

Is Germline Gene Editing Exceptional?

Myrisha S. Lewis*

Advances in gene editing have recently received significant scientific and media attention. Gene editing, especially CRISPR-Cas9, has revived multiple longstanding ethical debates, including debates related to parental autonomy, health disparities, disability perspectives, and racial and economic inequalities. Germline, or heritable, gene editing generates several newer, neglected bioethical debates, including those about the shared human germline and whether there is a “line” that humans should not cross.

This Article addresses several interrelated ethical and legal questions related to germline gene editing. Those questions address why, if at all, germline gene editing needs to be regulated and, if germline gene editing needs to be regulated, whether it can be regulated under existing law. Ultimately, this Article finds that germline gene editing should and can be regulated under existing law; however, the current federal-centric regime is not the optimal way to regulate this subset of gene editing.

Instead, this Article argues that germline gene editing should be regulated like traditional assisted reproductive technology, such as in vitro fertilization, instead of as an exceptional, federally-regulated medical product. Doing so would reduce regulatory barriers in access to innovation, and the technique would be subject to a significantly less burdensome and less federally dominated regime than it is today. Additionally, this Article’s proposed regulatory treatment of germline gene editing would increase access to the technique and remove the

*Associate Professor, William & Mary Law School; J.D., Columbia Law School; A.B., Harvard College. For their helpful comments and suggestions, I thank Aaron Bruhl, I. Glenn Cohen, Lolita Darden, Tara Grove, Lewis Grossman, Laura Heymann, Alli Larsen, Kim Mutcherson, Nate Oman, Rachel Rebouché, Sonia Suter, and the participants at: Biolawlapalooza 3.0; the University of Richmond’s Junior Faculty Forum; Arizona State University’s Annual Conference on the Governance of Emerging Technologies; the 2019 Law and Society Association Annual Meeting; the 2019 Baby Markets Roundtable; the 42nd Annual Health Law Professors Conference; the 13th Annual Lutie A. Lytle Black Women Law Faculty Workshop; the Third Annual Junior Faculty Forum on Law and STEM at Stanford Law School; the 2019 *Nova Law Review* Symposium; the University of Richmond Faculty Workshop; and the Fourth Annual Health Law Works-in-Progress Retreat at Seton Hall Law School.

federal government, which is prone to regulate based on social and political views, from the practice of medicine, in order to allow access to a procedure that could improve or save many lives.

I. INTRODUCTION	737
II. EMERGING TECHNOLOGIES IN GENE EDITING AND “TRADITIONAL” ART ...	743
A. Scientific Background	744
1. Genes	744
2. Somatic Gene Therapy.....	745
3. Germline Gene Editing.....	746
4. Assisted Reproductive Technology.....	749
B. Legal Background	752
1. Federal Funding Restrictions	756
2. Administrative Legal Barriers.....	758
3. Budget Riders.....	761
III. SOCIAL, POLITICAL, AND ETHICAL DEBATES THAT CAN INFLUENCE REGULATION.....	763
A. Concerns Related to Autonomy: The Consent of Future Persons and Parental Autonomy.....	767
1. Consent for Future Persons and Parental Autonomy....	767
B. Concerns Related to Disability Rights and Eugenics	771
1. Disability-Related Concerns.....	772
2. Eugenics Concerns	773
3. Disparities and Inequality.....	775
4. Hierarchy of Disease	777
C. Morality Concerns Related to the “Moral Status” of Embryos and the Proper Role of Humans	779
1. Hubris, Sanctity of Nature, and Religious Concerns.....	780
2. Commodification	782
D. Concerns Related to the Future of the Human Race	783
1. The Morality of Enhancement.....	784
2. The “Inviolability” of the Human Germline	787
3. The “Shared Human Identity”	788
IV. APPLYING TRADITIONAL ASSISTED REPRODUCTIVE TECHNOLOGY REGULATION TO EMERGING GERMLINE GENE EDITING TECHNOLOGIES	794
A. The Similarities Between Germline Gene Editing and Drugs/Biologics	795
B. Regulating Gene Editing Like Assisted Reproductive Technology.....	804
C. Lessons from Assisted Reproductive Technology	810
V. CONCLUSION.....	813

I. INTRODUCTION

Every year, women give birth to children with incurable diseases or diseases with devastating symptoms and extensive suffering.¹ Further, many of those diseases have genetic causes, which means that subsequent generations may also suffer from those diseases and could be burdened with the knowledge that they could pass on these conditions to their children and future generations.² Beyond the burdens on those who are directly impacted by these diseases, the healthcare system must cope with the financial and logistical impacts of these diseases.³ For example, recent debates have focused on the high price of American healthcare, especially for pharmaceuticals.⁴ Most recently, as politicians and the public focused on the high price of drugs, this debate intensified when the U.S. Food and Drug Administration (FDA) approved a drug to treat spinal muscular atrophy in children with a one-time cost of \$2.1 million.⁵ What if we could avoid the health and financial burdens of genetically-caused diseases?

Germline gene editing, which is the target of unique regulatory treatment in the United States, offers that possibility. Germline gene editing consists of two medical techniques: one that yields a heritable genetic modification, which could be passed on to future generations,

¹ See Carolyn Jacobs Chachkin, *What Potent Blood: Non-Invasive Prenatal Genetic Diagnosis and the Transformation of Modern Prenatal Care*, 33 AM. J.L. & MED. 9, 47–48 (2007); *Birth Defects Research*, MARCH OF DIMES <https://www.marchofdimes.org/research/birth-defects-research.aspx> (last visited Oct. 19, 2019).

² See Lori B. Andrews, *A Conceptual Framework for Genetic Policy: Comparing the Medical, Public Health, and Fundamental Rights Models*, 79 WASH. U. L.Q. 221, 247–48 (2001); Angela Liang, *The Argument Against a Physician's Duty to Warn for Genetic Diseases: The Conflicts Created by Safer v. Estate of Pack*, 1 J. HEALTH CARE L. & POL'Y 437, 443–44 (1998); ARNOLD CHRISTIANSON ET AL., MARCH OF DIMES, GLOBAL REPORT ON BIRTH DEFECTS, (2006), <https://www.marchofdimes.org/global-report-on-birth-defects-the-hidden-toll-of-dying-and-disabled-children-full-report.pdf>.

³ See, e.g., Nina Gonzaludo et al., *Estimating the Burden and Economic Impact of Pediatric Genetic Disease*, 21 GENETICS IN MED. 1781, 1787 (Dec. 20, 2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6752475/pdf/41436_2018_Article_398.pdf. But see CHRISTIANSON ET AL., *supra* note 2 at 10–11.

⁴ Ezekiel J. Emanuel, *Big Pharma's Go-To Defense of Soaring Drug Prices Doesn't Add Up*, ATLANTIC, (Mar. 23, 2019), <https://www.theatlantic.com/health/archive/2019/03/drug-prices-high-cost-research-and-development/585253>; Austin Frakt, *Something Happened to U.S. Drug Costs in the 1990s*, N.Y. TIMES, (Nov. 12, 2018), <https://www.nytimes.com/2018/11/12/upshot/why-prescription-drug-spending-higher-in-the-us.html>; Ben Hirschler, *How the U.S. Pays 3 Times More for Drugs*, SCI. AM. (Oct. 13, 2015), <https://www.scientificamerican.com/article/how-the-u-s-pays-3-times-more-for-drugs>.

⁵ Linda Carroll & Lauren Dunn, *\$2.1 Million Drug to Treat Rare Genetic Disease Approved by FDA*, NBC NEWS (May 24, 2019), <https://www.nbcnews.com/health/health-news/2-1-million-drug-treat-rare-genetic-disease-approved-fda-n1009956>.

and another that uses “traditional” assisted reproductive technology (“ART”), which does not involve genetic modification, namely, in vitro fertilization (“IVF”).⁶ In terms of accessing heritable genetic modification, however, options are severely limited, unlike the availability of traditional ART.⁷

The regulatory regime is especially hostile toward treatments with therapeutic uses that could *prevent* disease inheritance or *correct* defective genes by using genetic modification, such as germline gene editing.⁸ Thus, even though some trials related to gene editing in adults, as opposed to embryos, are going forward, access to preventive or germline gene editing remains limited.⁹ This access is limited because gene editing of embryos, like other techniques involving genetic modification, has been subjected to a federal-centric regime that hinders innovation.¹⁰

Some prospective parents, such as those who both carry recessive traits, cannot simultaneously naturally reproduce and have a genetically related child without risking passing the disease on to their children.¹¹ Germline gene editing is a solution to this problem. Current United

⁶ See *infra* Part II; Henry T. Greely, *CRISPR'd Babies: Human Germline Genome Editing in the 'He Jiankui Affair,'* 6 J. OF L. & BIOSCIENCES 111, 113 (2019) (“In short: germline editing creates changes that a person’s descendants can inherit, as opposed to changes that could not be passed on to future generations.”).

⁷ See Susan Winterberg et al., *Technology Factsheet Series: Genome Editing*, HARV. KENNEDY SCH. BELFER CTR. FOR SCI. & INT’L AFF. & CRCS CTR. FOR RES. ON COMPUTATION & SOC’Y (2019), <https://www.belfercenter.org/sites/default/files/2019-06/TechFactSheet/genomeediting%20-%206.pdf>; see also *infra* note 8.

⁸ See discussion *infra* Section II.B. of FDA treatment of forms of ART involving genetic modification. For more detailed accounts, see Myrisha S. Lewis, *The American Democratic Deficit in Assisted Reproductive Technology Innovation*, 45 AM. J.L. & MED. 130, 131–32, 149–55 (2019) [hereinafter Lewis, *The American Democratic Deficit*]; Myrisha S. Lewis, *How Subterranean Regulation Hinders Innovation in Assisted Reproductive Technology*, 39 CARDOZO L. REV. 1239, 1273–74 (2018) [hereinafter Lewis, *How Subterranean*].

⁹ See, e.g., Michael Nedelman & Minali Nigam, *Trial Underway in US Uses Gene-editing in People with Severe Sickle Cell Disease*, CNN (July 30, 2019), <https://www.cnn.com/2019/07/30/health/crispr-trial-sickle-cell>; Rob Stein, *In A 1st, Doctors in U.S. Use CRISPR Tool To Treat Patient with Genetic Disorder*, NPR (July 29, 2019), <https://www.npr.org/sections/health-shots/2019/07/29/744826505/sickle-cell-patient-reveals-why-she-is-volunteering-for-landmark-gene-editing-st>.

¹⁰ See *supra* note 8.

¹¹ See Eric Rakowski, *Who Should Pay for Bad Genes?*, 90 CAL. L. REV. 1345, 1349 (2002); see also *Tay-Sachs*, U.S. NAT’L LIBR. OF MED. (Feb. 11, 2020), <https://ghr.nlm.nih.gov/condition/tay-sachs-disease#inheritance>; *Tay-Sachs Disease*, NAT’L CTR. FOR ADVANCING TRANSLATIONAL SCIS., <https://rarediseases.info.nih.gov/diseases/7737/tay-sachs-disease/cases/50741> (last visited Nov. 20, 2020). *Tay-Sachs* is a disease where if both parents carried the recessive gene, they could pass on the trait to their children if they reproduced naturally.

States regulation, however, severely curtails a technique that could permit parents who are carriers of various inheritable diseases, such as Tay-Sachs, sickle cell anemia, Alzheimer's disease, Huntington's disease, inheritable forms of blindness, and cystic fibrosis, to prevent their children from inheriting or being carriers for those diseases.¹² This severely curtailed access to the technology is striking not only because of the possible delay in access to promising medical treatment but also because parents can make so many other decisions for their children (and future children), including use of IVF (which would be required for the gene editing of embryos); selection of embryos to implant using IVF; prenatal testing; enrollment of children in clinical trials; and many other decisions about the upbringing of their children, including their children's medical care.¹³

Often, new technologies with potential for uses that society views as harmful, such as germline gene editing, artificial intelligence, genomically modified organisms, robotics, and cloning, face requests for regulation.¹⁴ A November 2018 *Vanity Fair* article asked, "Is Gene Editing More Dangerous than Nuclear Weapons?" thus emphasizing the fear and concern surrounding potential uses of gene editing.¹⁵ ART,

¹² See *Genetic Disorders*, U.S. NAT'L LIBR. OF MED., <https://medlineplus.gov/genetic-disorders.html> (last visited Oct. 26, 2020); see, e.g., Sharon Begley, *Scientists Unveil The 'Most Clever CRISPR Gadget' So Far*, STAT News (Apr. 20, 2016), <https://www.statnews.com/2016/04/20/clever-crispr-advance-unveiled/>; Berly McCoy, *CRISPR Gene-editing 'Eliminates' HIV in Some Mice. What Does It Mean for Humans?*, PBS NEWS HOUR (July 2, 2019, 5:40 PM), <https://www.pbs.org/newshour/science/crispr-gene-editing-eliminates-hiv-in-some-mice-what-does-it-mean-for-humans>. But see Eric S. Lander, *What We Don't Know*, in 24 NAS INTERNATIONAL SUMMIT ON HUMAN GENE EDITING, COMMISSIONED PAPERS 24 (2015), https://www.nap.edu/resource/21913/gene_papers.pdf (noting that in terms of the genetic treatment of disease "if we really care about helping parents avoid cases of genetic disease, germline editing is not the first, second, third, or fourth thing that we should be thinking about").

¹³ See U.S. Food and Drug Admin., HHS, *Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products*, 78 Fed. Reg. 12937, 12944 (Feb. 26, 2013); *Troxel v. Granville*, 530 U.S. 57, 66–70, 72–73 (2000); *Prince v. Massachusetts*, 321 U.S. 158, 166 (1944); Sonia M. Suter, *A Brave New World of Designer Babies?*, 22 BERKELEY TECH. L.J. 897, 923 (2007). For more on parental autonomy and child welfare, see Section III.A.

