2020) (evaluating the progress and potential applications of the Chen et al. research group).

43. *See* Kevles, *supra* note 38.

gene-editing technology.[44] Scientists in Spain and France spearheaded the earliest advances towards CRISPR technology when they discovered the possibility of conferring viral immunity through archaeal research and biological weapons research around 2005.[45] By 2008, Dutch researchers uncovered CRISPR's precise cutting ability, and American scientists discovered its programmability.[46] At the same time, both German and Russian scientists added to the unveiling of CRISPR's full potential in adding tracrRNA and successfully transferring CRISPR in other bacteria.[47]

The discovery process of CRISPR culminated in three papers published in 2012. Almost simultaneously, Jennifer Doudna and Emanuelle Charpentier, who recently won the Nobel Peace Prize for their CRISPR research, published their findings that RNA could function *in vitro*, Feng Zhang reported his successful genome editing in mammalian cells, and George Church reported his successful genome editing of human cells.[48] Since the publication of those papers, CRISPR's potential has been recognized by the global public, as evidenced by the dramatic uptick of CRISPR in Google searches.[49] CRISPR's mechanics set it apart from other gene-editing technologies because it is easier to use, less expensive, and more accurate.[50] Today, scientists use CRISPR to test for genetic mutations in mammals, some including humans, but only in somatic cells.

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44. *See* Eric S. Lander, *The Heroes of CRISPR*, 164 CELL 18, 18–20 (2016) (outlining CRISPR's global discovery process).

45. Beginning in 1989, Fransisco Mojica studied archaeal microbes (single-celled organisms) in Mediterranean marshes off the Spanish coast when he first discovered palindromic, regularly spaced bases never seen before in microbes. He published several papers on the topic. Coinciding with Mojica's story, Gilles Vergnaud of France's Ministry of Defense also discovered the CRISPR pattern in their microbiological research. *See id.* at 18–22.

46. *See id.* (recounting Phillipe Horvath's Cas-9 research, John van der Oost's work for the Dutch National Science Foundation, and Luciano Marrafini and Erik Sontheimer's targeting research at the University of Chicago).

47. Emanuelle Charpentier and Jörg Vogel further found that tracrRNA was necessary for processing crRNA, and thus necessary for overall CRISPR function. TracrRNA helps process CRISPR and cleave it to DNA. Meanwhile in Russia, Virginijus Siksnys discovered that CRISPR could be transferred into other bacteria and maintain the same effects as it did in the original organism, making it easier and cheaper to use. *See id.* at 23–24.

48. *See id.* at 24–25.

49. *See id.* at 26.

50. *See* Sarah Polcz & Anna Lewis, *CRISPR-Cas9 and the Non-Germline Non-Controversy*, 3 J. L. & BIOSCIENCES 413, 414–15 (2016).

C. *The Ethics of CRISPR*

The use of CRISPR on humans sparks fundamental ethical concerns in the global community.[51] Typically, scholars divide these concerns between somatic and germline cell editing because each implicates distinct issues—germline modification will be inherited as a permanent part of the human gene pool, while somatic cell editing affects only an individual.[52] Within somatic cell editing, a further divide lies between whether one views somatic cell editing on a continuum of gene-editing technologies, or as a new, unprecedented technology.[53] The "continuum" school of thought, which includes organizations such as the International Summit on Human Gene Editing and the National Academies of Sciences, Engineering, and Medicine, believes that as long as certain safety and efficacy standards are met, somatic gene editing should be no different than other medical interventions.[54] The "unprecedented" school of thought agrees that somatic editing begs similar questions to other medical interventions, but concludes that it should ultimately be treated differently because of additional, significant questions surrounding the adequacy of existing regulations, the commercialization of gene-editing technologies, and the equity of access in such a dynamic field.[55]

The following examples illustrate those adequacy of governance, commercialization, and equity issues exclusive to the somatic application of CRISPR.[56] Concerning the adequacy of existing regulations, recent experiments suggest that certain genes can predispose individuals to violence based on their personal experiences, and CRISPR can be used to modify that gene to reduce the violent nature of the individual.[57] Given the low cost and availability of CRISPR treatment, if an individual refused to modify his or her "violent" genes and later committed a violent act, questions arise over how a person ought to be punished for refusing the treatment.[58] Similarly, but further down the road, governments could cut eligibility for disability funding and treatment for individuals who could be cured

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51. *See, e.g.*, Baltimore, Baylis, Berg, Daley, Doudna, Lander, Lovell-Badge, Ossorio, Pei, Thrasher, Winnacker & Zhou, *supra* note 5 (calling together the global scientific community in order to address changes in gene-editing technology because they are significant enough to merit a change in ethical standards).

52. *See* WHO, *supra* note 22, at 2; Polcz & Lewis, *supra* note 50, at 417–18; NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 83.

53. *See* WHO, *supra* note 22, at 2–3.

54. *See id.*

55. *See id.* at 3–4.

56. *See* Polcz & Lewis, *supra* note 50, at 417–22.

57. *See id.* at 418–19. These examples are somewhat theoretical given the current state of CRISPR (i.e., CRISPR has not been successful inserted into a human brain yet), but could certainly happen in the future.

58. *See id.*

by CRISPR but refuse.[59] Finally, application of CRISPR to somatic cells could enhance athletic performance, and because detection of gene therapy is difficult, a new kind of "gene-doping" advantage in sports could be hard to prevent.[60] Some of these modifications are time-sensitive, so the application of CRISPR on minors sparks controversy surrounding consent: Should guardians or children themselves provide consent for time-sensitive traits like height, or secondary sexual characteristics[61] for those who identify as transgender?[62] Other legal implications include allowing insurance companies to incentivize genetic modification for women with a predisposition to breast cancer through discovery of the BRCA1 gene, or those with a predisposition to a harmful addiction like nicotine.[63] Curbing criminal violence, changing legal entitlements to disability accommodations, and having the ability to choose one's own characteristics each implicate policy decisions far beyond the consenting individual, which blurs the rationale for dividing conversations based on germline and somatic editing.[64]

The commercialization of gene-editing technologies manifests clearly in the debate about enhancement and therapeutic use. The scientific community has tried to limit somatic editing to only therapeutic uses, though the distinction between therapeutic use and enhancement has become increasingly unclear.[65] The National Academies of Sciences, Engineering, and Medicine have defined therapy to encompass both the treatment and the prevention of

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59. *See id.* at 420–21.

60. *See id.* at 422–23.

61. Secondary sexual characteristics are those characteristics that develop after puberty, such as men's facial hair. *See, e.g.*, Elizabeth J. Susman, Renate M. Houts, Laurence Steinberg, Jay Belsky, Elizabeth Cauffman, Ganie DeHart, Sarah L. Friedman, Glenn I. Roisman & Bonnie L. Halpern-Felsher, *Longitudinal Development of Secondary Sexual Characteristics in Girls and Boys Between Ages 9½ and 15½ Years*, ARCH PEDIATRIC ADOLESCENCE MED. 1, 2 (2010).

62. *See id.* Currently, this type of modification would be very difficult to accomplish because it is multigenic.

63. *See* Polcz & Lewis, *supra* note 50, at 424; *see also* Mukherjee, *supra* note 17 (discussing the novelty of the label "pre-vivors" for individuals who survived a genetic disease he or she never actually had).

64. *See* Polcz & Lewis, *supra* note 50, at 423 (discussing the implications of changing "immutable" traits, and suggesting problems using this science on minors).

65. *See id.* (explaining the ability to change traits for individuals in order to better "suit their life choices"); NAT'L ACADS. OF SCIS. ENG'G AND MED., *supra* note 8, at 110 (recommending that public policy debates discuss the use of somatic cell genome editing outside of the treatment of disease or disability); Ruha Benjamin, *Interrogating Equity: A Disability Justice Approach to Genetic Engineering*, *in* COMMISSIONED PAPERS FOR THE INTERNATIONAL SUMMIT ON HUMAN GENE EDITING 48, 48–51 (2015), https://sites.nationalacademies.org/cs/groups/pgasite/documents/webpage/pga_170455.pdf (last visited August 31, 2020) [https://perma.cc/UZ5V-J8JA] (archived August 31, 2020) (discussing the fallacies associated with the "ableist" norms that somatic cell gene editing is developed to cure and exploring the balance between these cures and the desires of individuals to enhance the human body).

diseases, and enhancement as genetic "interventions that are intended to improve a bodily condition or function beyond what is needed to restore or sustain health."[66] The international scientific community generally condones therapeutic genetic modification as safe and beneficial, but some situations make distinguishing enhancement from therapy difficult.[67] To illustrate, most people consider it therapy when doctors reduce the cholesterol level of a patient with coronary heart disease or preventative therapy to genetically reduce that patient's sibling's cholesterol, but might consider it enhancement when doctors lower the cholesterol level of a healthy, young individual below what is "normal."[68] Definitionally, "normal" in a genetic conversation refers to what is typical for the human range of capabilities in phenotypical or physical manifestation of a trait, and "natural" refers to the genes that create the range of "normal" characteristics, whether advantageous or disadvantageous.[69] At the heart of these distinctions lies the question of how to define a disease.[70] Defining a disease can reveal societal preconceptions, for example, as many individuals may hold different opinions about whether a certain genetic traits and their resulting conditions need cures. For example, individuals who are deaf or blind often state they would not want to be cured of their deafness or blindness because it is a part of their identity, and they would not be the same person but for their condition.[71] Because defining a disease can differ greatly, individual nations should decide for themselves who will decide what is "normal" and what constitutes a "disease" in order to regulate somatic cell editing.[72]

Finally, somatic cell editing also implicates fairness concerns.[73] Some schools of thought focus on the fairness of the interventional effect of gene editing, rather than the distinctions previously mentioned.[74] Classifying what genetic characteristics are "fair" largely depends on what is considered "normal," and because the range of "normal" human characteristics for any one gene is so large, fairness is a very fluid category (think about the difference in humans' sprinting

66. NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 145.

67. *See id.*

68. *See id.* at 147.

69. *See id.* at 139.

70. *See id.* at 147–48; Mukherjee, *supra* note 17.

71. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 148; Mukherjee, *supra* note 17.

72. However, even individual countries defining terms like "disease" and "normal" is an imperfect solution because it usurps the individual's autonomy in making these decisions for oneself based on one's culture and experiences. See *infra* Part IV for further discussion.

73. *See, e.g.*, NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 147–50 (discussing the concept of fairness in the context of somatic cell gene editing).

74. *See id.* at 149.

speeds, for example).[75] Societies usually increase access for citizens through raising medical funding and insurance coverage to ensure equity for other medical interventions like hip replacements or laser eye surgery, but with CRISPR, societies have certainly restricted funding and insurance coverage.[76]

But supporters of a Rawlsian, equity-based theory of justice would argue the contrary.[77] Under this theory of equality-based reciprocity, fairness is less about individual access and more about societal distribution, so a genetic enhancement to an individual would only be tolerated if distributed equitably in such a way that advanced the common good.[78] In reality, genetic enhancement through gene editing would likely not be the principal source of inequality in a society, if it had any effect at all.[79]

Many countries prohibit germline cell modification because of its serious ethical implications.[80] There are three major ethical issues with germline modification: permanently affecting the health of future generations, producing unpredictable and possibly irreversible results, and the lack of consent because the people who would be affected by the modification have not yet been born.[81] The debate about germline cell editing can be examined through a study of the benefits and detriments of its use for basic research (using CRISPR to test for editing precision and efficiency) or clinical research (applying tested science to living humans).[82] Basic research, however, can require the use of human embryos, which sparks ethical controversy among scientists over the source of the embryo and the length of testing.[83] Clinical research is a hotly debated area of CRISPR application, with scholars disagreeing primarily about whether there is a need for CRISPR modification when other technologies can accomplish many of

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75. While training and practice can contribute to a faster speed, humans are born with baseline capacity for sprinting because of genetic factors like a fast twitch muscle. In this context, what is the "fair" level of fast twitch muscle modification—Usain Bolt or a high school track runner? *See id.*

76. *See id.*

77. *See id.* at 149–50.

78. *See id.*

79. *See id.*

80. For example, the United States had an effective moratorium on germline modification. *See id.* at 183–90.

81. *See* Polcz & Lewis, *supra* note 50, at 415 (quoting American Medical Association, *Opinion 2.11 Gene Therapy*, https://web.archive.org/web/20160406074109/https://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion211.page (last visited Nov. 10, 2020) [https://perma.cc/AZV8-SXSX?type=image] (archived Nov. 10, 2020)); NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 137–38.

82. *See* WHO, *supra* note 22, at 2–3; Rosario M. Isasi & Bartha M. Knoppers, *Mind the Gap: Policy Approaches to Embryonic Stem Cell and Cloning Research in 50 Countries*, 13 EUR. J. HEALTH L. 9, 12–16 (2006).

83. *See* WHO, *supra* note 22, at 4–6.

the same results, and about how best to regulate the technology.[84] The regulatory debate centers on the safety and morality of the intergenerational effects of gene editing on the germline. One's position usually reflects one's belief as to whether CRISPR is an unprecedented technology or like other assisted-conception technologies.[85] Still other concerns outside of safety and regulation arise, such as the lack of consent from future generations, the threat to the dignity of humankind, the changing of cultural norms, and the exacerbation of socioeconomic inequality.[86]

III. DIFFERENT APPROACHES TO REGULATING CRISPR

Given the complex ethical considerations surrounding CRISPR and its rapid rise to practical use over the last two decades, regulating it and the future of gene editing proves both extremely important and difficult.[87] The existing international framework is mostly made up of broad standards or goals, like the Universal Declaration on the Human Genome and Human Rights (Declaration) and the International Summit on Human Gene Editing.[88] These agreements permit countries to select their own regulations for gene editing. Countries' regulations reflect the view of their citizens, while also supporting the broad goals of the agreements.[89] The Oviedo Convention, a more

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84. *See id.* at 6–7 (considering the argument for a need of germline editing for couples who desire to have a genetically related child without passing on a genetic illness); NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION 96 (2018), http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-and-human-reproduction-FINAL-website.pdf (last visited Sept. 5, 2020) [https://perma.cc/ED2C-NA4P] (archived Sept. 5, 2020) (arguing that since genome editing is only justified when it is beneficial to the future child's health, and existing technologies accomplish that already, genome editing could be prohibited); Brooke E. Hrouda, *"Playing God?": An Examination of the Legality of CRISPR Germline Editing Technology Under the Current International Regulatory Scheme and the Universal Declaration on the Human Genome and Human Rights*, 45 GA. J. INT'L & COMPAR. L. 221, 241 (2016).

85. *See* WHO, *supra* note 22, at 8; Hrouda, *supra* note 84, at 232–33.

86. *See* WHO, *supra* note 22, at 9. *Compare* Inigo de Miguel Beriain, *Should Human Germ Line Editing be Allowed? Some Suggestions on the Basis of the Existing Regulatory Framework*, 33 BIOETHICS 105, 107–08 (2018) (arguing that the human germline is always changing, so changes made through gene editing should not require special consideration), *with* G.A. Res. 53/152, Declaration on the Human Genome and Human Rights (Dec. 9, 1998) (intimating that the human genome has an inherent dignity that must be protected from human intervention).

87. Hrouda, *supra* note 84, at 229–32.

88. General Conference of UNESCO, *Universal Declaration on the Human Genome and Human Rights*, arts. 1—2, U.N. Doc. A/53/152 (Dec. 9, 1998) [hereinafter *Declaration*]; Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine art. 1, Apr. 4, 1997, E.T.S. 164 [hereinafter Oviedo Convention].

89. Hrouda, *supra* note 84, at 229–32.

specific agreement, provides more concrete steps for countries that ratify it, but many decisions are still left up to individual nations.[90] The United States, the United Kingdom, and Japan each serve as meaningful examples of gene-editing research governance within an individual country. Each of these countries regulate gene-editing technologies in different ways, yet each are on the cutting edge of innovation in this field.[91]

A. *Existing Transnational Regulations*

Though science transcends national borders, much of the existing transnational law does not bind countries.[92] Undoubtedly, the Universal Declaration on the Human Genome and Human Rights exhibits an excellent philosophy concerning gene-editing technology, but merely influences specific regulation because it is not binding law.[93] The International Summit on Human Gene Editing compiled updated, thorough data from experts around the world concerning ethical dilemmas in editing the genome via somatic and germline cells, but again, it fails to bind any countries.[94] And finally, the Oviedo Convention binds ratifying nations to its broad terms, but leaves open many specific regulatory questions.[95] Though each of these agreements fall short of regulating gene editing internationally, they are extremely influential works on the ethics of responsible science.

1. Universal Declaration on the Human Genome and Human Rights

The United Nations Educational, Scientific, and Cultural Organization (UNESCO)'s Declaration is not binding on any nation.[96]

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90. Robert Andorno, *The Oviedo Convention: European Legal Framework at the Intersection of Human Rights and Health Law*, 2 J. INT'L BIOTECH. L. 133, 134–36 (2005).

91. Charo, *supra* note 19, ¶¶ 26-41.

92. *See, e.g.*, Hurst Hannum, *The Status of the Universal Declaration of Human Rights in National and International Law*, 25 GA. J. INT'L & COMPAR. L. 287, 317–18 (1996) (explaining that UN Declarations are simply a declaration of rights, but no more than that).

93. Hrouda, *supra* note 84, at 223.

94. *International Summit on Human Gene Editing*, NAT'L ACADS. OF SCIS., ENG'G, AND MED. (Dec. 3, 2015), http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a (last visited Sept. 5, 2020) [https://perma.cc/GS6S-SZH4] (archived Sept. 5, 2020).

95. Oviedo Convention, *supra* note 88, chs. II–XIV (presenting protocols for regulating everything from consent to public engagement for ratification).