¹⁴ For discussions of technologies that have generated scholarly and public calls for more (or basic) regulation, see Jane R. Bambauer, *Dr. Robot*, 51 U.C. DAVIS L. REV. 383, 384 (2017); Ryan Calo, *Robotics and the Lessons of Cyberlaw*, 103 CAL. L. REV. 513, 551–53 (2015); Mark Fenwick et. al., *Regulation Tomorrow: What Happens When Technology Is Faster Than the Law?*, 6 AM. U. BUS. L. REV. 561, 563 (2017); Henry T. Greely, *Neuroscience, Artificial Intelligence, Crispr—and Dogs and Cats*, 51 U.C. DAVIS L. REV. 2303, 2328 (2018); John O. McGinnis, *Accelerating AI*, 104 NW. U. L. REV. 366, 366–67 (2010).

¹⁵ See Nick Bilton, *The "Black Ball" Hypothesis: Is Gene Editing More Dangerous than Nuclear Weapons?*, VANITY FAIR (Nov. 28, 2018), <https://www.vanityfair.com/news/2018/11/is-gene-editing-more-dangerous-than-nuclear-weapons>; see also Eli Y.

specifically IVF, was similarly compared to the “atom bomb” when it was a new technique.¹⁶ Further, before IVF was a reality, observers noted that “the ‘brave new world’ of Aldous Huxley may be nearer realization.”¹⁷ Discussing gene editing and similar techniques in apocalyptic terms tends to lead to requests for overregulation and reduced access to medical innovation. Instead, this Article draws parallels between germline gene editing and most new and existing technologies or treatments, which come with advantages and disadvantages, including gene therapy and IVF, which were previously discussed in apocalyptic terms but are now widely available and subject to a substantially less burdensome regulatory regime.¹⁸

This Article argues that germline gene editing should be treated similarly to IVF, which is subject to physician self-regulation and state laws addressing the practice of medicine, instead of like a federally-regulated medical product.¹⁹ More specifically, this Article emphasizes a risk-based approach where regulatory regimes exist to manage risks or to compensate those who are harmed, as evidenced by the regulatory regimes created by environmental law, medical malpractice, pharmaceutical regulation, consumer protection, and tort law.²⁰

Adashi, *Fifty Years After Huxley: The Roadmap of Reproductive Medicine Revisited and Updated: The 2015 SRI-Pardi Distinguished Scientist Plenary Lecture of the Society for Reproductive Investigation*, 22 REPROD. SCI. 1330, 1330 (2015); see also *infra* note 77 and accompanying text (noting calls for moratoria or periods of time in which human germline gene editing not be attempted).

¹⁶ Jason Pontin, *Science is Getting Us Closer to the End of Fertility*, WIRED (Mar. 27, 2018), <https://www.wired.com/story/reverse-infertility>.

¹⁷ MARGARET MARSH & WANDA RONNER, *THE PURSUIT OF PARENTHOOD: REPRODUCTIVE TECHNOLOGY FROM TEST-TUBE BABIES TO UTERUS TRANSPLANTS* 20 (2019).

¹⁸ See *infra* Section II.B. (discussing the characterization of the regulatory regime surrounding IVF and other traditional ART techniques as “minimally regulated” or “unregulated” and the state regulation of ART). The term “gene therapy” generally applies to non-somatic or non-heritable genetic modification.

¹⁹ For more on state regulation of the practice of medicine and IVF see *infra* Section II.B. For more on self-regulation in the field of ART, see, for example, Jennifer L. Rosato, *The Children of ART (Assisted Reproductive Technology): Should the Law Protect Them from Harm?*, 2004 UTAH L. REV. 57, 66 (2004) (“The American Society for Reproductive Medicine (‘ASRM’) is the primary professional organization that oversees the field of reproductive medicine, and the Society of Assisted Reproductive Technology (‘SART’), an affiliated organization, specifically covers IVF programs, in addition to other types of ART programs.” (citations omitted)).

²⁰ See William Green, *The FDA, Contraceptive Marketing Approval and Products Liability Litigation: Depo-Provera and the Risk of Osteoporosis*, 68 FOOD & DRUG L.J. 115, 116–17 (2013); Anna B. Laakmann, *When Should Physicians Be Liable for Innovation*, 36 CARDOZO L. REV. 913, 916 (2015); Jonathan Remy Nash, *The Supreme Court and the Regulation of Risk in Criminal Law Enforcement*, 92 B.U. L. REV. 171, 192–97 (2012) (exploring the “paradigmatic risk regulation as undertaken by agencies in the context of

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 741

Scientific advances that potentially impact the gene pool elicit political, legal, and scientific controversy.²¹ Germline gene editing provides the promise of eventually eradicating certain diseases instead of just treating a disease after it has been inherited.²² Gene editing has been characterized as “an ideal method to correct inherited disorders.”²³ Many bodies of literature apply to the regulation of gene editing, including those that examine innovation, risk-regulation, bioethics, health law with an emphasis on food and drug law, administrative law, and intellectual property law.²⁴

This Article builds on my prior scholarship regarding the role of ethical and social considerations in scientific decision-making and uses those considerations to structure a system for regulating germline gene editing techniques.²⁵ This Article makes several contributions to the bioethics, food and drug law, and health law literatures. With respect to bioethics literature, this Article outlines the various reasons why individuals are opposed to gene editing technologies. This Article shows that many of those reasons are the same reasons that lead to opposition

environmental regulation”). See generally Mark Geistfeld, *Negligence, Compensation, and the Coherence of Tort Law*, 91 GEO. L.J. 585 (2003); Michele Goodwin, *A View from the Cradle: Tort Law and the Private Regulation of Assisted Reproduction*, 59 EMORY L.J. 1039, 1089–1100 (2010).

²¹ For a definition of the gene pool, see, for example, *The Collective Set of Alleles in a Population Is Its Gene Pool*, SCITABLE BY NATURE EDUC. (2014), <https://www.nature.com/scitable/topicpage/the-collective-set-of-alleles-in-a-6385985> (“The collection of all the genes and the various alternate or allelic forms of those genes within a population is called its gene pool.”).

²² *The Science and Ethics of Genetically Engineered Human DNA: Hearing Before the Subcommittee on Research and Technology of the H. Comm. on Sci., Space, and Technology*, 114th Cong. 1, 23 (2015), (statement of Dr. Elizabeth McNally), <https://www.govinfo.gov/content/pkg/CHRG-114hhrg97564/pdf/CHRG-114hhrg97564.pdf> [hereinafter *The Science and Ethics of Genetically Engineered Human DNA*].

²³ Donald B. Kohn et al., *Ethical and Regulatory Aspects of Genome Editing*, 127 BLOOD 2553, 2553 (2016). This characterization applies to both somatic and germline gene editing.

²⁴ See, e.g., Stuart Minor Benjamin & Arti K. Rai, *Fixing Innovation Policy: A Structural Perspective*, 77 GEO. WASH. L. REV. 1, 19 (2008) (citing Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 347 (2007)); Stuart Minor Benjamin & Arti K. Rai, *Who’s Afraid of the APA? What the Patent System Can Learn from Administrative Law*, 95 GEO. L.J. 269, 275 (2007). For more on gene editing from a patent perspective, see Green, *supra* note 20, at 115–17; Laakmann, *supra* note 20, at 916; Nash, *supra* note 20, at 192–97; Arti K. Rai, *Building A Better Innovation System: Combining Facially Neutral Patent Standards with Therapeutics Regulation*, 45 HOUS. L. REV. 1037, 1040 (2008); Jacob S. Sherkow, *Patent Protection for CRISPR: An ELSI Review*, 4 J.L. & BIOSCIENCES 565 (2017). See generally Mark Geistfeld, *Negligence, Compensation, and the Coherence of Tort Law*, 91 GEO. L.J. 585 (2003) (discussing “the . . . long-held belief that the tort system is designed to compensate physical injuries”).

²⁵ See Lewis, *The American Democratic Deficit*, *supra* note 8.

to IVF. With respect to the food and drug law literature, this Article examines the role that the FDA has taken in the regulation of gene modifying ARTs, before explaining why the FDA should not regulate gene modifying ARTs. As to the broader health law field, this Article analyzes the regulatory treatment of a controversial medical technique.

This Article recommends a regime for regulating germline gene editing that embodies values that are beneficial to researchers, the public, and governmental bodies. Science often outpaces the law, but in the time required for germline gene editing to be commercially ready, there is adequate time to improve the regulatory regime to actually accommodate that form of gene editing.²⁶ This would differ from the regulatory treatment of other techniques such as ART, for which the law has lagged behind science.

Part II of this Article provides background on traditional ART and innovative genetic technologies and ARTs before providing an overview of the American regulatory system that currently applies to gene editing and traditional ART. Part III explores bioethical debates that have arisen in the context of the technologies discussed in Part II, in addition to providing an overview of bioethical debates that are unique to germline gene editing technologies, in support of the argument that those morality-based objections are insufficient to support the federal treatment of germline gene editing. Part IV advocates for a regulatory treatment of germline gene editing technologies that is similar to that of traditional ART, namely IVF, by drawing on the regulatory and scientific challenges that accompany techniques involving genetic modification and ART.

²⁶ See *infra* Section II.B. (discussing self-regulation in the medical profession); see also NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES 31 (2018) [hereinafter NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES]; Lyria Bennett Moses, *Understanding Legal Responses to Technological Change: The Example of In Vitro Fertilization*, 6 MINN. J.L. SCI. & TECH. 505, 515–17 (2005); Anna Funk, *Human Gene Editing is Controversial. Shoukhrat Mitalipov Isn't Deterred*, DISCOVER MAG., (April 15, 2019), <http://discovermagazine.com/2019/may/repairing-the-future> (“Mitalipov estimates the gene editing technology [for use on embryos] won’t be ready for clinical trials—meaning tests in real pregnancies—for another five to 10 years.”); Rob Stein, *First U.S. Patients Treated With CRISPR As Human Gene-Editing Trials Get Underway*, NPR (Apr. 16, 2019, 11:01 AM), <https://www.npr.org/sections/health-shots/2019/04/16/712402435/first-u-s-patients-treated-with-crispr-as-gene-editing-human-trials-get-underway> (“[I]t will be many years before any CRISPR treatment could become widely available.”).

II. EMERGING TECHNOLOGIES IN GENE EDITING AND “TRADITIONAL” ART

As evidenced by the number of Nobel Prizes awarded concerning genetic innovation and the sums generated by patents on DNA-related technology, genetic advances are significant.²⁷ Germline gene editing, which would occur before a child is born and result in heritable changes, requires the use of ART, namely IVF, which is legal in the United States.²⁸ ART, unlike gene editing, is not subject to patent restrictions.²⁹

This Part provides relevant scientific and legal background, including the history of the regulation of traditional ART and the FDA’s unexpected assertions of jurisdiction over techniques involving the combination of ART and genetic modification. In prior works, I have outlined the FDA’s gradual assertion of jurisdiction over techniques that combine ART and genetic modification (what I have referred to as “AARTs”) and germline genetic modification before arguing that these techniques, involving genetic modification like cytoplasmic and mitochondrial transfer, should be treated similarly to IVF, which falls within state-regulated practice of medicine, as opposed to within the federal regulation of medical products.³⁰ This Article takes a similar position related to germline gene editing.

²⁷ See, e.g., 1972: *First Recombinant DNA*, NAT’L INSTS. OF HEALTH, NAT’L HUM. GENOME RES. INST. (Apr. 26, 2013), <https://www.genome.gov/25520302/online-education-kit-1972-first-recombinant-dna>; *The Birth of Biotech*, MIT TECH. REV. (July 1, 2000), <https://www.technologyreview.com/s/400767/the-birth-of-biotech/>; *The Nobel Prize in Chemistry 1980*, NOBEL PRIZE, <https://www.nobelprize.org/prizes/chemistry/1980/summary> (last visited May 4, 2019); *The Nobel Prize in Physiology or Medicine 1962*, NOBEL PRIZE, <https://www.nobelprize.org/prizes/medicine/1962/summary> (last visited May 4, 2019).

²⁸ See, e.g., Eli Adashi & I. Glenn Cohen, *Heritable Genome Editing: Edited Eggs and Sperm to the Rescue?*, 322 JAMA (2019); *Heritable Genome Editing: Action Needed To Secure Responsible Way Forward*, NUFFIELD COUNCIL ON BIOETHICS (July 17, 2018), <http://nuffieldbioethics.org/news/2018/heritable-genome-editing-action-needed-secure-responsible>; Yanting Zeng et al., *Correction of the Marfan Syndrome Pathogenic FBN1 Mutation by Base Editing in Human Cells and Heterozygous Embryos*, 26 MOLECULAR THERAPY 2631, 2631 (2018), <https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016%2818%2930378-2#%20> (discussing the potential combination of gene editing and PGD).

²⁹ See, e.g., Jon Cohen, *CRISPR Patent Fight Revived*, 365 SCI. 15–16 (July 5, 2019), <https://science.sciencemag.org/content/365/6448/15.2/tab-pdf>.

³⁰ See discussion *infra* Section II.B.

A. *Scientific Background*

1. Genes

There are a number of terms related to genetics, ART, and the regulation of medical products that are important for discussing the regulatory treatment of gene editing. As a foundational matter, genes are the source of hereditary traits in humans and other living organisms.³¹ Genes are a part of the human genome.³² Within the human genome, 23 pairs of chromosomes contain “approximately 22,000 genes.”³³ Each of these approximately 22,000 genes is “encoded as DNA” contained in the nucleus of the cell.³⁴ But genes are not static. The term “mutation” refers to a change in the genetic sequence.³⁵ While “[s]ome mutations are harmless . . . others can cause disease or increase the risk of disease. As a result, the study of genetics can lead to valuable medical breakthroughs.”³⁶

³¹ *Assoc. for Molecular Pathology v. Myriad Genetics*, 569 U.S. 576, 580 (2013).