96. *See, e.g.*, Hannum, *supra* note 92, at 317–18 (explaining that UN Declarations are simply a declaration of rights, but no more than that); Hrouda, *supra* note 84, at 223. The United Nations defines a declaration as an instrument that "clarif[ies] the state's position and do[es] not purport to exclude or modify the legal effect of a treaty." *See* United Nations Treaty Collection, *Glossary*, https://treaties.un.org/Pages/Overview.aspx?path=overview/glossary/page1_en.xml (last

The principles laid out in the Declaration are broad, normative goals designed to protect the human genome.[97] The United Nation's Twenty-Ninth General Assembly unanimously adopted the Declaration in 1997, and it has been widely supported since.[98] Despite its lack of binding authority, the Declaration has taken an influential place in international biomedical law as a customary common law.[99] The United States, the United Kingdom, and Japan have indicated approval and inclusion of the Declaration in their national governance as member countries of the United Nations.[100]

The Declaration has three main principles: that the human genome is part of the heritage of humanity, that individual human life should be respected regardless of genetic makeup, and that genetic discrimination cannot be tolerated.[101] This first principle is found in the first two articles of the Declaration, which proclaim that that the human genome underpins all of humanity and therefore should be respected as an integral part of human dignity.[102] Article 10 of the Declaration adds to the first principle by adding the second two principles: "No research or research applications concerning the human genome . . . should prevail over respect for the human rights, fundamental freedoms and human dignity of individuals or . . . groups of people."[103] Additionally, Article 12 ensures equal access to the benefits of genetic research on the human genome to all individuals.[104] The Declaration continues on to emphasize the necessity of informed consent in genetic research, yet allows research to progress without it if the individual does not have the capacity to consent and there is a direct health benefit, minimal risk and burden, or, in the case of a human embryo, a third party consents to the research.[105] Finally, in Article 16, the Declaration encourages individual countries to enact

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visited Sept. 5, 2020) [https://perma.cc/5FJF-T2W5] (archived Sept. 5, 2020) (explaining that declarations are not always binding).

97. *The Universal Declaration on the Human Genome and Human Rights*, UNESCO (2019), https://en.unesco.org/themes/ethics-science-and-technology/human-genome-and-human-rights (last visited Sept. 5, 2020) [https://perma.cc/U9GZ-X5Q3] (archived Sept. 5, 2020).

98. *See id.*; Hrouda, *supra* note 84, at 223 n.8.

99. Hrouda, *supra* note 84, at 223.

100. *Member Nations*, UNITED NATIONS (2020), https://www.un.org/en/member-states/ (last visited Feb. 26, 2020) [https://perma.cc/RH7M-PMV6] (archived Sept. 5, 2020).

101. *UNESCO Adopts Universal Declaration on the Human Genome and Human Rights*, EUREKALERT! (Nov. 11, 1997), http://www.eurekalert.org/pub_releases/1997-11/U-UAUD-111197.php (last visited Sept. 5, 2020) [https://perma.cc/Q69F-MTYJ] (archived Sept. 5, 2020) (breaking down the Declaration into smaller parts); Hrouda, *supra* note 84, at 232–33 (discussing three basic principles in the Declaration).

102. *Declaration*, *supra* note 88, arts. 1–2; *see* Hrouda, *supra* note 84, at 233–34.

103. *Declaration*, *supra* note 88, art. 10; *see* Hrouda, *supra* note 84, at 234.

104. *Declaration*, *supra* note 88, art. 12.

105. *Id.* art. 5(a)–(e); *see* Hrouda, *supra* note 84, at 235.

their own ethics committees to constantly assess the ethical concerns of that country's research.[106]

The Declaration's wide acceptance illustrates the global approval of protecting the dignity of the human.[107] Within the Declaration, protecting the dignity of the human stands for the proposition that there is fundamental value in one human being recognizing another for his or her value as a human.[108] Implicit in that conception of human dignity lies the acceptance of human diversity, which symbolically includes everything down to the human genome.[109] The Declaration subdues common fears about gene editing by emphasizing equality of access,[110] necessity of patients' informed consent,[111] and continued, individual assessment of governance by each country.[112]

The Declaration falls short in some ways. The International Bioethics Committee, the governing body charged with enforcing the Declaration, has yet to decide whether or not "germline interventions" contradict human dignity under the treaty.[113] If the Committee did so, then germline editing would be illegal under the treaty. Additionally, the Declaration rests upon the assumption that the human genome is inherently protected under universal human rights, but some scientists have argued that there is no such thing as a distinctly human genome—that even nonhumans have genomes similar to humans, so no special protection of the human genome needs to be afforded in the name of universal human rights.[114]

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106. *Declaration*, *supra* note 88, art. 16.

107. *See* Hrouda, *supra* note 84, at 234.

108. *See* Mette Labach, *What is Human Dignity?*, NAT'L U. IR. 1, 1–2 (2004), http://eprints.maynoothuniversity.ie/392/1/Human_Dignity.pdf (last visited Sept. 5, 2020) [https://perma.cc/2G75-HC2T] (archived Sept. 5, 2020) (positing a historical account of what human dignity means).

109. *See id.* (emphasizing the value of each individual recognizing others).

110. *See, e.g.*, NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 147–50 (discussing the concept of fairness in the context of somatic cell gene editing).

111. *See, e.g.*, *id.* at 30–34 (stating the principles underlying the United States' requirement of voluntary, informed consent from the patient).

112. *See, e.g.*, *id.* at 45–48 (explaining the role of IRBs in the United States' system of governance provides an example of continued, individualized assessment of research governance).

113. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 115.

114. *Id.* (arguing that UNESCO's symbolic importance of the human genome might be biological fiction since there is no set of genomic variations humans have that nonhumans do not have, and if there were distinct human variations, it would preclude any further evolution).

2. International Summit on Human Gene Editing

The International Summit on Human Gene Editing (Summit) aims to unify participating countries on bioethical policies through occasional meetings where experts present different findings to inform the Summit's statement.[115] Each of these two Summits included experts from all over the world.[116] The first Summit's statement encouraged cautious and scrutinizing regulation of somatic cell editing moving forward, but specifically forbade germline editing as too dangerous in light of the lack of research and understanding in 2015.[117] The second Summit was held in Hong Kong, which is where Dr. He announced his completed modification of human embryos in November 2017, discussed in Part I.[118] Each Summit produced commissioned papers, presentations, and guidelines for the international community, though none of these were binding on any nation.[119] The official statement from the 2018 Summit meeting affirmed careful governance but approved somatic cell research and again strongly discouraged germline research until a later time.[120]

The International Summit represents a new vision for self-governance of scientific research—allowing professional bodies, learned societies, and national academies to create rules based off their expertise and data and enforce them as a community.[121] The 1975 Asilomar conference, which served almost as a template for the International Summit, highlighted the value of self-regulation. Scientists met at the conference to discuss protocols for the development of recombinant DNA technology and produced widely accepted biosafety practices.[122] Spurred by advances in CRISPR research, the scientific community pushed for self-regulation in gene-editing technology, which culminated in the International Summit.[123]

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115. *International Summit on Human Gene Editing*, *supra* note 94.

116. *Id.*

117. *Id.*

118. Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9.

119. *Id.*; Baltimore, Baylis, Berg, Daley, Doudna, Lander, Lovell-Badge, Ossorio, Pei, Thrasher, Winnacker & Zhou, *supra* note 5.

120. Baltimore, Baylis, Berg, Daley, Doudna, Lander, Lovell-Badge, Ossorio, Pei, Thrasher, Winnacker & Zhou, *supra* note 5; Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9.

121. *See* Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9 (releasing only a statement from the summit for countries to incorporate into their existing protocol and regulation).

122. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 129. *But see* Charo, *supra* note 19 (suggesting that self-regulation among scientists led to overly strict guidelines and shortage of supplies gametes and embryos needed for research in the US).

123. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 129 (describing the earliest CRISPR scientists' move for regulation of CRISPR, specifically barring germline modification and creating internationally agreed upon objectives for CRISPR research).

3. Oviedo Convention

The Council of Europe emphasized the dignity of the human genome in its 1997 European Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, now known as the Oviedo Convention.[124] The Convention's treaty was adopted by nineteen European countries, with the United Kingdom, France, and Germany notably missing. [125]

Unlike UNESCO agreements and the International Summit, the Oviedo Convention requires each ratifying nation to adopt the recommendations as laws in their own countries upon ratification, without using any of the common European institutions to enforce the law.[126] The Convention is also an attempt to regulate the entirety of human bioethics, not just genetic research or other individual components of human rights or biomedicine.[127]

However, like the UNESCO agreements, the Convention provides a general framework on which each country should base its own specific protocols.[128] The Convention can only be protected in courts of an individual nation, not the European Court of Human Rights, which many scholars point out as a flaw in the treaty.[129] Where the Convention provides for relative human rights, the common law of the European Court of Human Rights may apply because the language used is practically identical.[130]

More than anything, the Oviedo Convention emphasizes the dignity of the inheritance of the human genome over scientific progress

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124. *See* Andorno, *supra* note 90, at 133 (explaining that the Council of Europe is made up of 46 European nations with the mission of promoting both human rights and democratic values in Europe). The Council of Europe held the European Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, now known as the Oviedo Convention, in 1997.

125. *See id.* at 134 (explaining that the United Kingdom did not adopt the Convention because it was too restrictive, Germany refused because it was too permissive, and France refused because of its own simultaneous bioethics law reform).

126. *See id.* at 134–36; Oviedo Convention, *supra* note 88, art. 1. This means that the adopting countries of the Oviedo Convention must agree with every word of the Convention and defend it in their own courts.

127. *See* Oviedo Convention, *supra* note 88, pmbl. (using generalized terms like "biology" and "medicine" affecting "human dignity"); Andorno, *supra* note 90, at 134.

128. *See* Oviedo Convention, *supra* note 88, chs. II–XIV (presenting protocols for regulating everything from consent to public engagement for ratification); Andorno, *supra* note 90, at 134.

129. *See* Oviedo Convention, *supra* note 88, art. 1, para. 2 ("Each Party shall take in its internal law the necessary measures to give effect to the provisions of this Convention."); Andorno, *supra* note 90, at 135–36 (specifically noting that without judicial enforcement in each member country, the rights laid out in the Convention will have no real power).

130. *See* Andorno, *supra* note 90, at 136.

or societal preference.[131] In that spirit, it seeks to protect equality of access to healthcare for all humans, the right to informed consent, and the right to privacy of information.[132] While it protects against genetic discrimination and forbids modifications of the human genome completely, it fails to take a position on human cloning.[133] The Convention sets up a general framework for biomedical research, but defers the task of defining "embryo research" to the individual nations.[134] Without defining embryo research, the Convention fails to resolve the controversy surrounding the use of embryos in research, which is a fundamental part of gene-editing research.[135]

The Oviedo Convention directly prohibits interventions on the human genome in Article 13.[136] However, when the Convention was drafted in 1997, the technology was not close to making germline modifications a reality.[137] With CRISPR's invention, many member states are pressing to revisit Article 13 via Article 32, which allows the Convention to be revised starting five years after its ratification.[138]

B. *Sample Countries*

At the national level, countries have adapted their existing systems to the growth of gene-editing technology with varying degrees of success. The United States uses its regulatory system to delegate regulatory authority over scientific development to specialized government agencies, which are designed to be responsive to the American public.[139] The United Kingdom maintains extensive statutory control of all reproductive technology, both pre- and post-market.[140] Finally, the Japanese government delegates much of the initiative of scientific regulation to academic societies and the

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131. *See id.* at 137; Oviedo Convention, *supra* note 88, pmbl., art. II.

132. *See* Oviedo Convention, *supra* note 88, arts. 3, 5–10; Andorno, *supra* note 90, at 138–39.

133. *See* Oviedo Convention *supra* note 88, arts. 11, 13; Andorno, *supra* note 90, at 140–41. Interestingly, the Convention specifically bans sex selection *in vitro*.

134. *See* Andorno, *supra* note 90, at 141–42.

135. *See id.* at 142.

136. *See* Oviedo Convention, *supra* note 88, art. 13.

137. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 117.

138. *See id.*

139. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 103–05, 171–72 (outlining the process of FDA approval of somatic cell gene editing clinical testing, standard laboratory practices including consent, and IRB continued review of ethics and safety).

140. *See* Robin Lovell-Badge, *The Regulation of Human Embryo and Stem-Cell Research in the United Kingdom*, NATURE REVS. 998, 1000 (2008) (statutorily requiring HFEA approval, donor consent, and independent ethics committee approval of gene-editing technologies).

public.[141] Though these approaches differ, their regulatory systems serve as a model for other countries because they are on the cutting edge of gene editing.

1. The United States: Innovation Leads to Hesitancy

Currently in the United States, somatic cell clinical applications and research for treatment or prevention of disease and disability are moving forward, while clinical applications and research on germline editing are firmly prohibited.[142] The Food and Drug Administration (FDA) regulates somatic cell applications and research.[143] Somatic cell research is treated like other laboratory research—this includes internal biosafety review, general laboratory practice standards, and special policies applicable to the use of human cells, tissue, or embryos in research.[144]

In the United States, research proposals involving CRISPR must be approved through a multistep process. First, the FDA must approve a confidential Investigational New Drug (IND) application, and then the FDA and an institutional review board (IRB) continually review the progress and techniques over the period of research.[145] In addition to the reviews done by the IRB and the FDA, meetings held at the National Institutes of Health (NIH)'s Novel and Exceptional Technology and Research Advisory Committee (NExTRAC) facilitate public engagement.[146] The NIH's review aims to determine the amount of funding, if any, that it will give to the research proposal.[147]

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141. *See* Anu Shukla-Jones, Steffi Friedrichs & David E. Winickoff, *Gene Editing in an International Context: Scientific, Economic and Social Issues Across Sectors* 22, 27–28 (OECD Sci., Tech., & Indus., Working Paper No. 04, 2018) (noting a Japanese Cabinet Office member offered Japan's panel and public engagement sessions as an example of inclusive regulation).

142. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 183–90 (discussing the existing U.S. regulations of somatic cell application and research and germline cell application and research and recommending regulations for the advancement of gene-editing technology both in the U.S. and generally); Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9 (prohibiting gene editing of human germline cells).

143. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 184–86 (focusing on somatic cell application and research governance).

144. *See id.* at 184 (policies factor in any identifying information that could be found in the material, requiring a form of consent from the subject and additional institutional board review [IRB] if any is found).

145. *See id.* at 103, 171 (outlining the process of approval of somatic cell gene editing clinical testing).

146. *See id.* at 103.

147. *See* Hrouda, *supra* note 84, at 230–31. Other sources of funding besides the NIH are available.

The NIH approves those somatic applications with easily trackable and identifiable risks.[148] Nonbinding guidance from the FDA implies that the less chance of long-term risk, the less monitoring throughout the clinical research will be required.[149] If allowed on the market, a gene-altering drug would have special warning labels, require patient consent, be subject to post-market data analysis, and be subject to complete withdrawal from the market should any indication of danger or ineffectiveness be shown.[150] Interestingly, though, the United States does not regulate how physicians use the product once it has been released to the market.[151]

American citizens have shown support for the clinical use of somatic cell gene editing for the prevention of disease and disability using the democratic processes already in place in the government—by participating in congressional elections and public commenting under the Administrative Procedure Act.[152] Additionally, the NIH and the NExTRAC make their reviews open to the public (in person or via broadcast) and send findings to an email list of those who signed up for updates.[153] Finally, there are seven national ethics committees that work to encourage public participation in decision-making and advise the federal government on its policymaking on these topics.[154]

However, the death of Jesse Gelsinger in 1999 indelibly marked the discussion about somatic cell gene editing research in the United States.[155] Gelsinger was a patient of Dr. Wilson at the University of Pennsylvania. Specifically, Gelsinger was a participant in his trial aiming to modify somatic cells in children born with orinithine transcarbamylase (OTC).[156] Gelsinger died due to an adverse reaction to the vector through which the doctors had delivered the gene-editing

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148. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 104 (noting these reviews take into account "stakeholder and societal perspectives about the value of benefits and the tolerability of risks, . . . the existence and effectiveness of alternative treatments, disease severity, risk tolerance of affected patients, and potential for additional insight from postmarket data").

149. *See id.* (suggesting 15 years of posttrial observation).

150. *See id.* at 104–05 (also noting that the potential off-label use of these drugs might merit further restriction).

151. *See* Charo, *supra* note 19. The FDA does not regulate clinical practice, but doctors and drug/device representatives are partially regulated through the Health and Human Services agency through laws like HIPPA. *See Introduction: About HHS*, DEP'T OF HEALTH AND HUM. SERVS., https://www.hhs.gov/about/strategic-plan/introduction/index.html (last visited Sept. 5, 2020) [https://perma.cc/25FS-V3A7] (last archived Sept. 5, 2020).

152. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 169.

153. *See id.* at 170–71.

154. *See id.* at 172.

155. *See* Lynn Smith & Jacqueline Fowler Byers, *Gene Therapy in the Post-Gelsinger Era*, 4 JONA'S HEALTHCARE L., ETHICS & REG. 104, 107 (2002).