³² NUFFIELD COUNCIL ON BIOETHICS, *GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES*, *supra* note 26, at 7 (noting that the “genome is the complete set of genes”); *see also* Greely, *supra* note 6, at 115 (explaining why the author uses the term “genome editing” instead of “gene editing”);

³³ *Myriad*, 569 U.S. at 580. *But see* Human Genome Project Information Archive 1990–2003, *About the Human Genome Project* (Mar. 26, 2019), https://web.ornl.gov/sci/techresources/Human_Genome/project/index.shtml (noting that there are “approximately 20,000-25,000 genes in human DNA”). *See also* Cassandra Willyard, *New Human Gene Tally Reignites Debate*, *NATURE* (Jun. 19, 2018), <https://www.nature.com/articles/d41586-018-05462-w>.

³⁴ *Myriad*, 569 U.S. at 580; John A. Robertson, *Procreative Liberty in the Era of Genomics*, 29 *AM. J.L. & MED.* 439, 439 (2003). *See generally* J.D. Watson & F.H.C. Crick, *Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid*, 171 *NATURE* 737 (1953).

³⁵ *Myriad*, 569 U.S. at 582.

³⁶ *Id.* *See also* *Genetic Disorders*, MEDLINEPLUS, U.S. NAT’L LIBR. OF MED. (Apr. 17, 2018), <https://medlineplus.gov/geneticdisorders.html>.

You can inherit a gene mutation from one or both parents. A mutation can also happen during your lifetime. There are three types of genetic disorders:

- Single-gene disorders, where a mutation affects one gene [like] sickle cell anemia . . .
- Chromosomal disorders, [like Down syndrome] where chromosomes (or parts of chromosomes) are missing or changed. Chromosomes are the structures that hold our genes . . .
- Complex disorders, [like colon cancer] where there are mutations in two or more genes. Often your lifestyle and environment also play a role.

Id.

2. Somatic Gene Therapy

In recent years, media coverage has frequently addressed germline gene editing and gene therapy.³⁷ Genetic engineering has existed since 1972 when researchers published articles in the *Proceedings of the National Academies of Sciences* on their use of recombinant DNA technology.³⁸ The first human clinical trials involving gene therapy took place in 1990.³⁹ Germline gene editing of embryos implicates reproductive cells such as egg or sperm as opposed to somatic cells, the other types of cells in the body.⁴⁰ While it is expected that somatic cell gene therapy only changes an individual patient's genes (and is therefore not heritable), genome editing introduces heritable genetic modifications.⁴¹ Gene therapy, or gene transfer, which only affects an individual's somatic cells, does not engender the same opposition as germline gene editing.⁴²

³⁷ See *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 3.

³⁸ There were a number of publications related to recombinant DNA in 1972 and 1973. See Russell Spivak et al., *Germ-line Gene Editing and Congressional Reaction in Context: Learning from Almost 50 Years of Congressional Reactions to Biomedical Breakthroughs*, 30 J.L. & HEALTH 20, 23 n.9 and accompanying text (2017). For more on recombinant DNA technologies, see Stanley Cohen et al., *Construction of Biologically Functional Bacterial Plasmids In Vitro (R factor/restriction enzyme/transformation/endonuclease/antibiotic resistance)*, 70 PROC. NAT'L ACAD. OF SCI. 3240, 3244 (1973), <https://www.pnas.org/content/pnas/70/11/3240.full.pdf>; Eileen M. Kane, *Human Genome Editing: An Evolving Regulatory Climate*, 57 JURIMETRICS J. 301, 301-02 (2017); Jennifer Khan, *The CRISPR Quandary*, N.Y. TIMES MAG. (Nov. 9, 2015), <https://www.nytimes.com/2015/11/15/magazine/the-crispr-quandary.html>; *1972: First Recombinant DNA*, NAT'L INSTS. OF HEALTH (Apr. 26, 2013), <https://www.genome.gov/25520302/online-education-kit-1972-first-recombinant-dna>.

³⁹ *How Does Gene Therapy Work?*, SCI. AM. (May 13, 2008), <https://www.scientificamerican.com/article/experts-gene-therapy>; see also *How Does Gene Therapy Work?*, MEDLINEPLUS, U.S. NAT'L LIBR. OF MED. (Apr. 30, 2019), <https://ghr.nlm.nih.gov/primer/therapy/procedures>.

⁴⁰ *Somatic Cells*, NAT'L HUM. GENOME RES. INST., <https://www.genome.gov/genetics-glossary/Somatic-Cells> (last visited June 3, 2019).

⁴¹ See Katrine S. Bosley et al., *CRISPR Germline Engineering—The Community Speaks*, 33 NATURE BIOTECHNOLOGY 478, 485 (2015).

⁴² *Id.*; see also Marcy Darnovsky & Katie Hasson, *CRISPR's Twisted Tales: clarifying misconceptions about heritable genome editing*, 63 PERSPS. IN BIO. & MED. 155, 158 (2020); Sarah Polcz & Anna Lewis, *CRISPR-CAS9 and the Non-Germline Non-Controversy*, 3 J.L. & BIOSCIENCES 413, 413-14 (2016); Nicholas Wade, *Scientists Seek Ban on Method of Editing the Human Genome*, N.Y. TIMES (Mar. 20, 2015), <https://www.nytimes.com/2015/03/20/science/biologists-call-for-halt-to-gene-editing-technique-in-humans.html>.

3. Germline Gene Editing

Germline gene editing technology like CRISPR-Cas9 modifies DNA contained in the nucleus of the cell (“nuclear DNA”) as opposed to DNA outside of the nucleus such as mitochondrial DNA, which has been the target of other forms of ART that arguably do not implicate the human germline.⁴³ As noted in the Introduction, germline gene editing offers the ability to prevent a future child from contracting a disease altogether by removing the genetic mutation that would result in disease.⁴⁴ Germline gene editing could also reduce the likelihood that individuals will be affected by diseases with genetic risk factors, such as breast cancer.⁴⁵ The definition of the term “germline” is disputed: some think that it incorporates only changes to nuclear DNA, while others argue that it includes changes to non-nuclear DNA, such as mitochondrial

⁴³ See *What is DNA?*, NAT’L INSTS. OF HEALTH, U.S. NAT’L LIBR. OF MED., <https://ghr.nlm.nih.gov/primer/basics/dna> (“DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms. Nearly every cell in a person’s body has the same DNA. Most DNA is . . . nuclear DNA[], but a small amount of DNA can also be found in the mitochondria . . .”) (last visited Oct. 18, 2020). Compare Lucía Gómez-Tatay, José M. Hernández-Andreu & Justo Aznar, *Mitochondrial Modification Techniques and Ethical Issues*, 6 J. CLINICAL MED. 1, 3 (2017) (noting that gene editing could be adapted to act on mitochondrial DNA, but “to prevent the transgenerational transmission of mitochondrial diseases, it needs to act on the germline[,]” and that the technology does not yet work well with mitochondrial DNA), with Rosamund Scott & Stephen Wilkinson, *Germline Genetic Modification and Identity: the Mitochondrial and Nuclear Genomes*, 37 OXFORD J. LEGAL STUD. 886, 887 (2017) (stating that, in 2016, the US Institute of Medicine “held that [Mitochondrial Replacement Therapy] . . . constitute[s] genetic modification and that, since mitochondria are maternally inherited, . . . [it] amount[s] to germline modification if female offspring are born”). For more information on the many uses and advances in CRISPR, see Sharon Begley, *CRISPR Advances Are Coming Fast. Here’s Your Guide*, STAT PLUS, <https://www.statnews.com/feature/crispr/tracker>. For a brief history of the development of CRISPR, including competing claims as to who first created the technology, see Greely, *supra* note 6, at 2326–29. For more on the disputes related to the meaning of the term “germline,” see David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCI. 36, 37 (2015).

⁴⁴ See *supra* Part I.

⁴⁵ See GERMAN ETHICS COUNCIL, INTERVENING IN THE HUMAN GERMLINE: OPINION: EXECUTIVE SUMMARY & RECOMMENDATIONS 12 (Aileen Sharpe trans., 2019), <https://www.ethikrat.org/fileadmin/Publikationen/Stellungnahmen/englisch/opinion-intervening-in-the-human-germline-summary.pdf> (“The correction of a germline mutation in the Breast Cancer 1 (BRCA1) gene could, for example, reduce the breast cancer risk of a woman affected by this form of familial breast cancer from about 75 percent to the level of the general female population of about 12 percent.”). But see Sharon Begley, *You Had Questions for David Liu About CRISPR, Prime Editing, and Advice to Young Scientists. He Has Answers*, STAT NEWS (Nov. 6, 2019), <https://www.statnews.com/2019/11/06/questions-david-liu-crispr-prime-editing-answers> (“BRCA1 and BRCA2 variants that predispose individuals to cancer, and many other genetic variants like these, could in principle be addressed by genetic therapies. However, there are a number of challenges associated with using gene editing for this purpose.”).

DNA.⁴⁶ In this Article, the term germline genetic modification refers to the use of technology that modifies nuclear DNA.

While human gene therapy has been possible since 1980, gene editing technology has existed since at least 2003.⁴⁷ Gene editing technology allows genes to be “deleted, inserted or replaced by a different piece of DNA.”⁴⁸ The gene editing technology, CRISPR-Cas9, which is the focus of most gene editing-related media coverage, first appeared in scientific literature in 2012.⁴⁹

Germline gene editing, like many innovations (including somatic gene therapy), is accompanied by safety concerns.⁵⁰ These concerns include those related to mosaicism and off-target effects.⁵¹ Mosaicism exists when an organism includes both edited and unedited cells; this is significant because the goal of gene editing is to edit all of the cells such that the genetic modification is uniform.⁵² “Off-target effects” are also

⁴⁶ Ainsley J. Newson & Anthony Wrigley, *Is Mitochondrial Donation Germ-Line Gene Therapy? Classifications and Ethical Implications*, 31 *BIOETHICS* 55, 57–58 (2017).

⁴⁷ Kane, *supra* note 38, at 303, 307.

⁴⁸ See *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 3 (citing Andrew Pollack, *A Powerful New Way to Edit DNA*, *N.Y. TIMES* (Mar. 3, 2014), <https://www.nytimes.com/2014/03/04/health/a-powerful-new-way-to-edit-dna.html>).

⁴⁹ See George Q. Daley et al., *After the Storm—A Responsible Path for Genome Editing*, 380 *NEW ENG. J. MED.* 897, 897 (2019). For an explanation of how the CRISPR-Cas9 technology operates, see Andrew Pollack, *A Powerful New Way to Edit DNA*, *N.Y. TIMES* (Mar. 3, 2014), <https://www.nytimes.com/2014/03/04/health/a-powerful-new-way-to-edit-dna.html?searchResultPosition=16>. CRISPR-Cas9 is a gene editing method; it is not, however, the only method of editing genes. See, e.g., *What Are Genome Editing and CRISPR-Cas9?*, NAT'L INSTS. OF HEALTH, U.S. NAT'L LIBR. OF MED., <https://ghr.nlm.nih.gov/primer/genomeresearch/genomeediting> (last visited Oct. 18, 2020).

Several approaches to genome editing have been developed. A recent one is known as CRISPR-Cas9, which is short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9. The CRISPR-Cas9 system has generated a lot of excitement in the scientific community because it is faster, cheaper, more accurate, and more efficient than other existing genome editing methods.

Id.

⁵⁰ See, e.g., Francoise Baylis, *Human Germline Genome Editing and Broad Societal Consensus*, 1 *NATURE HUM. BEHAVIOR* 1, 1 (2017); NAT'L ACAD. SCIS., ENG., & MED., *HUMAN GENOME EDITING* 237, 302 (2017) [hereinafter NAT'L ACADS. SCIS., ENG'G & MED., *HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE*].

⁵¹ See, e.g., Baylis, *supra* note 50, at 1; NAT'L ACADS. SCIS., ENG'G & MED., *HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE*, *supra* note 50, at 116.

⁵² See Hong Ma et al., *Correction of a Pathogenic Gene Mutation in Human Embryos*, 548 *NATURE* 413, 415 (2017) (discussing efforts to avoid mosaicism in embryos); see also Bosley et al., *supra* note 41, at 480 (statement of Dr. Jennifer Doudna) (“[I]f the ‘edited’ individual is chimeric for the intended correction, they may still have diseased cells in critical tissues.”). For more information on mosaicism, see NAT'L ACAD. OF SCIS., *HERITABLE*

referred to as “unintended consequences.”⁵³ It is possible that the gene editing will not do exactly what the editor intended, as seen with twins who were born as a result of an experiment by Dr. He Jiankui, a now-disgraced Chinese scientist who announced the birth of the first “CRISPR babies”; neither of the twins born after the germline gene editing had the exact modified gene that the doctor intended.⁵⁴ According to Dr. He, the first CRISPR babies, who were edited to prevent HIV transmission, suffered from mosaicism, with one baby having cells that were both edited and unedited.⁵⁵ Additionally, the gene that Dr. He Jiankui targeted did not necessarily confer automatic protection against HIV-1.⁵⁶ Further, the targeted mutation, CCR5, corresponds to increased susceptibility to West Nile virus, influenza, enhanced memory, and possibly a shortened life span.⁵⁷ Other research indicates that the CCR5 gene could be connected to improved stroke recovery outcomes.⁵⁸

Many articles related to gene editing also focus on off-target effects.⁵⁹ Off-target effects occur when scientists target one gene for editing and inadvertently impact other non-targeted genes.⁶⁰ Over time, scientists have minimized the off-target effects of gene editing, but off-target effects remain a cause for concern among both scientists and ethicists.⁶¹

HUMAN GENOME EDITING 68–69 (2020) [hereinafter NAT’L ACADS. SCIS., HERITABLE HUMAN GENOME EDITING].