156. *See id.* at 106 (explaining OTC as a disease where an X chromosome is either missing or defective, preventing the liver from producing enough OTC to remove ammonia from the blood).

material.[157] The FDA and NIH barred Dr. Wilson from participating in clinical trials without restrictions until February 2010 and required him to write a letter detailing his experiences from the trial before returning to clinical trials.[158] The NIH's and FDA's investigations attributed blame to the research team specifically concerning the patient consent form, which led both patients and the FDA to believe no deaths occurred in the previous testing on animals.[159] The later investigation also highlighted the neglect of the university's IRB for allowing the trial to continue on Gelsinger, whose ammonia levels were abnormal at the time of the fatal injection.[160] Finally, as later came to light, the lead doctor had a financial interest in the trial's success, which led to a lawsuit from the Gelsingers.[161]

In response to the inundation of review requests the NIH received after Gelsinger's death, the FDA and NIH harmonized their requirements, which streamlined the supervision burden on researchers to balance the confidentiality for businesses looking to profit from the technology in trial (because much of the review process is open to the public) and appropriate disclosures throughout trials for safety and accountability.[162] However, the damage that Gelsinger's death caused to the public trust in the field of gene-editing research and the responsibility cast on IRBs was undeniably severe.[163]

Gene-editing research in the United States slowed partly because of Gelsinger's death and because of the functional bar on research using human embryos without the goal of pregnancy. The Dickey-Wicker Amendment prohibits federal funding for research using human embryos without the goal of pregnancy, but some states and

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157. *See id.* at 107.

158. *See* Robert Steinbrook, *The Gelsinger Case*, *in* OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS 110, 116 (Ezekiel J. Emanuel, Christine C. Grady, Robert A. Crouch, Reidar K. Lie, Franklin G. Miller & David D. Wendler eds., 2008); Robert Fretwell Wilson, *The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research*, 36 AM. J.L. & MED. 295, 301 (2010) (focusing on Dr. Wilson's punishment, including his letter).

159. *See* Steinbrook, *supra* note 158, at 116; *see also* Wilson, *supra* note 158, at 303–16 (taking an in-depth look at Dr. Wilson's financial interest in Gelsinger's trial, specifically discussing the consent form at issue).

160. *See* Smith & Byers, *supra* note 155, at 108 (recounting the investigation's findings on the IRB); Wilson, *supra* note 158, at 306 (noting Gelsinger's unusual ammonia levels).

161. *See* Smith & Byers, *supra* note 155, at 104–05.

162. *See id.* at 108–09.

163. *See* Mark Yarborough & Richard R. Sharp, *Public Trust and Research a Decade Later: What Have We Learned Since Gelsinger's Death?*, 97 MOLECULAR GENETICS & METABOLISM 4, 4–5 (2009) (comparing Gelsinger's death with a more recent patient's death and arguing that for the sake of public trust in science, disclosure and accountability must be strengthened).

private organizations can still fund the research.[164] Even so, the FDA would not approve any research or clinical application that would modify the human genome, specifically germline editing, because its long-term, unpredictable risks would not survive the FDA's rigorous risk/benefit analysis.[165]

Overall, while the American system of regulating gene-editing research is slow-moving because of the amount of bureaucratic approval necessary to begin trials, it is not impossible to overcome.[166] The significant ambiguity in defining disease and disability illustrates why the American process remains so slow.[167] In light of the Gelsinger tragedy, this slowness can be interpreted as deliberate caution unlikely to change anytime soon.[168]

Despite the government's hesitance, however, American scientists continue to hold their place on the cutting edge of gene-editing research—which acknowledges the fact that the American research budget is the largest in the world, both due to public and private funding.[169] The American regulatory system seeks to exert tight control over products pre-market, during the basic and clinical research stages, but once the product is on the market, the American system releases more control than most countries.[170] Once the product gets on the market, doctors are permitted to use and prescribe the product however they desire, which might not be for the same use that the drug was approved.[171]

Interestingly, the American regulation of gene-editing research does not involve the academic science community often—at most, their members might serve on independent review boards, funding committees, and the FDA committees.[172] Though it neglects learned scientific societies to an extent, the American regulatory system incorporates public engagement into its very framework, ensuring that the public opinion on gene editing is honored throughout the process of

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164. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 184 (suggesting that most jurisdictions prohibit germline modifications that do not have reproduction as the end goal, but that existing research guidelines could be adapted to adequately regulate this use).

165. *See id.* at 188–89.

166. *See id.* at 103–04, 171 (noting the regulatory process necessary for gene-editing research).

167. *See id.* at 191.

168. *See id.* at 192 ("Regulatory agencies should not at this time authorize clinical trials of somatic or germline genome editing for purposes other than treatment or prevention of disease or disability."); Yarborough & Sharp, *supra* note 163, at 4–5 (arguing for more disclosure and accountability in order to salvage the American public's trust in science).

169. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 109.

170. *See* Charo, *supra* note 19, at 42.

171. *See id.* (nodding to the idea that once a drug is approved for the market in America, it is permissible for off-label uses as well).

172. *See id.* at 41–42 (noting that the oversight of gene-editing technology falls under the FDA's jurisdiction with no necessary checks from academic communities).

regulating its research.[173] Finally, the American legal framework follows the recommendations of the International Summit on Human Gene Editing in that it currently allows clinical applications of somatic cell editing to progress, but functionally prohibits germline editing.[174]

2. The United Kingdom: Flexible but Strong Intervention

The UK regulates somatic cell research under the advanced therapy medicinal products (ATMP) legal framework, which comes from the European Union (EU).[175] In order to get a somatic cell therapy product on the market in the UK, both the European Medicines Agency and the UK Medicines and Healthcare Products Regulatory Agency must authorize the product's manufacturing.[176] There are two ways around the authorizations mentioned: the hospitals exemption and the specials exemption.[177] The hospital exemption applies specifically to ATMPs, but both exemptions approve a medicinal product that is created for a specific patient.[178]

The British government has eagerly regulated gene therapy and its evolving research since the 1980s.[179] After the birth of the first IVF baby, Louisa Brown, the government recognized a need for government regulation in such a powerful scientific area and set up the Warnock Committee to propose such regulation.[180] Instead of building its approach around a general prohibition on human embryo research and fertility research, the Warnock Committee proposed a framework that would allow flexibility, eventually through licensing under the Human Fertilisation and Embryology (HFE) Act and the Human Fertilisation and Embryology Authority (HFEA).[181] The Warnock Committee also created and enacted the widely accepted fourteen-day limitation on

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173. *See id.* at 40 (noting the regulatory public comment process). *But see* Martin Gilens & Benjamin I. Page, *Testing Theories of American Politics: Elites, Interest Groups, and Average Citizens*, 12 PERSP. ON POL. 564, 575–77 (2014) (suggesting that regulatory capture by American elites and corporate interest groups exert much more influence over the lawmaking process than the expressed policy preferences of average citizens). While the American regulatory process aims to include public preference in the notice and comment period, many scholars argue that the regulatory process has failed to do so because it has been captured by corporate interest groups and affluent preferences.

174. *See* Baltimore, Baylis, Berg, Daley, Doudna, Lander, Lovell-Badge, Ossorio, Pei, Thrasher, Winnacker & Zhou, *supra* note 5; Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9.

175. Davies, *supra* note 28, at 15.

176. *Id.*

177. *Id.*

178. *Id.*

179. *See* Lovell-Badge, *supra* note 140, at 999 (producing a timeline showing regulations since 1978).

180. *See id.* at 998; *see also* Hrouda, *supra* note 84, at 226–27 (arguing that Aldous Huxley's fears about "the Fertilizing Room" were realized when Louisa Brown was born).

181. *See* Lovell-Badge, *supra* note 140, at 998.

research on human embryos that many countries adopted since 1984.[182]

The HFE Act of 1990 specified that the research using human embryos must be necessary to one of the following enumerated purposes: (1) promoting advances in the treatment of infertility, (2) increasing the knowledge about the causes of miscarriages, (3) developing more effective techniques for contraception, and/or (4) developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.[183] It also created the HFEA to review each proposed project for licensing under one of the previously listed purposes. Additionally, the HFEA requires the competence of the research team, the approval of an independent ethics committee, the consent of the embryo donors for the specific experiments, and the donors must have received counseling.[184] In 2001, three more purposes were added to the HFE Act: (1) increasing knowledge about the development of embryos, (2) increasing knowledge about serious disease, and (3) enabling any such knowledge to be applied in developing treatments for serious disease.[185] It also required that any human embryonic-stem cell line derived in the United Kingdom must be deposited in the UK Stem Cell Bank.[186] Also in 2001, Parliament quickly passed the Human Reproductive Cloning Act, which prohibited the implantation of a human embryo created by means other than fertilization in a woman.[187] In 2004, the government included the removal, storage, and use of human tissue and organs in the purview of the Human Tissue Authority under the Human Tissue Act.[188]

Under these laws, research conducted for reproductive purposes could be licensed in the United Kingdom if it fulfills each of the criteria needed, but heritable genome editing, for any purpose, is prohibited completely.[189] The contradiction here—that cells may be reconstructed

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182. The fourteen-day rule prohibits the use of human embryos in research after they are fourteen days old. *See id.* at 999; Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 25, 27–28 (comparing Japan and UK regulations on embryo research, specifically noting their common 14-day rule). *But see* Insoo Hyun, Amy Wilkerson & Josephine Johnston, *Embryology Policy: Revisit the 14-day Rule*, 533 NATURE 169, 170–71 (2016) (suggesting an extension to the globally-accepted 14-day rule because of advancing technology that has allowed scientists to sustain embryos longer).