⁵³ NAT’L ACADS. SCI., ENG’G & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE, *supra* note 50, at 122; *see also* NAT’L ACADS. SCIS., HERITABLE HUMAN GENOME EDITING, *supra* note 52, at 67–68.

⁵⁴ *See* Henry T. Greely, *He Jiankui, Embryo Editing, CCR5, The London Patient, and Jumping to Conclusions*, STAT NEWS (Apr. 15, 2019), <https://www.statnews.com/2019/04/15/jiankui-embryo-editing-ccr5>.

⁵⁵ *See* Gina Kolata & Pam Belluck, *Why Are Scientists So Upset About the First Crispr Babies?*, N.Y. TIMES (Dec. 5, 2018), <https://www.nytimes.com/2018/12/05/health/crispr-gene-editing-embryos.html>.

⁵⁶ *See id.*

⁵⁷ *See* Darnovsky & Hasson, *supra* note 42, at 156; Sara Reardon, *Gene Edits to ‘CRISPR babies’ Might Have Shortened Their Life Expectancy*, NATURE (June 4, 2019), <https://www.nature.com/articles/d41586-019-01739-w>.

⁵⁸ *See* Greely, *supra* note 6, at 159–60 (discussing the connection between CCR5 and stroke recovery and noting that “[t]he evidence of benefit in stroke recovery, if any, applies only to Nana,” who is one of the so-called CRISPR babies).

⁵⁹ *See, e.g.*, Ma et. al, *supra* note 52, at 416.

⁶⁰ *Id.*

⁶¹ *See, e.g.*, Letter from Burt Adelman, M.D., Special Advisor, Novo Ventures, et al. to Alex Azar II, Secretary, U.S. Dep’t of Health & Human Services (Apr. 24, 2019), <https://www.asgct.org/global/documents/clinical-germline-gene-editing-letter.aspx> (calling for a moratorium on germline gene editing but not somatic gene editing). *But see* Yanting Zeng et al., *Correction of the Marfan Syndrome Pathogenic FBN1 Mutation by Base Editing in Human Cells and Heterozygous Embryos*, 26 MOLECULAR THERAPY 2631,

When considering the risks and benefits of germline gene editing as opposed to other treatment options, there are a limited number of diseases that germline gene editing would address better than other methods of treatment.⁶² Nevertheless, germline and somatic gene editing offer the possibility of great medical promise.⁶³

4. Assisted Reproductive Technology

ART has incited religious, ethical, and political controversy since 1978 when the first baby was born as a result of IVF.⁶⁴ Controversy has also accompanied other forms of ART and medical screening techniques related to reproduction, including the use of preimplantation genetic diagnosis (“PGD”), amniocentesis, and sperm banks.⁶⁵ Most recently, mitochondrial transfer, a form of ART involving genetic modification to prevent maternal mitochondrial disease transmission, has similarly led to intense debate and opposition, with clinical trials going forward in the United Kingdom but not in the United States.⁶⁶ ART safety concerns include those related to the drugs used to stimulate egg production; continued correlations between ART and adverse maternal-fetal outcomes; and some often-dismissed concerns about ART’s long-term effects.⁶⁷

Germline gene editing could improve the efficacy of traditional ART.⁶⁸ For example, PGD is used in combination with forms of ART such as IVF.⁶⁹ PGD can screen embryos created using IVF for genetic

2631, 2634 (2018) (discussing the results of an experiment in which base editing was used to eliminate off-target effects).

⁶² *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 64 (providing the answers to post-hearing questions of Dr. Elizabeth McNally, which observed that “[t]echnology and its medical application are judged based on the risk-benefit ratio”).

⁶³ *See supra* Part I.

⁶⁴ In IVF, an egg is fertilized by sperm in a laboratory. Adam Eley, *How Has IVF Developed Since the First ‘Test-tube Baby’?*, BBC NEWS (Jul. 23, 2015), <https://www.bbc.com/news/health-33599353>; *see also* June Carbone & Jody Lyneé Madeira, *Buyers in the Baby Market: Toward a Transparent Consumerism*, 91 WASH. L. REV. 71, 102 (2016); Moses, *supra* note 26, at 522–26, 536–45.

⁶⁵ R. Alta Charo, *Who’s Afraid of the Big Bad (Germline Editing) Wolf?*, 63 PERSPS. IN BIOLOGY & MED. 93, 93 (2020).

⁶⁶ *See Lewis, The American Democratic Deficit*, *supra* note 8, at 146–49 (discussing debate and opposition to mitochondrial transfer).

⁶⁷ *See infra* note 391 and accompanying text; *see also* Martha Field, *Compensated Surrogacy*, 89 WASH. L. REV. 1155, 1159 (2014).

⁶⁸ NAT’L ACADS. SCIS., HERITABLE HUMAN GENOME EDITING, *supra* note 52, at 120.

⁶⁹ *See, e.g.*, Jeani Chang et al., *Outcomes of In Vitro Fertilization with Preimplantation Genetic Diagnosis: An Analysis of the United States Assisted Reproductive Technology Surveillance Data, 2011–2012*, 105 FERTIL. & STERIL. 394 (2016); NUFFIELD COUNCIL ON

abnormalities, with the goal of allowing individuals to select embryos that do not contain those abnormalities.⁷⁰ PGD cannot address all genetic abnormalities or diseases but can detect “single- gene defects or chromosomal abnormalities” such as Down Syndrome or Tay-Sachs.⁷¹ PGD can also be used for sex selection and to affirmatively select for certain traits, such as a genetic match for a sibling in need of a tissue transplant.⁷² Embryos that meet the requested constraints are then implanted for pregnancy.⁷³ In certain instances, PGD reveals that “[m]any embryos are unsuitable for transfer because they are affected by . . . genetic disease or are of poor quality.”⁷⁴ This concern is exacerbated when there are fewer embryos to choose from due to limitations like compromised fertility.⁷⁵

It is expected that there are very limited circumstances in which germline gene editing is the only option; however, parents still might prefer germline gene editing to PGD for the potential positive health outcomes of their future children.⁷⁶ Combining germline gene editing with PGD “could rescue otherwise viable embryos that were carrying the abnormal allele and theoretically double the probability of the birth

BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 1. PGD is also referred to as “preimplantation genetic testing.” Chang et al., *supra* note 69, at 394–95.

⁷⁰ See Jaime S. King, *Predicting Probability: Regulating the Future of Preimplantation Genetic Screening*, 8 YALE J. HEALTH POL’Y, L. & ETHICS, 283, 285 (2008); *Preimplantation Genetic Diagnosis: PGD*, AMER. PREGNANCY ASSOC., <https://americanpregnancy.org/infertility/preimplantation-genetic-diagnosis> (last visited Jul. 27, 2019). PGD is also used to create children with certain genetic characteristics so that they can be “matches” for older siblings. These children are sometimes referred to as savior siblings. See, e.g., Susannah Baruch, *Preimplantation Genetic Diagnosis and Parental Preferences: Beyond Deadly Disease*, 8 HOUS. J. HEALTH L. & POL’Y 245, 256 (2008); Ferris Jabr, *Are We Too Close to Making Gattaca a Reality?*, SCI. AM.: BRAINWAVES (Oct. 28, 2013), <https://blogs.scientificamerican.com/brainwaves/are-we-too-close-to-making-gattaca-a-reality>.

⁷¹ *PGD Q&A*, CTR. FOR ADVANCED REPRODUCTIVE SERV., <https://www.uconnfertility.com/specialized-programs/pre-implant-genetic-diagnosis-program/pgd-qa> (last visited Sept. 14, 2020); see also *PGD Detected Diseases*, CTR. FOR ADVANCED REPRODUCTIVE SERV., <https://www.uconnfertility.com/specialized-programs/pre-implant-genetic-diagnosis-program/pgd-detected-diseases> (last visited Sept. 14, 2020).

⁷² See *supra* note 71. See also S. Sheldon & S. Wilkinson, *Should Selecting Saviour Siblings Be Banned?*, 30 J. MED. ETHICS 533, 533 (2004).

⁷³ Sheldon & Wilkinson, *supra* note 72, at 533.

⁷⁴ Daley et al., *supra* note 49, at 899.

⁷⁵ *Id.*; see also Eli Y. Adashi & I. Glenn Cohen, *The Case for Remedial Germline Editing—The Long-term View*, 323 J. MED. ETHICS 1762, 1762–63 (2020) (discussing the limitations of PGD as compared to germline gene editing).

⁷⁶ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 115, 120.

of the healthy baby.”⁷⁷ Thus, ART’s effectiveness could improve due to a higher probability that embryos that would usually be discarded in traditional ART could instead result in a healthy pregnancy and childbirth. Combining gene editing with PGD could also create “savior siblings” for families seeking tissue matches for existing children who need stem cell transplants, a use that some would likely consider controversial.⁷⁸ Yet scholars have also noted that, in some instances, germline gene editing and PGD will be mutually exclusive.⁷⁹ Nevertheless, from both practical and bioethical perspectives, for those who are opposed to ART based on the destruction of embryos (or its contribution to the number of leftover embryos), combining PGD with germline gene editing or using germline gene editing alone might eventually reduce the number of discarded embryos in ART, although further innovation will destroy embryos in the research process.⁸⁰

⁷⁷ Daley et al., *supra* note 49, at 899.

⁷⁸ See Andrew Joseph, *Could Editing the DNA of Embryos with CRISPR Help Save People Who Are Already Alive?*, STAT NEWS (Sept. 16, 2019), <https://www.statnews.com/2019/09/16/could-editing-the-dna-of-embryos-with-crispr-help-save-people-who-are-already-alive>.

⁷⁹ See Adashi & Cohen, *supra* note 75, at 1763.

The [two international] panels [considering remedial germline editing (RGE)] would do well to recognize the potential substantial advantages of RGE over PGD, and that the 2 techniques are mutually exclusive. They cannot be sequentially applied to maximize the number of transferable embryos because RGE is applied at the time of fertilization and it is ill-suited to correct genetic defects identified by PGD in day 5 blastocysts. Given PGD’s unavoidable limitations, future efforts at curtailing heritable monogenic disorders would do well to prioritize safe and effective RGE.

Id.

⁸⁰ See Sharon Begley, *U.S. Scientists Edit Genome of Human Embryo, But Cast Doubt on Possibility of ‘Designer Babies’*, STAT NEWS (Aug. 2, 2017), <https://www.statnews.com/2017/08/02/crispr-designer-babies/>; Pam Belluck, *In Breakthrough, Scientists Edit a Dangerous Mutation from Genes in Human Embryos*, N.Y. TIMES (Aug. 2, 2017), <https://www.nytimes.com/2017/08/02/science/gene-editing-human-embryos.html>. But see Giulia Cavaliere, *Background Paper: The Ethics of Human Genome Editing*, WHO EXPERT ADVISORY COMM. ON DEVELOPING GLOBAL STANDARDS FOR GOVERNANCE AND OVERSIGHT OF HUMAN GENOME EDITING 5, <https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Ethics-paper-March19.pdf> (noting that germline gene-editing research involves the destruction of human embryos). For more information on the controversy that accompanies research on human embryos, see NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 80–81.

B. Legal Background

Subjecting germline gene editing in the U.S. to administrative hurdles is part of a longstanding federal regulatory hostility to gene modifying techniques in the United States. Despite the practice-products divide in which the federal government regulates medical products and states regulate the practice of medicine, there is little federal regulation of traditional ART, and most regulation comes from states.⁸¹ Most commentators characterize traditional ART as “minimally regulated,” “unregulated,” or non-uniformly regulated.⁸² This characterization stems from the general inapplicability of federal statutes to traditional ART, with most regulation coming from state regulation of the practice of medicine, although a few federal regulations do apply to laboratory conditions.⁸³ States have also responded to

⁸¹ For more on the practice-products distinction, which corresponds to state jurisdiction over the practice of medicine through mechanisms such as the licensing of health professionals and state tort law regimes and federal jurisdiction over the pre-marketing approval of products, such as drugs, devices, and biologics, see Barbara J. Evans, *Distinguishing Product and Practice Regulation in Personalized Medicine*, 81 *CLINICAL PHARMACOLOGY & THERAPEUTICS* 288, 288 (2007); Patricia J. Zettler, *Pharmaceutical Federalism*, 92 *IND. L.J.* 845, 892 (2017); Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 *SAN DIEGO L. REV.* 427, 434–54, 460–64 (2015). For more on the practice-products divide in the regulation of innovative therapies including gene editing and gene therapy, see Myrisha S. Lewis, *Innovating Federalism in the Life Sciences*, 92 *TEMPLE L. REV.* 383, 402–10 (2020).

⁸² See Lewis, *How Subterranean*, *supra* note 8 at 1241 n.1, 1251–53 (providing a summary of prevailing views on the regulation of traditional ART).

⁸³ Federal regulations do apply to ART and PGD; however, those regulations tend to focus on compliance-related issues such as “donor material safety, transparency, and reporting requirements, as is the case with IVF, or on quality control of the laboratories (though not necessarily the actual diagnostics) used for PGD” as opposed to restricting access to the techniques or the method of technique used. NAT’L ACADS. SCI., ENG’G & MED., *HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE*, *supra* note 50, at 131. For examples of federal regulation that applies to ART, see 42 U.S.C. § 264 (2012); 21 C.F.R. § 1271.3(d) (2016); U.S. FOOD & DRUG ADMIN., *ELIGIBILITY DETERMINATION FOR DONORS OF HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS* (2007); Final Rule and Notice, 69 Fed. Reg. 29,786, 29,787 (May 25, 2004); Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447 (Jan. 19, 2001). But see Seema Mohapatra, *Global Legal Responses to Prenatal Identification and Sex Selection*, 13 *NEV. L.J.* 690, 701 (2013) (discussing the FDA’s jurisdiction over MicroSort, a sperm-sorting device that was in the process of obtaining FDA approval until 2011 when “the FDA informed [the Genetics and IVF institute where clinical trials related to MicroSort were occurring] that it would no longer be allowed to enroll any more families in the FDA clinical trial for family-balancing purposes”). Medical devices are also regulated by the FDA. See, e.g., U.S. FOOD AND DRUG ADMIN., *OVERVIEW OF DEVICE REGULATION* (2020), <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation>. Medical devices are not discussed in this Article as the FDA treats somatic and germline gene editing as drugs and/or biologics, not devices.

certain technologies that could lead to the creation of children, namely by enacting statutes banning human cloning.⁸⁴

In previous articles, I have noted that this characterization of ART as “minimally regulated” or “unregulated” is accurate only insofar as it relates to traditional ART, which is ART not involving genetic modification. ART involving genetic modification is unexpectedly subject to the federal government’s burdensome regime that applies to regulated products.⁸⁵ This Article is part of that thread of scholarship and explores another form of genetic modification in ART, namely, the combination of IVF with genome modification, over which the FDA surprisingly declared jurisdiction, as discussed below.⁸⁶ Like my other articles, this Article, when deciding between two potential regulators for forms of ART involving genetic modification, selects states (and their accompanying hands-off regime) over the federal government.⁸⁷ That selection stems not only from a jurisdictional objection to treating a medical technique like a drug but also from a normative perspective about which regulator is the most transparent and may further parental autonomy and innovation in a way that will lead to a diversity of outcomes.⁸⁸ In other words, the regulation of germline gene editing would be better carried out by physicians (who are regulated by states) than the federal government.

Most of the commentary related to the regulation of germline gene editing has focused on the relevance of moratoria and guidelines in the applicable scientific community, as well as the role of the FDA in the regulation of somatic and germline gene editing in the United States.⁸⁹ This FDA-centric view is surprising because states have jurisdiction over the practice of medicine, and the federal government has jurisdiction over the tools used in the practice of medicine, such as

⁸⁴ The Article differentiates cloning technology from reproductive technology because cloning involves copying one individual as opposed to reproduction which focuses on two individuals. For more on state statutes banning reproductive cloning, see Judith F. Daar, *The Prospect of Human Cloning: Improving Nature or Dooming the Species?*, 33 SETON HALL L. REV. 511, 515 (2003); Charles Thomas, *Novel Assisted Reproductive Technologies and Procreative Liberty: Examining in Vitro Gametogenesis Relative to Currently Practiced Assisted Reproductive Procedures and Reproductive Cloning*, 26 S. CAL. INTERDISC. L.J. 623, 636 n.98 (2017).

⁸⁵ See *infra* pp. 760–61.

⁸⁶ See *Id.*

⁸⁷ See *Id.*

⁸⁸ See Lewis, *The American Democratic Deficit*, *supra* note 8, at 157–63

⁸⁹ See, e.g., Eric S. Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, 567 NATURE 165, 165 (2019); Carrie D. Wolinetz & Francis S. Collins, *NIH Supports Call for Moratorium on Clinical Uses of Germline Gene Editing*, NATURE (Mar. 13, 2019), <https://www.nature.com/articles/d41586-019-00814-6>.

medical devices and fertility drugs.⁹⁰ Thus, for the regulation of traditional ART, the only federal statute specifically enacted to address ART is the Fertility Clinic Success Rate Act, which implements a reporting regime administered by the Centers for Disease Control (not the FDA) but lacks an enforcement mechanism.⁹¹

The FDA has proclaimed jurisdiction over somatic and germline gene editing, even though the practice of medicine does not fall within federal jurisdiction.⁹² As a practical matter, this means that the FDA does not approve surgical techniques or traditional ART techniques like IVF, for example.⁹³ While courts resolved the FDA's questioned jurisdiction over innovative new therapies, such as regenerative medicine techniques and stem cell treatments, in the FDA's favor, the FDA's asserted jurisdiction over reproductive techniques involving genetic modification has yet to be litigated.⁹⁴

Medicine, innovation, and reproduction are all accompanied by risk. The FDA does not punish physicians for medical malpractice, as state tort law provides remedies for harms incurred as a result of medical treatment (medical malpractice), and states license physicians through licensing regimes.⁹⁵ Thus, those harmed by gene editing could

⁹⁰ See *supra* note 81 (discussing the practice-products divide between the state-regulated practice of medicine and federally-regulated medical products).

⁹¹ See 42 U.S.C. §§ 263a-1-7 (2012) (codifying the Fertility Clinic Success Rate Act).

⁹² *Information About Self-Administration of Gene Therapy*, U.S. FOOD & DRUG ADMIN. (Nov. 21, 2017), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy> ("FDA considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy. . . . Clinical studies of gene therapy in humans require the submission of an investigational new drug application (IND) prior to their initiation in the United States, and marketing of a gene therapy product requires submission and approval of a biologics license application (BLA)."); see also Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 15 (noting "Congress[s] repeated[] . . . assurances that the FDA's authority to license therapeutic products would not interfere with the practice of medicine"); *The FDA's New Policy Steps and Enforcement Efforts To Ensure Proper Oversight of Stem Cell Therapies and Regenerative Medicine*, U.S. FOOD & DRUG ADMIN., (Aug. 28, 2017) (Statement from FDA Commissioner Scott Gottlieb, M.D.), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573443.htm> (noting the "close calls" between state and federal jurisdiction posed by new treatments and medical fields)

⁹³ See, e.g., Nancy M.P. King, *The Line Between Clinical Innovation and Human Experimentation*, 32 SETON HALL L. REV. 573, 575 (2002).

⁹⁴ See, e.g., *United States v. Regenerative Scis.*, 741 F.3d 1314, 1317–21 (D.C. Cir. 2014); *United States v. US Stem Cell Clinic*, 403 F. Supp. 3d 1279, 1285–1301 (S.D. Fla. 2019).

⁹⁵ See, e.g., BARRY R. FURROW ET AL., *HEALTH LAW: CASES, MATERIALS, AND PROBLEMS* 87 (7th ed. 2013); Lori B. Andrews, *The Shadow Health Care System: Regulation of Alternative*

avail themselves of remedies under state tort law like other patients.⁹⁶ While this ex post approach does not prevent risk, risk-free medicine and innovation are not required in other areas (and cannot co-exist with these areas), including ART and PGD.⁹⁷ Even though germline gene editing could lead to intergenerational risk, as germline gene editing would affect a future child and that future child's children, the regulatory system has addressed transgenerational harms before, such as in the case of the multigenerational harms of diethylstilbestrol (DES) exposure.⁹⁸ Some state statutes focus on the availability of insurance coverage for ART, but states do not regulate the actual techniques used in ART; although states do regulate physicians through licensing regimes and criminal law.⁹⁹ States also recognize the impacts of ART within the framework of family law.¹⁰⁰ Further, ethical norms have evolved in ART, including those discussed and promulgated by organizations such as the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine.¹⁰¹ In this way, traditional ART is regulated similarly to surgical techniques, which are subject to little regulatory oversight, whereas techniques involving the

Health Care Providers, 32 Hous. L. Rev. 1273, 1298–1308 (1996); David M. Studdert et al., *Medical Malpractice*, 350 New Eng. J. Med. 283, 283 (2004).

⁹⁶ See, e.g., Michele Goodwin, *A View from the Cradle: Tort Law and the Private Regulation of Assisted Reproduction*, 59 EMORY L.J. 1039, 1089–1100 (2010) (discussing current and potential applications of tort law to ART); Gary E. Marchant, *Legal Risks and Liabilities of Human Gene Editing*, 13 SCITECH LAW. 26, 27–29 (2016) (discussing the prospective causes of action available to those injured through germline gene editing research or clinical use).

⁹⁷ See, e.g., Bratislav Stankovic, *"It's a Designer Baby!"—Opinions on Regulation of Preimplantation Genetic Diagnosis*, 2005 UCLA J.L. & TECH. 3, 20 (noting the inaccuracy of genetic tests).

⁹⁸ See NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 88 (discussing transgenerational changes in the context of germline gene editing); Marianthi-Anna Kioumourtoglou et al., *Association of Exposure to Diethylstilbestrol During Pregnancy with Multigenerational Neurodevelopmental Deficits*, 172 JAMA PEDIATRIC 670, 675 (2018); Suryanarayana V. Vulimiri & Ofelia Olivero, *Introduction: Special Issue on Transplacental/Transgenerational Mutagenesis and Carcinogenesis*, 60 ENVTL. & MOLECULAR MUTAGENESIS 392, 392–93 (2019); Ctrs. for Disease Control and Prevention, *About DES*, <https://www.cdc.gov/des/consumers/about/index.html> (last visited Dec. 21, 2020). See *infra* notes 322–23 (discussing DES exposure and the regulatory regime's response).

⁹⁹ Lewis, *The American Democratic Deficit*, *supra* note 8, at 155.

¹⁰⁰ *Id.*

¹⁰¹ For a discussion of each of these organizations, see MARSH & RONNER, *supra* note 17, at 186–87.

combination of ART and genetic modification are subject to substantially more burdensome regimes.¹⁰²

This Part provides an overview of the various legal provisions that apply to aspects of germline gene editing, including the minimally regulated IVF, which is combined with the highly regulated genetic modification. This Article advocates for extending the current regime for the state-based regulation of traditional, or non-gene modifying, ART to germline gene editing and other forms of ART involving genetic modification. The remainder of this Part provides background on how the federal regulatory regime has been applied to germline gene editing. This analysis indicates how the federal government has acted in a hostile manner toward gene editing by regulating it to the point of effective preclusion. This hostility has surfaced through (1) federal funding restrictions, (2) barriers imposed through administrative law, and (3) Congressional restrictions on administrative agencies. Part IV will build on this overview by showing how the application of federal regulation to ART involving genetic modification is not only misplaced but also involves the federal regulatory system's hostility to germline genetic modification, which manifests similar risks to ART and approved gene therapy products.

1. Federal Funding Restrictions

Federal funding restrictions have had a significant impact on medical innovation requiring embryonic research as germline gene editing requires. For example, various conservatives have "opposed federal funding of embryo research because they believed that life begins at the moment when the sperm and egg unite."¹⁰³ This same opposition also limited funding for IVF research, which led to private funding and private innovation in IVF.¹⁰⁴ Eventually, these informal failures to provide funding to IVF research became codified in the Dickey-Wicker Amendment, a federal budget rider that has been renewed every year since 1996 and limits funding of research involving the (controversial) creation or destruction of embryos.¹⁰⁵

¹⁰² See generally King, *supra* note 93 (discussing the limited oversight over clinical innovation).

¹⁰³ MARSH & RONNER, *supra* note 17, at 72, 108.

¹⁰⁴ *Id.* at 73.

¹⁰⁵ *Id.* at 144, 176; see also NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 80–81. For more on the controversy related to the destruction of embryos and research on embryos, see *infra* Section II.A.4.

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 757

The National Institutes of Health (NIH) have influenced scientific innovation and the federal drug approval process.¹⁰⁶ The NIH is an operating division of the U.S. Department of Health and Human Services that “invests about \$41.7[] billion annually in medical research.”¹⁰⁷ The NIH has its own research campus, employs over 6,000 scientists, and disburses funding for medical innovation through a system of competitive grants.¹⁰⁸ NIH funding recipients are subject to a number of provisions, including mandatory federal regulations and oversight by various bodies.¹⁰⁹ Historically, one of those bodies, the Recombinant DNA Advisory Committee, commonly referred to as the “RAC,” was a federal advisory committee whose guidelines applied to recipients of federal funding.¹¹⁰ The RAC reviewed “human gene transfer protocols subject to the NIH Guidelines”;¹¹¹ the Guidelines “were applicable to all experiments performed at, or sponsored by, any institutions receiving NIH funding.”¹¹²

The FDA asserted jurisdiction over gene therapy in 1986, and “required the submission of a protocol for approval to the [NIH’s Recombinant DNA Advisory Committee] RAC” in addition to the submission of an investigational new drug (IND) application to the FDA for human gene therapy trials.¹¹³ At the same time, the RAC has long

¹⁰⁶ See MARCY E. GALLO ET AL., CONG. RES. SERV., R44824, *ADVANCED GENE EDITING: CRISPR-CAS9*, 17–18 (2018).

¹⁰⁷ NAT’L INSTS. OF HEALTH, BUDGET (Jan. 24, 2019), <https://www.nih.gov/about-nih/what-we-do/budget>.

¹⁰⁸ *Id.* See *Grants Compliance & Oversight*, NAT’L INST. OF HEALTH, <https://grants.nih.gov/policy/compliance.htm> (last visited Jan. 10, 2020).

¹⁰⁹ See *id.* (discussing federal regulations and oversight applicable to parties with NIH grants). See generally NAT’L INSTS. OF HEALTH, NIH GRANTS POLICY STATEMENT (2019), <https://grants.nih.gov/grants/policy/nihgps/nihgps.pdf> (discussing the policies applicable to grant recipients).

¹¹⁰ See Jordan Paradise, *U.S. Regulatory Challenges for Gene Editing*, 13 SCI. TECH. LAW. 10, 12 (2016). (“Technically, private institutions are not subject to the RAC-IRB-FDA framework, yet adherence is the norm; market entry of any commercial drug, device, or biologic product always requires affirmative FDA review and approval or clearance.”); see also *Recombinant DNA Advisory Committee*, NAT’L INSTS. OF HEALTH, <https://osp.od.nih.gov/biotechnology/recombinant-dna-advisory-committee> (last visited Sept. 25, 2018) (“The Recombinant DNA Advisory Committee (RAC) was established by NIH in 1974 to provide recommendations to the NIH Director and a public forum for discussion of the scientific, safety, and ethical issues related to basic and clinical research involving recombinant or synthetic nucleic acid molecules.”).