183. Lovell-Badge, *supra* note 140, at 1000.

184. *See id.* (describing HFEA functions); Human Fertilisation and Embryology Act 1990, c. 37 § 8 (Eng.) (laying out the specific functions of the HFEA).

185. Lovell-Badge, *supra* note 140, at 1000.

186. *Id.*

187. *See id.* at 999–1000. *See generally* Human Reproductive Cloning Act 2001, c. 23 (Eng.).

188. *See generally* Human Tissue Act 2004, c. 30 (Eng.).

189. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 100; R. Isasi, E. Kleiderman & B.M. Knoppers, *Editing Policy to Fit the Genome? Framing Genome Editing Policy Requires Setting Thresholds of Acceptability*, 351 SCIENCE 337, 337–38 (2016).

for reproductive research, but the germline must not be modified—developed because of advancing technology in preventing mitochondrial disease and Parliament's desire to make room for that cure to develop.[190]

Concerning the United Kingdom's recent exit from the EU, science in the United Kingdom could look different in the near future.[191] While the United Kingdom and EU's hyper-governance of gene-editing science does not differ dramatically, the flow of funding and ease of collaboration with other EU countries might be a setback for science in the United Kingdom.[192] However, because of the skilled and established scientists in the United Kingdom, private funding and governmental restructuring could compensate for the lost funding.[193] In addition, UK businesses and scientists could continue to comply with EU laws in order to conduct business and research with other countries.[194]

In comparison to the United States, the United Kingdom's eager government regulation of gene-editing research is certainly extensive: it maintains control over permissibility (i.e., the prohibition on germline modification and the permissibility of research for reproductive purposes) and over practical matters (i.e., type of cells involved, activities done in the research, and purposes for which the activities are done and the cells are used).[195] However, both countries use regulatory bodies for initial approval, an independent review board for continued oversight, and patient consent as the three main pillars of good gene-editing research.[196] While the American regulations are detailed and practical, the United Kingdom's regulations are driven by idealistic goals.[197] Where the United States releases much of the

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190. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 102–03.

191. *See* Andrew H. Baker, Robin R. Ali & Adrian J. Thrasher, *Impact of BREXIT on UK Gene and Cell Therapy: The Need for Continued Pan-European Collaboration*, 27 HUM. GENE THERAPY 1, 1 (2016) (suggesting that science in the UK would be fine if Brexit occurred, but it could be a setback for European science if collaboration is not continued).

192. *See id.*

193. *See id.* at 2.

194. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 119.

195. *Id.* at 105.

196. *Compare* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 103–05, 171–72 (outlining the process of FDA approval of somatic cell gene editing clinical testing, standard laboratory practices including consent, and IRB continued review of ethics and safety), *with* Lovell-Badge, *supra* note 140, at 1000 (statutorily requiring HFEA approval, donor consent, and independent ethics committee approval of gene-editing technologies).

197. *Compare* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 183–90 (examining the US's regulatory approach to germline and somatic cell research and application, which evaluates one proposal at a time through a public rulemaking process), *and* Charo, *supra* note 19 (arguing that detailed administrative rules can be more responsive than legislation), *with* Lovell-Badge, *supra* note 140, at 1000 (describing the HFE Act centering around guiding purposes and promulgating more specific legislation from it).

control over medicinal products once they are on the market, the United Kingdom retains a strong hand in regulating products and their uses even in the market.[198] The Nuffield Council on Bioethics credits the United Kingdom's success in widespread compliance with the HFEA to the fact that real practitioners involved in learned societies had a hand in creating the regulations.[199] Finally, the United Kingdom incorporates public opinion by outsourcing interactive activities to independent and nongovernmental agencies instead of infusing public opinion into the rulemaking process, like the United States does.[200] While the United Kingdom's positions might remain more consistent because its laws are not directly dependent on public feedback,[201] it might be more efficient to have a centralized organization like the government incorporate both law and public opinion, as in the United States.[202] Either way, scholars have continually emphasized the importance of public engagement when it comes to scientific regulations because of its universal effects on humanity.[203]

3. Japan: Flourishing under Regulatory Reluctance

Japan's relationship with general bioethics is different than the United States and the United Kingdom because it incorporates academic societies in a more potent capacity.[204] At first, Western ideas about bioethics strongly influenced Japanese academia via newly translated literature.[205] In response, as early as the 1970s, the Japanese government began to adopt policies concerning informed consent of patients, brain death, and quality of life.[206] As scientific research began to expand, the government selected a committee to meet regularly and, with public involvement, promulgate administrative guidelines for scientific research.[207] The committee

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198. *See* Charo, *supra* note 19.

199. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 84, at 106.

200. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 175.

201. *See* Charo, *supra* note 19 (noting that legislation for biotechnology is generally more politically credible as well).

202. NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 175; *see* Charo, *supra* note 19 (pointing out that regulations can be more responsive to the public than the "blunt instrument" of legislation).

203. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 163–64.

204. *See* Akira Akabayashi, *Bioethics in Japan, 1980-2009: Importation, Development, and the Future*, 1 ASIAN BIOETHICS R. 267, 268 (2009) (arguing that Japanese bioethics began with the academic debate over brain death and organ transplant in the 1980s, and was finally resolved by law as a prophylactic reaction to the academic, public, and political debate that lasted over two decades).

205. *See id.* at 267.

206. *See id.* at 268–69 (explaining the Japanese concern for bioethics through the "Tokai University Euthanasia Judgment," where a scientist was sentenced to two years in prison for administering potassium chloride to a terminally ill patient).

207. *See id.* at 270–71 (describing what the author deems to be Phase II of the Development of Japanese research ethics).

incorporated a public comment system later, which allowed for the public to engage in policymaking in an organized, efficient way.[208] Due to these regulations, ethics committees in scientific institutions became ubiquitous and started catching scientific fabrications and misconduct more often.[209] Governmental and academic institutions created internal offices for a new whistle-blower reporting system in order to address conflicts of interest or other unethical research.[210] In 2004, the Cabinet Office Council for Science and Technology Policy's Expert Panel on Bioethics published a report called the "Fundamental Policy on Handling of Human Embryos," which explained that the government viewed human embryos as "sprouts of human life" that could be used in scientific research with the proper honor and respect.[211] As institutions began to actually conduct genomic research, they required stringent protection of patients' personal information and provided genetic counseling throughout the process, according to the Ethical Guidelines for Human Genome and Gene Analysis Research, one of the most rigorous research guidelines in the world.[212] Unfortunately, while bioethics has certainly flourished in Japan, the medical system has suffered from a dramatic decline in doctors and funding recently because of heightened premiums for health insurance.[213]

Specifically, Japan's government commissioned a panel of experts from scientific fields to create new guidelines for gene-editing research.[214] In doing so, the expert panel held multiple public engagement sessions with its own citizens and other countries in order to understand the issues from many perspectives.[215] Japanese regulations of human embryo research built on Japan's 2004 policy, which disallowed the creation of human embryos for research unless it met each of four criteria: (1) scientific significance in life science and medicine cannot be obtained other than through the use of human embryos, (2) the benefits or anticipated benefits are socially appropriate, (3) there is assurance of human safety, and (4) safeguards

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208. *See id.* (describing what the author deems to be Phase II of the Development of Japanese research ethics).

209. *See id.* at 271 (describing what the author deems to be Phase II of the Development of Japanese research ethics); *see, e.g.*, David Swinbanks, *Gene Therapy Gets Double Dose of Screening*, 367 NATURE 399, 399 (1994) (discussing the establishment and function of ethics committees in response to 1993 legislation in both the Moriyama and Niigata Universities).

210. *See* Akabayashi, *supra* note 204, at 271 (describing what the author deems to be Phase II of the Development of Japanese research ethics); *see also, e.g.*, Swinbanks, *supra* note 209.

211. *See* Akabayashi, *supra* note 204, at 272.

212. *See id.* at 273.

213. *See id.* at 274.

214. *See* Shukla-Jones, Friedrichs, & Winickoff, *supra* note 141, at 22 (recounting a presentation on public engagement in Japan from two Cabinet Office members).

215. *See id.* at 22, 27–28.

are placed to avoid raising concerns of reducing human beings to tools or means.[216] The panel's recommendations prohibited germline editing in clinical research, but encouraged research into better understanding the function of genetics at an early developmental stage.[217] It allowed the use of surplus embryos for research, limited the handling period of human embryos for research to fourteen days, and required secure disposal of human embryos used in research.[218]

But Japan's inclusive and innovative regulations were not the government's first response to the growth of gene-editing technology.[219] After the Panel presented the aforementioned report in 2016, confusion broke out. The Panel itself did not have the power to create, implement, and enforce guidelines based on its findings, and had charged the relevant academic societies with the responsibility of self-regulation accordingly.[220] The academic societies pushed back, arguing that the government should pay for and create regulations for the scientific community.[221] As the relationship between the Panel and the academic societies began to dissolve, Chief Cabinet Secretary Suga declared that the "Japanese government must become responsibly involved in genome-editing technology."[222] From this statement came the expert panel and interim report, both of which scholars consider vague and unenforceable.[223]

Where the United States tests the same drug more than once before approval, Japanese regulations make a single initial evaluation of a drug's risk that categorizes it into a higher or lower level of oversight based on the dangers of its risks.[224] Further, what is interesting about Japan's production of gene-editing regulation is that it works best as a reactive measure—from the bottom up.[225] The Japanese government only took an interest in scientific regulations after the Japanese public pushed back against physician-assisted suicide.[226]

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216. *Id.* at 27–28.

217. *See id.*

218. *See id.*

219. *See* Eisuke Nakazawa, Keiichiro Yamamoto, Aru Akabayashi & Akira Akabayashi, *Regulations on Genome Editing of Human Embryos in Japan: Our Moral Moratorium*, 27 CAMBRIDGE Q. HEALTHCARE ETHICS 360, 362 (2018).

220. *Id.*

221. *See id.*

222. *Id.*

223. *Id.* at 263. *See also* Heidi Ledford, *The Landscape for Human Genome Editing: A View of International Regulations Suggests Where in the World a CRISPR Baby Could Be Born*, 526 NATURE 310, 310–11 (2015) (suggesting that Japan's guidelines fall into the same unenforceable category as China's).

224. *See* Charo, *supra* note 19.

225. *See* Nakazawa, Yamamoto, Akabayashi & Akabayashi, *supra* note 219; *see also* Akabayashi, *supra* note 204, at 270 (describing Japan's choice to regulate bioethical policy decisions through administrative guidelines crafted substantially from public response at committee meetings).

226. *See* Akabayashi, *supra* note 204, at 269–70.

Where the United Kingdom and the United States have both regulated scientific protocol from top down, or from the government to the scientific professional community, to the public consumers, Japan has taken the opposite approach in waiting for the public to request the government's intervention before it gets involved in scientific developments.[227] All three countries incorporate the public's opinions, value governmental transparency and patient consent, and intervene significantly in the scientific research process.[228] Each of the countries incorporate these values into a system that promotes ethical scientific advancement, yet the United States emphasizes deliberate progress through its extensive,[229] detailed regulatory process for funding; the United Kingdom legislates based on unifying, broad ideals;[230] and Japan regulates according to the needs of academic societies.[231]

VI. THE INTERNATIONAL GENE-EDITING ETHICS COMMISSION

Gene editing of both somatic and germline cells affects biological science globally and is growing more quickly than governments can manage.[232] Considering some countries are already using somatic cell editing in clinical research and germline editing could follow closely behind, realistic and effective regulation of gene-editing research has never been more crucial.[233] Soft-law agreements that express broad

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227. *Compare* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 103–05, 171–72 (outlining the process of FDA approval of somatic cell gene editing clinical testing, standard laboratory practices including consent, and IRB continued review of ethics and safety), *with* Lovell-Badge, *supra* note 140, at 1000 (statutorily requiring HFEA approval, donor consent, and independent ethics committee approval of gene-editing technologies), *and* Shukla-Jones, Friedrichs, & Winickoff, *supra* note 141, at 22, 27–28 (explaining that a Japanese Cabinet Officer's example of public engagement sessions illustrates the prioritization of public opinion in Japanese scientific regulation).

228. *Compare* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 103–05, 171–72 (outlining the process of FDA approval of somatic cell gene editing clinical testing, standard laboratory practices including consent, and IRB continued review of ethics and safety), *with* Lovell-Badge, *supra* note 140, at 1000 (statutorily requiring HFEA approval, donor consent, and independent ethics committee approval of gene-editing technologies), *and* Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 22, 27–28 (giving a Cabinet Office member offering Japan's panel and public engagement sessions as an example of inclusive regulation).

229. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 103–05, 171–72.

230. *See* Lovell-Badge, *supra* note 140, at 1000–01.

231. *See* Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 22, 27–28.

232. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8, at 57 ("As noted by former FDA Commissioner Robert Califf, '[s]cientific advances do not adhere to national boundaries and therefore it is critical that we understand the evolving views of our international counterparts.'").

233. *See* Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 38 (stating that because human applications are a reality for gene editing now, countries must

principles about the human genome, though noble and integral to biosafety of humankind, have failed to properly motivate scientists to comply with transnational beliefs about genome editing.[234] Additionally, differing regulations among different countries lead to confusion at best, and inaction at worst.[235]

In response, this Note proposes to form The International Gene-Editing Ethics Commission (Commission), an entity made up of democratically elected representatives of participating countries.[236] This Commission is distinct from other international committees, such as The International Summit on Human Gene Editing, because it harnesses the power of scientific publication to incentivize scientists across the globe to become members bound by its ethical guidelines.[237] The Commission would compile a valuable database of gene-editing data that is available only to member countries, evaluate research proposals, promulgate mandatory ethical standards, and provide significant funding to those research proposals that commit to undergo

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distinguish between somatic, with which most countries are comfortable, and germline editing, with which most countries are not comfortable and create regulations for both kinds).

234. *See, e.g.*, Andorno, *supra* note 90, at 134 (noting that important scientific communities like the United Kingdom, Germany, and France rejected even the most binding international treaty, the Oviedo Convention); Hannum, *supra* note 92, at 322–23.

235. *See* Melillo, *supra* note 16, at 771 (emphasizing the need for global consensus concerning the regulation of gene editing); Preetika Rana, *How a Chinese Scientist Broke the Rules to Create the First Gene-Edited Babies*, WALL ST. J. (May 10, 2019), https://www.wsj.com/articles/how-a-chinese-scientist-broke-the-rules-to-create-the-first-gene-edited-babies-11557506697?mod=wsj_vanderbilt3 [https://perma.cc/ZH9Z-2VPJ] (archived Aug. 31, 2020) (outlining Dr. He's communications with other scientists about his CRISPR clinical applications, which mostly consisted of scientists urging caution and attempting to create a deliberate ignorance about his experiment).

236. *See* Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 30 (summarizing experts' opinions about the benefits and dangers of international harmonization of gene-editing technology regulation, most of whom agreed that harmonization is worth trying); *see also* Charo, *supra* note 19. This Commission would aim for the successful and influential impact of the Council for International Organizations of Medical Sciences, which creates global standards for human subjects, but it would differ because it specifically addresses gene-editing research and clinical applications rather than medical science as a whole. "Democratically elected representatives" may look different for different countries. For instance, in the United States, it is most likely that the President would have to appoint the US representatives to this Commission in order to comply with the US Constitution. Importantly, though, since the President is elected by the American public, these appointments are, at least partially, democratic. My hope is that these representatives would be democratically elected through the available processes in each participating country.

237. *See* NAT'L ACADS. OF SCIS., ENG'G, AND MED., *supra* note 8; Baltimore, Charo, Daley, Doudna, Kato, Kim, Lovell-Badge, Merchant, Nath, Pei, Porteus, Skehel, Tam & Zhai, *supra* note 9 (discussing how the International Summit on Human Gene Editing offers little incentive to member nations other than publicly available expert findings and its ethical guidelines are not binding on any nation); *see also* Charo, *supra* note 19 (stating that the Council for International Organizations of Medical Sciences creates global standards for human subjects).

regular reviews by the commission as well as the reviews required by their own countries. Most importantly, the Commission would create and enforce a clear whistle-blower framework to allow scientists to handle a future situation like that with Dr. He more effectively. In order to become a member nation, the country must demonstrate its commitment to transparency, responsible science, and promoting well-being of the entire human race, as well as of individuals.

The International Gene-Editing Ethics Commission has four main features: (1) a database, (2) research funding, (3) a proposal evaluation system, and (4) mandatory ethical standards. The database and the research funding serve as incentives to join the Commission, in an effort to promote the ethical advancements of gene-editing technology.

A. *The Incentives: Information and Funding*

Moving forward, the scientific community must be adequately incentivized to faithfully comply with globally established regulations in research, both basic and clinical. In his article reflecting on Jesse Gelsinger's death, Dr. Wilson noted that

> It should be recognized . . . that academic medicine is a competitive profession with the primary measure of success being recognition by your colleagues of your research accomplishments. This recognition is critical to sustaining one's research agenda through the successful competition for grants and the awarding of academic promotions and tenure.[238]

Given the powerful motivator of publication for medical researchers, academic societies and journals hold influential power over the global scientific community.[239] Japan's struggle between academic societies and governmental regulation also points to a need for a body outside of academia and government to order the incentives of the community correctly.[240] To ensure ratification in scientifically-influential nations like the United Kingdom,[241] membership in the Commission must be extremely valuable so that countries are incentivized to join. These incentives must also be valuable in order to incentivize international,

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238. James M. Wilson, *Lessons Learned from the Gene Therapy Trial for Ornithine Transcarbamylase Deficiency*, 96 MOLECULAR GENETICS & METABOLISM 151, 155 (2009) https://reader.elsevier.com/reader/sd/pii/S109671920800499X?token=1E4DB222E5B01B2440CF54697F343D7F8F53168665D71003D45002A7606CCA261B513232DB88733D1CDE4E2686D036B3 [https://perma.cc/WEC3-G652] (archived Aug. 31, 2020).