¹¹¹ See also *The NIH Review Process for Human Gene Transfer Trials*, NAT’L INSTS. OF HEALTH, <https://osp.od.nih.gov/biotechnology/faq-onthe-nih-review-process-for-human-gene-transfer-trials/> (last visited Sept. 25, 2018).

¹¹² Kane, *Human Genome Editing*, *supra* note 38, at 306.

¹¹³ *Id.* at 307; Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53248, 53251, (U.S. Food &

held the institutional view that it would not “entertain proposals to modify the human germline.”¹¹⁴ Thus, individuals seeking to research human germline gene editing face significant financial restrictions.¹¹⁵ While these financial restrictions do not automatically equate to marketing or regulatory restrictions, as detailed in the next subsection, the FDA has exhibited a similar hostility to germline genetic modification.

2. Administrative Legal Barriers

The FDA administers a regulatory regime intended to ensure that a number of medical products marketed for approval in the United States, including drugs, biologics, and medical devices, are safe and effective.¹¹⁶ Since 1993, the FDA has asserted responsibility for the regulation of gene therapy.¹¹⁷ The FDA has stated that it would regulate gene therapy as a biologic and/or drug.¹¹⁸ The FDA has proclaimed that it will treat germline gene editing in the same manner as gene

Drug Admin. Oct. 14, 1993), <https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/UCM148113.pdf>; see also U.S. FOOD & DRUG ADMIN., Statement of Policy for Regulating Biotechnology Products, 51 Fed. Reg. 23,310, 23,311, (U.S. Food & Drug Admin. Jun. 26, 1986) <https://www.govinfo.gov/content/pkg/FR-1986-06-26/pdf/FR-1986-06-26.pdf> (“Nucleic acids or viruses used for human gene therapy will be subject to the same requirements as other biological drugs. It is possible that scientific reviews of these products will also be performed by the National Institutes of Health.”)

¹¹⁴ *Statement on NIH Funding of Research Using Gene-editing Technologies in Human Embryos*, NAT’L INSTS. OF HEALTH, (Apr. 28, 2015), <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos>. For more on the RAC, see Francis S. Collins & Scott Gottlieb, *The Next Phase of Human Gene-Therapy Oversight*, 379 NEW ENG. J. MED. 1393, 1393–95 (2018) [hereinafter Collins & Gottlieb, *The Next Phase of Human Gene-Therapy Oversight*]; NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 56–57.

¹¹⁵ See Paradise, *supra* note 110 (noting the influence of NIH-funding restrictions on those who are not even individual funding recipients); see also Collins & Gottlieb, *supra* note 114, at 1393–95 (detailing the current roles of the FDA and the NIH in the regulation of gene therapy products).

¹¹⁶ See, e.g., U.S. FOOD & DRUG ADMIN., *What Does FDA Regulate?* (Aug. 22, 2018), <https://www.fda.gov/aboutfda/transparency/basics/ucm194879.htm>. For more on the difference between drugs and biologics, see W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023, 1026, 1032–33 (2016).

¹¹⁷ See Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53248, 53251 (U.S. Food & Drug Admin. Oct. 14, 1993), <https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/UCM148113.pdf>.

¹¹⁸ Collins & Gottlieb, *supra* note 114, at 1393–95.

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 759

therapy.¹¹⁹ As a matter of “ethical controversy,” the National Academy of Sciences (NAS) has noted that there is a “broad international consensus” that not only permits but encourages somatic cell gene therapy as long as it is proven “safe and effective.”¹²⁰ In 2017, the FDA approved the first gene therapy product for use in the United States, in addition to two other gene therapy products for marketing in the United States.¹²¹

In previous works, I have traced the FDA’s unexpected regulation of forms of ART involving genetic modifications of various degrees.¹²² The regulation of reproductive technology is unexpected due to the aforementioned practice-products divide, and the FDA’s regulatory assertion essentially means that reproductive techniques (or the children created as a result) are drugs and/or biologics.¹²³ Despite the dearth of federal statutes that apply to traditional ART, the FDA has asserted jurisdiction over forms of ART requiring genetic modification,

¹¹⁹ U.S. Food and Drug Admin., *Information About Self-Administration of Gene Therapy* (Nov. 21, 2017), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy>.

FDA considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy. . . . Clinical studies of gene therapy in humans require the submission of an investigational new drug application (IND) prior to their initiation in the United States, and marketing of a gene therapy product requires submission and approval of a biologics license application (BLA).

Id. When this Article uses the term “gene therapy,” it is referring to somatic or non-heritable genetic modification.

¹²⁰ NAT’L ACADS. SCIS., ENG’G & MED., *HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE*, *supra* note 50, at 147; *see also* NAT’L ACADS. OF SCI., *HERITABLE HUMAN GENOME EDITING*, *supra* note 52, at 126–29 (discussing effectiveness in the context of germline gene editing).

¹²¹ Collins & Gottlieb, *supra* note 114, at 1393–95; *Information About Self-Administration of Gene Therapy*, U.S. FOOD & DRUG ADMIN. (Nov. 21, 2017), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy>; Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53248, 53251 (U.S. Food & Drug Admin. Oct. 14, 1993), <https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/UCM148113.pdf> (defining gene therapy).

¹²² *See generally* Myrisha S. Lewis, *Halted Innovation: The Expansion of Federal Jurisdiction over Medicine and the Human Body*, 2018 UTAH L. REV. 1073 (2018) [hereinafter Lewis, *Halted Innovation*]; Lewis, *How Subterranean*, *supra* note 8.

¹²³ *Id.* For more on the difficulty of applying the FDA’s statutory requirements to controversial procedures related to reproduction, see Richard A. Merrill & Bryan J. Rose, *FDA Regulation of Human Cloning: Usurpation or Statesmanship?*, 15 HARV. J.L. & TECH. 85, 123–24 (2001); Gail H. Javitt & Kathy Hudson, *Regulating (for the Benefit of) Future Persons: A Different Perspective on the FDA’s Jurisdiction to Regulate Human Reproductive Cloning*, 2003 UTAH L. REV. 1201, 1227–28 (2003); Lewis, *How Subterranean*, *supra* note 8, at 1264.

including cytoplasmic transfer, mitochondrial transfer, and more recently, germline gene editing.¹²⁴ These jurisdictional assertions have come in the form of letters sent by the FDA to physician-researchers asserting that their work requires an IND application, despite the states regulating the practice of medicine.¹²⁵ FDA jurisdictional assertions have also come in the form of agency declarations on its website, which include not only cytoplasmic transfer and mitochondrial transfer, two techniques that arguably do not involve heritable genetic modification, but also germline genetic modification.¹²⁶ These FDA actions have deterred innovation even though the FDA regulates medical products and not techniques or the practice of medicine.¹²⁷

¹²⁴ See, e.g., Lewis, *How Subterranean*, *supra* note 8, at 1243–47; *infra* notes 113, 119 (providing the FDA's declarations of jurisdiction over gene therapy and germline gene editing). The FDA has also asserted jurisdiction over cloning which is not a form of ART.

¹²⁵ Lewis, *How Subterranean*, *supra* note 8, at 1250, 1254–56.

¹²⁶ See *Advisory on Legal Restrictions on the Use of Mitochondrial Replacement Techniques to Introduce Donor Mitochondria into Reproductive Cells Intended for Transfer into a Human Recipient*, U.S. FOOD & DRUG ADMIN. (Mar. 16, 2018) <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/advisory-legal-restrictions-use-mitochondrial-replacement-techniques-introduce-donor-mitochondria>; *FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P's) Product List*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/fda-regulation-human-cells-tissues-and-cellular-and-tissue-based-products-hctps-product-list> (last updated Feb. 1, 2018). For more on the dispute over the definition of germline, see NAT'L ACADS. SCI., ENG'G & MED., *MITOCHONDRIAL REPLACEMENT TECHNIQUES: ETHICAL, SOCIAL, AND POLICY CONSIDERATIONS* 88–89 (2016); Radhika Viswanathan, *3 Biological Parents, 1 Child, and an International Controversy*, VOX (July 28, 2018, 10:00 AM), <https://www.vox.com/2018/7/24/17596354/mitochondrial-replacement-therapy-three-parent-baby-controversy>; NUFFIELD COUNCIL ON BIOETHICS, *NOVEL TECHNIQUES FOR THE PREVENTION OF MITOCHONDRIAL DNA DISORDERS: AN ETHICAL REVIEW* 58 (2012) (“In spite of the separability of alterations to nuclear and mitochondrial genes which some commentators argue for, the Working Group will however refer to the techniques of PNT and MST as ‘germline therapies’ because they introduce a change that is incorporated into the (mitochondrial) genes of the resulting people, and so will be incorporated into the germline that they will go on to develop. This terminology seems appropriate because before the cell reconstruction procedure was performed and the relevant parts of the mother’s and donor’s egg or embryo combined, the person that would have originally resulted from their mother’s egg or embryo had it been left unchanged would have had a different genetic makeup (and thus, a different germline). We refer to the techniques of PNT and MST as ‘germline therapies’ while acknowledging that some changes to the mitochondrial genes have germline effects that are different from the germline effects of changes to nuclear genes.”); *Mitochondrial Replacement Therapy*, UNITED MITOCHONDRIAL DISEASE FOUND., <https://www.umdf.org/mitochondrial-replacement-therapy/> (last visited Aug. 5, 2020) (“[Mitochondrial replacement therapy] is NOT genetic manipulation, but rather a technological innovation and an expansion of in vitro fertilization, a clinically-approved technique used for four decades.”).

¹²⁷ See *supra* note 81 and accompanying text (discussing the practice-products divide).

3. Budget Riders

Since 2015, the Consolidated Appropriations Act has prohibited the FDA from using any of its funds to consider IND applications that involve human germline editing.¹²⁸ Specifically, the budget rider refers to a “heritable genetic modification,” a term that is not defined and has resulted in some scholarly debate.¹²⁹ This budget rider came after decades of FDA regulatory actions, such as Untitled Letters, which targeted researchers providing techniques involving genetic modification but fell short of direct enforcement action.¹³⁰ While some members of Congress have expressed disagreement with the budget rider, Congress has renewed the budget rider every year since 2015. That renewal has been accompanied by laudatory statements related to its preservation of “the sanctity of life.”¹³¹ These life-based arguments

¹²⁸ See Katherine Drabiak, *Emerging Governance of Mitochondrial Replacement Therapy: Assessing Coherence Between Scientific Evidence and Policy Outcomes*, 20 DEPAUL J. HEALTH CARE L. 1, 27 (2018) (citing NAT’L ACADS. SCI., ENG’G & MED., MITOCHONDRIAL REPLACEMENT TECHNIQUES: ETHICAL, SOCIAL, AND POLICY CONSIDERATIONS 2 (2016)) (observing that “the [NAS] report recently questioned whether [mitochondrial replacement therapy] constitutes heritable germline modification, asserting it would require additional legal analysis which makes the application of the spending prohibition uncertain”); Russell Spivak et al., *Germ-line Gene Editing and Congressional Reaction in Context: Learning from Almost 50 Years of Congressional Reactions to Biomedical Breakthroughs*, 30 J.L. & HEALTH 20, 22–23 (2017).

¹²⁹ NAT’L ACADS. SCI., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 191 (citing Consolidated Appropriations Act of 2016, H.R. 2029, 114th Cong., 1st Sess. (2015), <https://www.congress.gov/114/bills/hr2029/BILLS-114hr2029enr.pdf>) (last visited January 4, 2017). For more on the potential applicability (or inapplicability) of the budget rider to techniques such as mitochondrial transfer, see Glenn Cohen, *Circumvention Medical Tourism and Cutting Edge Medicine: The Case of Mitochondrial Replacement Therapy*, 25 IND. J. GLOBAL LEGAL STUD. 439, 442 (2018); Katherine Drabiak, *Emerging Governance of Mitochondrial Replacement Therapy: Assessing Coherence Between Scientific Evidence and Policy Outcomes*, 20 DEPAUL J. HEALTH CARE L. 1, 27 (2018) (citing to NAT’L ACADS. OF SCI., ENG’G & MED, MITOCHONDRIAL REPLACEMENT TECHNIQUES: ETHICAL, SOCIAL, AND POLICY CONSIDERATIONS 2 (2016)); Joshua D. Seitz, *Striking A Balance: Policy Considerations for Human Germline Modification*, 16 SANTA CLARA J. INT’L L. 60, 95 (2018).

¹³⁰ See Lewis, *How Subterranean*, *supra* note 8 and accompanying text; see also *supra* notes 126–27 (noting the debate over the germline and what is “heritable” genetic modification).

¹³¹ Eli Adashi & I. Glenn Cohen, *Heritable Genome Editing: Edited Eggs and Sperm to the Rescue?*, JAMA F. (Oct. 3, 2019) (providing the following comments of two members of Congress on the “Consolidated Appropriation Act of 2016, the moratorium prohibits the US Food and Drug Administration from addressing research ‘in which a human embryo is intentionally created or modified to include heritable genetic modification.’ Expounding on the bill in question, Rep Harold D. Rogers (R, Kentucky) noted that it ‘preserves the sanctity of life,’ adding ‘new provisions prohibiting genetic editing of human embryos.’ Rep Robert B. Aderholt (R, Alabama) said the “prohibition on gene

connect to bioethical concerns regarding the proper role of humans on earth and to previous debates on the morality and legality of abortion discussed in Part III.¹³² Ultimately, due to the budget rider, private, domestic clinical trials would still be restricted because, according to the FDA, FDA acceptance of a new drug or biologic application would be required for systemic trials related to these techniques according to the FDA.¹³³

At the same time, federal bans do not prohibit innovation, but they can reduce access to innovation domestically and/or drive it abroad. For example, New York-based physicians who work on mitochondrial transfer in the U.S. have traveled to Mexico to provide techniques to U.S.-based patients (with the aim of leading to a human birth) in contravention of federal law, which prohibits the use of the technique in the U.S. without an IND application.¹³⁴ Similarly, a researcher working on mitochondrial transfer, a technique involving inheritable genetic modification, entered into a partnership to conduct research in Korea instead of in the United States, where federal funding is limited due to restrictions.¹³⁵ In the context of germline gene editing, some have expressed concern that such a moratorium could eventually lead to “genome editing tourism” where scientists move to countries with lax rules on germline gene editing to continue researching and ultimately providing the technique to patients.¹³⁶ Such tourism would mean that

editing of human embryos . . . is a tremendous victory for those who are concerned about life.”).

¹³² *Id.* (“Given that the prospect of editing of the human embryo genome is caught up in the debate over abortion, proponents of gene editing will be hard-pressed to secure the broad political support required for its actualization.”).

¹³³ *See, e.g.*, U.S. FOOD & DRUG ADMIN., GUIDANCE FOR CLINICAL INVESTIGATORS, SPONSORS, AND IRBs: INVESTIGATIONAL NEW DRUG APPLICATIONS (INDS)—DETERMINING WHETHER HUMAN RESEARCH STUDIES CAN BE CONDUCTED WITHOUT AN IND 5–7 (Sept. 2013), <https://www.fda.gov/downloads/drugs/guidances/ucm229175.pdf>.

¹³⁴ *See* Michelle Roberts, *First ‘Three Person Baby’ Born Using New Method*, BBC NEWS (Sept. 27, 2016) <https://www.bbc.com/news/health-37485263>; *see also* John Zhang et al., *Live Birth Derived From Oocyte Spindle Transfer to Prevent Mitochondrial Disease*, 34 REPROD. BIOMEDICINE ONLINE 36, 361–68 (2017).

¹³⁵ David Cyranoski & Boer Deng, *Stem-Cell Star Lands in Same Venture as Disgraced Cloner*, NATURE (Feb. 11, 2015), <https://www.nature.com/news/stem-cell-star-lands-in-same-venture-as-disgraced-cloner-1.16907>. Some states, like California, have created regimes that provide funding for activities like stem cell research that have faced political opposition at the federal level in the United States. *See* June Carbone, *Negating the Genetic Tie: Does the Law Encourage Unnecessary Risks?*, 79 UMKC L. REV. 333, 360 (2010).

¹³⁶ *See* Bosley et al., *supra* note 41, at 483 (statement of Anthony Perry, Department of Biology and Biochemistry at the University of Bath); *see also* Letter to Honorable Alex Azar II, Secretary of the U.S. Dept. of Health and Human Services (Apr. 24, 2019) <https://www.asgct.org/global/documents/clinical-germline-gene-editing-letter.aspx>.

germline gene editing would be limited to patients who can afford to travel abroad and require physicians and researchers to travel abroad in order to conduct research and patient care.¹³⁷ Potential genome editing tourism also leads to a concern that those providing these techniques to patients may be unscrupulous researchers who may not properly inform patients or work in furtherance of patient health.¹³⁸

III. SOCIAL, POLITICAL, AND ETHICAL DEBATES THAT CAN INFLUENCE REGULATION

Germline gene editing not only raises previous bioethical debates related to ART but also generates new debates related to the regulation of new medical products and technologies.¹³⁹ It is important to address the bioethical debates that arise due to germline gene editing and also make clear which of the ethical concerns that accompany gene editing also stem from reproduction or assisted reproduction in general.

Gene editing technologies (both somatic and reproductive) have led to much scientific, legal, and ethical discussion.¹⁴⁰ Both scientists and regulators are concerned about the safety and effectiveness of gene editing technologies.¹⁴¹ Due to inheritable changes and lack of long-term research, regulators, scientists, and ethicists generally treat germline gene editing as legally, ethically, and scientifically distinct from gene therapy and traditional ART.¹⁴²

¹³⁷ NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 190 (referring to "regulatory havens" with "lenient or nonexistent regulations").

¹³⁸ See Francis S. Collins, *Statement on Claim of First Gene-Edited Babies by Chinese Researcher* (Nov. 28, 2018), <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-claim-first-gene-edited-babies-chinese-researcher> (statement by Francis S. Collins, National Institutes of Health Director).

¹³⁹ See also NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 2–3 (discussing the role of language in discussions of genome editing and the meanings and use of the concepts of "moral" "ethical" and "activity [of] bioethics").

¹⁴⁰ See, e.g., Paradise, *supra* note 110, at 11.

¹⁴¹ See discussion *infra* Parts III and IV (discussing safety and effectiveness concerns in FDA regulation); see also Yanting Zeng et al., *Correction of the Marfan Syndrome Pathogenic FBN1 Mutation by Base Editing in Human Cells and Heterozygous Embryos*, 26 MOLECULAR THERAPY 2631, 2635 (2018), <https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016%2818%2930378-2#%20> (referring to "safety and efficiency" of gene editing and stating "[b]esides efficiency, a successful gene therapy needs perfect precision and specificity.").

¹⁴² See Kane, *supra* note 38, at 302–03. But see Julia D. Mahoney & Gil Siegal, *Beyond Nature? Genomic Modification and the Future of Humanity*, 81 LAW & CONTEMP. PROBS. 195, 212 (2018) (arguing that "drawing a [regulatory] bright line between somatic and heritable genome editing is not persuasive on either moral or practical grounds").

There are many bases for these anti-genetic modification views, including science-fiction movies and classic literature that highlight the perils of human hubris, and the general thought that such a change is simply “not something we should do.”¹⁴³ Evidence of these anti-genetic modification perspectives appears not only in statements of certain members of the public but also in many politicians’ statements, including members of both the Democratic and Republican parties.¹⁴⁴ These anti-genetic modification perspectives also motivate federal regulation.¹⁴⁵ There are three significant categories of opposition to genome editing: safety concerns, efficacy concerns, and morality concerns. Nonetheless, many discussions of gene editing, especially germline gene editing, group all of these concerns together and refer to them collectively.¹⁴⁶ Addressing these concerns together often leads to a blending of the standard in FDA product approval for “safety and effectiveness,” with concerns related to political, social, and moral issues.¹⁴⁷ Yet when some commentators discuss “safety and

¹⁴³ See, e.g., Steven Pinker, *The Moral Imperative for Bioethics*, BOSTON GLOBE (Aug. 1, 2015), <https://www.bostonglobe.com/opinion/2015/07/31/the-moral-imperative-for-bioethics/JmEkoyzITAu9oQV76JrK9N/story.html>; see also Bosley et al., *supra* note 41, at 481.

¹⁴⁴ See, e.g., John P. Holdren, *A Note on Genome Editing*, OBAMA WHITE HOUSE ARCHIVE: WHITE HOUSE BLOG (May 26, 2015, 10:40 AM), <https://obamawhitehouse.archives.gov/blog/2015/05/26/note-genome-editing>; Sarah Karlin, *Gene Editing: The Next Frontier in America's Abortion Wars*, POLITICO (Feb. 16, 2016), <https://www.politico.com/story/2016/02/gene-editing-abortion-wars-219230>.

¹⁴⁵ See Lewis, *How Subterranean*, *supra* note 8; Lewis, *The American Democratic Deficit*, *supra* note 8; Javitt & Hudson, *supra* note 123, at 1216–17; see also NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, NAT'L INSTS. OF HEALTH (Apr. 2016), <https://osp.od.nih.gov/biotechnology/nih-guidelines>; Francis S. Collins, *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT'L INSTS. OF HEALTH (Apr. 28, 2015), <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos>; Carrie D. Wolinetz & Francis S. Collins, *NIH Supports Call for Moratorium on Clinical Uses of Germline Gene Editing*, NATURE (Mar. 13, 2019), <https://www.nature.com/articles/d41586-019-00814-6>.

¹⁴⁶ See, e.g., *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 20 (statement of Dr. Jennifer Doudna); Joseph Morton, *Fortenberry Shares Story of Daughter's Heart Defects During Talks of Human Gene Editing Research*, OMAHA WORLD-HERALD (Jun. 5, 2019), https://www.omaha.com/livewellnebraska/health/fortenberry-shares-story-of-daughter-s-heart-defects-during-talks/article_412afcac-feaa-597a-a00c-8cddb58ce65d.html (Congressman Fortenberry “reiterated that science has to be tied to ethical considerations and that lifting the prohibitions [on germline gene editing] would send a signal to maverick researchers that the restraints are off, a move that would endanger everyone”). See comments of Congressmembers discussed *supra* note 131 and *infra* notes 236–37.

¹⁴⁷ See, e.g., 21 U.S.C. § 355(a); 21 U.S.C. § 393(b)(2)(B); Jeffrey M. Drazen et al., *The FDA, Politics, and Plan B*, 350 NEW ENG. J. MED. 1561, 1561–62 (2004); Lisa Heinzlering,

effectiveness,” they are actually incorporating political and social concerns instead of keeping them separate.¹⁴⁸ As will be discussed *infra*, if a product is deemed “safe and effective,” this does not mean that the product or technology is completely “safe,” but rather, that its benefits and risks have been identified, and the risks merit the potential reward.¹⁴⁹

In prior works, I have argued that the FDA’s jurisdiction over techniques involving reproduction and genetic modification is misplaced. In those prior works, I have emphasized that political and social views influence the FDA’s already problematic decision-making process, already noted for its obscurity, especially as it relates to techniques that combine ART with genetic modification.¹⁵⁰ Further, a number of recent events, as chronicled in the medical and legal literatures, have emphasized the impacts of politics on scientific decision-making.¹⁵¹ This Article separates those safety, efficacy, and morality concerns. This Part, combined with Part IV, aims to show that

The FDA’s Plan B Fiasco: Lessons for Administrative Law, 102 GEO. L.J. 927, 939–48 (2014); Alastair J.J. Wood et al., *A Sad Day for Science at the FDA*, 353 NEW. ENG. J. MED. 1197, 1197–98 (2005). The term “safety and efficacy” also arises in other countries’ analysis of the appropriateness of gene editing. See, e.g., GERMAN ETHICS COUNCIL, *supra* note 45, at 57 (“In principle, the less obvious any medical need is, the stricter the safety and efficacy requirements and, by extension, the innocuousness requirements for germline interventions will have to be.”).

¹⁴⁸ See Kathryn A. Watts, *Controlling Presidential Control*, 114 MICH. L. REV. 683, 709 (2016) (providing the statement of FDA Commissioner Hamburg: “It is our responsibility at FDA to approve drugs that are safe and effective for their intended use based on the scientific evidence”). Outside of the reproductive context, there is increasing concern about the impacts of politics on the decisions of public health agencies. For examples of this, see the following: Helen Branswell, *As Controversies Swirl, CDC Director Is Seen as Allowing Agency to Buckle to Political Influence*, STAT NEWS (Sept. 16, 2020), <https://www.statnews.com/2020/09/16/as-controversies-swirl-cdc-director-is-seen-as-allowing-agency-to-buckle-to-political-influence>; Nick Valencia & Kristen Holmes, *Trump’s HHS Alters CDC Documents for Political Reasons, Official Says*, CNN (Sept. 12, 2020, 8:06 PM), <https://www.cnn.com/2020/09/12/politics/cdc-trump-science-reports/index.html>.

¹⁴⁹ See 21 U.S.C. § 355(a); NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 139; Baltimore et al., *supra* note 43, at 37 (“As with any therapeutic strategy, higher risks can be tolerated when the reward of success is high, but such risks also demand higher confidence in their likely efficacy. And, for countries whose regulatory agencies focus on safety and efficacy but not on broader social and ethical concerns, another venue is needed to facilitate public conversation.”); Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 457–58, 502 (2010).

¹⁵⁰ See, e.g., Lewis, *The American Democratic Deficit*, *supra* note 8, at 149–56, 166–69.

¹⁵¹ *Id.* at 144, 149; see also Drazen et al., *supra* note 147, at 1561–62; Wood et al., *supra* note 147, at 1197–98; Heinzerling, *supra* note 147, at 930–58.

many of the bioethical and safety concerns that accompany germline gene editing are the same or similar to the concerns that accompany reproduction, drugs, and biologics, including gene therapy.¹⁵² As such, the regulatory regime does not need to respond to germline gene editing as if it were an exceptional technology requiring substantially different regulation than traditional ART or products the FDA regulates. This Article dispels those “morality concerns” and explains why they should not lead to gene editing’s treatment as an exceptional medical product, especially if the safety of germline gene editing merits its use.¹⁵³

This Article presents a comprehensive, balanced view of the bioethical debates surrounding germline gene editing. There are many sources of bioethical opposition to assisted reproduction (including IVF) and germline gene editing. This Part of the Article is both descriptive and normative. This Part of the Article identifies and thematizes the commonly occurring ethical objections to germline gene editing. There are at least ten commonly occurring objections to germline gene editing. Many of those reasons are common to ART, including IVF, a technique that is widely available (and legal) in the United States. These “ethical” reasons are also referred to as “societal” or “moral” concerns. This Part of the Article groups those commonly occurring ethical concerns and notes the interrelated nature of many of those concerns. This Article groups those commonly occurring bioethical debates that can influence regulation. This Part shows how the ethical concerns of ART are similar to the ethical concerns that accompany germline gene editing; these ethical concerns have not prohibited the legality of traditional ART. This Part also presents the germline gene editing-specific concerns before arguing that those concerns should not prohibit the legality of germline gene editing. After laying this foundation, Part IV focuses on the safety concerns common

¹⁵² See *What is Gene Therapy?*, U.S. FOOD AND DRUG ADMIN. (July 25, 2018), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy> (“Gene therapy products are biological products regulated by the FDA’s Center for Biologics Evaluation and Research (CBER). Clinical studies in humans require the submission of an investigational new drug application (IND) prior to initiating clinical studies in the United States. Marketing a gene therapy product requires submission and approval of a biologics license application (BLA).”).