239. *See infra* Part III.B.3 (discussing Japan's journey to regulation of gene-editing technology).

240. *See id.*; Shukla-Jones, Friedrichs, & Winickoff, *supra* note 141, at 22 (using a Cabinet Office member offering Japan's panel and public engagement sessions as an example of inclusive regulation).

241. Andorno, *supra* note 90, at 134 (noting the United Kingdom did not adopt the Convention because it was too restrictive, Germany refused because it was too permissive, and France refused because of its own simultaneous bioethics law reform).

specific regulations—an accomplishment not yet achieved by other international agreements. Ideally, the Commission would utilize the influence of the major peer-reviewed, scientific journals by favoring scientists' papers from member countries. Though this perk would likely require substantial funding on the front end and scientists might resent the favoritism, the scientific community's concern for safe, ethical research would help motivate funding from universities and nations around the world.

B. *The Purpose: Ethical Advancement of Gene Editing*

While one important function of the Commission would be to provide an efficient epicenter for scientists to share their findings and help each other advance across borders, its most crucial function would be the accountability created among its members through the promulgation of ethical standards for gene-editing research and a whistle-blower framework to enforce these standards. Had this been available to many scientists who heard about Dr. He's research before he went forward with his clinical application, there is a possibility that he could have been prevented from altering the human genome permanently and without permission.[242] Dr. He's clinical application of CRISPR had many negative consequences, among which are the lack of consent from the human population before permanently altering the human genome. Without understanding the effect of genome editing or its ramifications throughout future generations, this unapproved experiment changed the human genome as we knew it.

The Commission's standards would be created by those appointed to the Commission, with each member country appointing two citizens to represent them in the Commission. The Commission would meet to propose and discuss ideas for ethical standards and submit the finished product to the public for approval. Learning from the Japanese and American approaches that emphasize public engagement,[243] the Commission would create a public notice and comment period, similar to the American procedures laid out in the Administrative Procedure Act,[244] before enacting new regulations. Adding a check on the

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242. *See* Cyranoski, *supra* note 1 (discussing the scientists who knew about He's clinical research before it actually happened and whether they should have done more to prevent it).

243. Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 22, 27–28; *see* Charo, *supra* note 19 (noting that the oversight of gene-editing technology falls under the FDA's jurisdiction).

244. Administrative Procedure Act, 5 U.S.C. §§ 551–59 (2018) (outlining the process of producing administrative regulations through notice and comment rulemaking, which includes public engagement). *See also* Gilens & Page, *supra* note 173. I would like to note that the American regulatory process is not a perfect solution because of the regulatory capture problem discussed previously. I would suggest regulating this

Commission through the public helps avoid a future situation like the one with Dr. He—the pace of the use of gene-editing technology on humans could then match with the public's preference.[245] Dr. He's modification of germline editing came before much of the world assented to germline editing. Had his project been subject to regulation created based on public opinion, then, it would have been prohibited. Additionally, public engagement in the use of science also breaks any aristocratic barriers created by elite scientific academia and encourages public trust in the scientific community.[246] Finally, because humanity as a whole will be affected by the use of germline editing, incorporating public opinion into the regulatory process ensures that the rules reflect the will of the people.

Specifically, the Commission could solicit public opinions from many different countries through online polls and surveys in order to gauge and quantify the public sentiment towards new technology and its applications. Realistically, it would be important to break this down into a short explanation of the technology and then ask whether the survey-taker would be comfortable with the technology (1) being used in basic research and (2) being used on a family member in a clinical trial. That way, the Commission can combat potential cognitive barriers by making people think about use on a loved one, instead of a faceless test subject. Once the public approves the standards, member countries would be informed of them and held to them.

The Commission would enforce the publicly-enacted standards through a whistle-blower system for the scientific community.[247] Taking a page out of the International Summit on Human Gene Editing's book, self-regulation among scientists seems to be a more effective way to enforce scientific protocol transnationally than through a broader treaty like the UNESCO Declaration, or even the Oviedo Convention, that allows countries to create laws based on its broad principles. This framework would provide a system for scientists who are concerned by experiments or research that threaten one of the fundamental principles of the Commission to anonymously report their concern to the Commission, who will then investigate the issue and impose sanctions if necessary.

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notice and comment period in such a way that corporate interest groups and elite voices are not so controlling. Perhaps there could be a spending limit for lobbying these preferences to the Committee that equalizes the playing field, for example.

245. *See* Cyranoski, *supra* note 1.

246. *See generally* Christi J. Guerrini, G. Evan Spencer & Patricia J. Zettler, *DIY CRISPR*, 97 N.C. L. REV. 1399 (2019) (discussing the dangers of the growing use of CRISPR by nonscientists in the US).

247. Arthur Kantrowitz, *Elitism vs. Checks and Balances in Communicating Scientific Information to the Public*, 4 HEALTH SAFETY & ENV'T. 101, 103, 107–08 (1993) (advocating an extension of the scientific community's traditional self-policing nature in order to hold scientists accountable for their publicly-expressed policy preferences instead of relying on their credentials and prestige alone).

The Commission only has its own internal power and authority to penalize members who violated the guidelines. Possible sanctions could include monetary penalties to the relevant institution, which would incentivize the institution as a whole to monitor its researchers closely. Privileges of membership (funding and database access) could also be suspended as a penalty for violating guidelines. As a last resort for serious offenses, an institution's, or even a country's, membership could be suspended or revoked.

The International Commission would encourage the already strong sense of communication among the participating scientific communities such that it benefits all scientists involved through helpful databases, workshops, and collaborations. While this would benefit scientific advancement generally, it would also encourage transparency among peers.[248] The whistle-blower framework would allow peers to warn the Commission if a peer overstepped an ethical line through an anonymously written form. Anonymity would allow the whistle blower to avoid any stigmatization that might come with reporting a peer's infraction, but the writing ensures that the whistle blower has taken time to articulate the problems with the peer's experiment.

C. *Practicality*

This Commission is not a panacea for the regulation of advancing biotechnology. In particular, this solution relies on the assumption that many nations will be able to come to agreement on a code of ethics for scientific technology as it evolves further. Given how differently the United States, the United Kingdom, and Japan have regulated technology nationally, agreement might only be achieved through broad language, which this Note has already argued as ineffective. However, given the Committee's strong incentive for membership and harnessing of academia, this solution provides a different, more viable approach to international regulation.

Additionally, the practicality of obtaining scientific journals' agreement to favor member nations' work could be a hurdle to this solution's success for several reasons. First, scientific journals seek to publish work based on its merits, and less on who wrote it. Scientists themselves might push back against the Commission since their careers depend on their country's membership, over which they have little control. Second, it could further divide the public from academia.

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248. But it could also cause biotechnology to become politicized to an underproductive extent. *See* Shukla-Jones, Friedrichs & Winickoff, *supra* note 141, at 3, 28–30 (presenting global experts' hesitations on international governance of gene-editing technologies, including politicization and forcing countries to accept values of another country in terms of bioethics, but citing that a flexible framework could cure these issues).

In a similar vein, whether or not regulation can ever accurately capture public opinion, especially on a scale as large as proposed here, remains an issue for this Committee's rulemaking procedures.[249] Even given these concerns, this solution provides a middle ground between vague international agreements and specific, binding agreements. Vague international agreements gain universal adoption, but varying kinds of implementation. Specific, binding agreements gain less support, but more uniform implementation. This solution provides a way to gain wide acceptance to the broad goal of the Commission, but specific, uniform adherence to the specific guidelines developed by participating countries.

V. CONCLUSION

Despite the scientific community's best efforts to restrain advancing technology to allow for international ethical standards to catch up, Dr. He's experiment exemplifies that science can be hard to control. Specifically, gene editing has been at the forefront of human thought since we have existed—through the most primal selection of sexual mates, to Mendel's pea plants, to Nazism, to assisted reproductive technology, to CRISPR itself.[250] Through that lens, Dr. He's jumping into germline editing without international approval should not be so surprising. The international scientific community began a conversation about this issue, and countries attempted to regulate this issue independently, but those two forces must unite in finding a way forward. By streamlining the scientific community's expertise and already existing lines of communication via peer-review and the internet to trigger a quick legal response in the appropriate country, the International Gene-Editing Ethics Commission will allow scientists to use technologies like CRISPR safely across the globe. The question is no longer whether to edit the human genome, but how to do so ethically and safely.

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249. *See* Gilens & Page, *supra* note 173.

250. *See infra* Part II.A (discussing how historical eugenic thought serves as a warning sign to regulate CRISPR internationally).

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