¹⁵³ As discussed *infra* notes 319–21, even FDA approval does not guarantee that a technique or a product is “safe” as all medical procedures and products are accompanied by risk. Some commentators, such as Marcy Darnovsky, would still aim to prohibit germline gene editing even if it were characterized as “safe.” See, e.g., Rob Stein, *Breaking Taboo, Swedish Scientist Seeks to Edit DNA of Healthy Human Embryos*, NPR (Sept. 22, 2016), <https://www.gmwatch.org/en/news/archive/2016/17227-breaking-taboo-swedish-scientist-seeks-to-edit-dna-of-healthy-human-embryos>.

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 767

to germline gene editing and somatic gene editing and how common these concerns are to both, then argues that even the germline gene editing-specific concerns should not be construed to support federal regulation of the technique.

A. *Concerns Related to Autonomy: The Consent of Future Persons and Parental Autonomy*

Concerns related to autonomy tend to fall within two larger threads: those related to the autonomy of future generations and those related to the autonomy of parents over their future children. With ART, those concerns tend to focus on both the concerns of the children who would be conceived using ART and their inability to consent to their parents' actions, and the concerns of the parents who generally have broad abilities to make decisions for their future children. These concerns are exacerbated by germline gene editing, which implicates not only future children but also the children who would come after those children because the changes would affect future generations. These intergenerational concerns will be discussed in this Section and Section D.

1. Consent for Future Persons and Parental Autonomy

One objection to both germline gene editing and ART is the impact on future generations without their consent.¹⁵⁴ Concerns for future persons not only include their lack of consent but also what impacts their parents' decision-making might have on them. For example, if parents can select future traits, then children who were selected for those purposes, such as enhanced intelligence or height, may feel pressure to "live up to" those genetic traits.¹⁵⁵ While consent-based discussions tend to focus on the child who would be immediately produced as a result of germline modification, extending the argument about the "shared human identity" reveals that there is also a concern for subsequent generations who would be produced by someone who had undergone genetic modification.¹⁵⁶

¹⁵⁴ Polcz & Lewis, *supra* note 42, at 415.

¹⁵⁵ Suter, *supra* note 13, at 963, 968.

¹⁵⁶ See *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 44. For more on the bioethical concept of the "shared human identity," see *infra* Section III.D.3.

On the other hand, others would argue that germline gene editing and genetic modification are part of a larger trajectory that focuses on both scientific discovery and parental autonomy. This idea of parental autonomy is often invoked to counter the argument that germline gene editing could “interfere with a child’s ‘right to an open future’” as many parental choices do.¹⁵⁷ While parental decision-making does face limitations such as those that aim to protect children from child abuse and neglect, parents have significant autonomy in the rearing of their children and reproductive decision-making.¹⁵⁸ For example, as Julian Savulescu has noted, parents have tried for centuries to improve the health and intellect of their children.¹⁵⁹ Professor Savulescu has gone as far as to say that parents have a duty to improve the intellect and physical health of their children.¹⁶⁰ This argument has been summarized as “do good, whenever possible.”¹⁶¹

Parents are already able to select desirable embryos through various non-gene modifying forms of ART techniques that permit parents to select embryos with genetically desirable traits or even preferred genders, which often leads to scholarly and public critique of whether parents should undertake such actions.¹⁶² Procreative autonomy is often discussed in the context of parental decision-making, including prenatal testing and other decisions that enable parents to

¹⁵⁷ R. Alta Charo, *Who's Afraid of the Big Bad (Germline Editing) Wolf?*, 63 *PERSPS. IN BIOLOGY & MED.* 93, 95 (2020) (citing J. FEINBERG, *FREEDOM AND FULFILLMENT* (1992)).

¹⁵⁸ See generally *Prince v. Massachusetts*, 321 U.S. 158, 165 (1944); *Troxel v. Granville*, 530 U.S. 57, 65 (2000); Doriane L. Coleman, Kenneth A. Dodge & Sarah K. Campbell, *Where and How to Draw the Line Between Reasonable Corporal Punishment and Abuse*, 73 *L. & CONTEMP. PROBS.* 107, 107–08 (2010); Rebecca Vermette, *A Case for an Exception in the Domain of Parental Autonomy with Testing for Huntington Disease*, 18 *MICH. ST. J. MED. & L.* 29, 31 (2014); Cara D. Watts, *Asking Adolescents: Does a Mature Minor Have a Right to Participate in Health Care Decisions*, 16 *HASTINGS WOMEN'S L.J.* 221, 224 (2005).

¹⁵⁹ See Julian Savulescu, *Genetic Interventions and the Ethics of Enhancement of Human Beings*, 32 *GAZETA DE ANTROPOLOGIA*, Nov. 2016, <http://www.gazeta-antropologia.es/wp-content/uploads/GA-32-2-07-Julian-Savulescu.pdf>.

¹⁶⁰ See Julian Savulescu, *Procreative Beneficence: Why We Should Select the Best Children*, 15 *BIOETHICS* 413, 413–16 (2001).

¹⁶¹ ETHICS COMM. OF THE AM. SOC'Y FOR REPROD. MED., *Transferring Embryos with Genetic Anomalies Detected in Preimplantation Testing: An Ethics Committee Opinion*, 107 *FERTILITY & STERILITY* 1130, 1134 (2017) (noting that “good” is determined through the eyes of the parents who would be exercising procreative beneficence).

¹⁶² Julia D. Mahoney & Gil Siegal, *Beyond Nature? Genomic Modification and the Future of Humanity*, 81 *LAW & CONTEMP. PROBS.* 195, 205 (2018) (discussing “the present generation’s use of PGD and selective termination”).

decide which children they would like to have.¹⁶³ Prenatal testing, similarly to germline gene editing, leads to concerns that parents may feel that they should obtain prenatal testing or terminate their pregnancies due to the existence of detected abnormalities that cannot be resolved with in utero treatment.¹⁶⁴ The scope of procreative autonomy, however, remains undefined.¹⁶⁵

At the same time, some scholars note that an underemphasized aspect of embryo selection through PGD and selective termination of undesirable fetuses after prenatal testing is that doing so “affects the genetic profiles of future generations[, thus, while] one argument against human germline editing is that it may lead to the modification of genes that confer benefits as well as cause harm[,] . . . it is . . . a risk that we are already running.”¹⁶⁶

The continued legality of traditional ART in many ways responds to the issue of parental decision-making (albeit without the genetic component in most instances) by deferring to parental autonomy.¹⁶⁷ Generally, parents make decisions for their children, and parental decision-making falls within the constitutional right to parental autonomy.¹⁶⁸ Parents even make decisions for fetuses when they decide, for example, to use pre-birth interventions such as fetal

¹⁶³ See, e.g., Suter, *supra* note 13, at 924 n. 154; see also NAT'L ACADS. SCI., HERITABLE HUMAN GENOME EDITING, *supra* note 52, at 42–52.

¹⁶⁴ *Id.* at 927–28; Samuel R. Bagenstos, *Disability, Life, Death, and Choice*, 29 HARV. J.L. & GENDER 425, 438–39 (2006).

¹⁶⁵ John A. Robertson, *Embryos, Families, and Procreative Liberty: The Legal Structure of the New Reproduction*, 59 S. CAL. L. REV. 939, 955 (1986) (discussing procreative liberty).

¹⁶⁶ Julia D. Mahoney and Gil Siegal, *Beyond Nature? Genomic Modification and the Future of Humanity*, 81 LAW & CONTEMP. PROBS. 195, 205 (2018) (citations omitted). For more on PGD and prenatal testing, see NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 113.

¹⁶⁷ Traditional ART does not involve genetic modification; however, two techniques of ART do involve genetic modification, cytoplasmic transfer and mitochondrial transfer. For more on cytoplasmic transfer and mitochondrial transfer (and the regulatory system's response to the techniques), see *infra* Section II.B.2.

¹⁶⁸ For more on parental autonomy, see Elaine M. Chiu, *The Culture Differential in Parental Autonomy*, 41 U.C. DAVIS L. REV. 1773, 1792 (2008); E. Gary Spitko, *Reclaiming the “Creatures of the State”: Contracting for Child Custody Decisionmaking in the Best Interests of the Family*, 57 WASH. & LEE L. REV. 1139, 1181–89 (2000); see also Bosley et al., *supra* note 41, at 478, 482 (providing the statement of Robin Lovell-Badge at The Francis Crick Institute: “[P]arents are always seeking ways to give their children an advantage in life, and we do not consider this unethical. Sending a kid to a good school, for example, can have a transgenerational effect. However, a germline genetic change may be passed down without subsequent generations having a choice (except the same technology could be used to reverse the enhancement).”).

surgeries to improve their future children's health.¹⁶⁹ While physicians perform surgical techniques on existing individuals who can consent to the procedures; traditional ART, in utero treatments, and treatments of children all involve the inability of children to consent.

Parents can influence their children's genetic makeup in many ways other than by using germline gene editing, such as through natural reproduction, selection of sperm and egg donors, and genetic screening.¹⁷⁰ Critics of assisted reproduction, like Leon Kass, characterize natural reproduction as "a combination of nature and chance, not human design"; however, that characterization lacks some nuance.¹⁷¹ In natural reproduction, trait selection tends to be uncriticized, unmentioned, and unregulated: the idea that parents choose mates based on the traits that they would like to pass on to their children has not led society (and the law) to try to regulate these reproductive matters.¹⁷² Similarly, parents' "selective breeding" in which parents decide with whom they would like to reproduce has generally not been the focus of ethical opposition in the realm of reproduction.¹⁷³ Thus, there is no regime to prevent people from reproducing on the basis that doing so would pass on "undesirable" or "desirable" traits to offspring.¹⁷⁴

¹⁶⁹ See, e.g., Ahmet Baschat, *Preventing and Treating Birth Defects: What You Need to Know*, JOHNS HOPKINS MED., <https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/preventing-and-treating-birth-defects-what-you-need-to-know> (last visited Nov. 5, 2019). For more on fetal surgery in the context of germline gene editing, see NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 107–09.

¹⁷⁰ I. Glenn Cohen, *What (If Anything) Is Wrong with Enhancement? What (If Anything) Is Right with It?*, 49 TULSA L. REV. 645, 648, 682 (2014); Rakowski, *supra* note 11, at 1367.

¹⁷¹ Leon R. Kass, *The Wisdom of Repugnance*, NEW REPUBLIC, June 2, 1997, at 21.

¹⁷² See, e.g., Rakowski, *supra* note 11, at 1345. *But see* JUDITH AREEN ET AL., FAMILY LAW: CASES AND MATERIALS 71–72 (6th ed. 2012) (discussing prohibitions on incest).

¹⁷³ See, e.g., *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 6 (providing the statement of Subcommittee Chairwoman Barbara Comstock that "humans have been altering the genomes of species through selective breeding for thousands of years"); Julian Savulescu, *New Breeds of Humans: The Moral Obligation to Enhance*, 10 REPROD. BIOMED. ONLINE 36, 36 (2005) ("Selective mating has been occurring in humans ever since time began."); see also John A. Robertson, *Procreative Liberty in the Era of Genomics*, 29 AM. J.L. & MED. 439, 450–52 (2003); Savulescu, *supra* note 160, at 418 (defining "procreative autonomy").

¹⁷⁴ Rima Kundnani, *Protecting the Right to Procreate for Mentally Ill Women*, 23 S. CAL. REV. L. & SOC. JUST. 59, 67–70 (2013). *But see* AREEN ET AL., *supra* note 172, at 71–72 (discussing prohibitions on incest); Mindy K. Fersel, *Liberty and Justice for All? Protecting the Right to Privacy for Incapacitated Individuals: The Need for Comprehensive Sterilization Legislation in All Fifty States*, 20 CARDOZO J.L. & GENDER 827, 828–30, 839–49 (2014); Greely, *supra* note 54, at 161 (noting that "the Common Rule has special

B. Concerns Related to Disability Rights and Eugenics

Disability-related and eugenics concerns accompany techniques involving ART and germline gene editing. At the outset, it is important to note that “[t]he disability rights community is not monolithic, and its attitudes toward genetic technologies such as prenatal screening can vary from supportive to skeptical.”¹⁷⁵ As will be discussed *infra*, many individuals are concerned about the implications of techniques that deem certain traits desirable or undesirable. For some, those concerns are rooted in the particularly negative connotation of the word “eugenics,” which is associated with discriminatory practices, including genocide, forced sterilization, institutionalization, and anti-miscegenation laws in the United States, Germany, and the United Kingdom.¹⁷⁶ Proponents of these discriminatory practices aimed to rid society of certain races or traits that more powerful groups deemed “undesirable”; these practices existed before the advent of ART.

Parents often combine ART with PGD which allows them to choose “suitable” embryos for implantation and to discard unsuitable embryos. Like germline gene editing, PGD has been criticized for the possibility that it could “exacerbate a social environment that is hostile to people with disabilities more generally.”¹⁷⁷ Further, fetal diagnostic techniques allow parents to terminate pregnancies when testing reveals that the fetuses have diseases that the parents do not want their future children to have.¹⁷⁸ At the same time, supporters of germline gene editing note

requirements for” research involving children, fetuses, and embryos intended for implantation); Corey G. Johnson, *Female Inmates Sterilized in California Prisons Without Approval*, NBC BAY AREA (July 8, 2013, 11:27 AM), <https://www.nbcbayarea.com/news/california/Female-Inmates-Sterilized-in-California-Prisons-Without-Approval-214634341.html>; Kalhan Rosenblatt, *Judge Offers Inmates Reduced Sentences in Exchange for Vasectomy*, NBC NEWS (July 21, 2017), <https://www.nbcnews.com/news/us-news/judge-offers-inmates-reduced-sentences-exchange-vasectomy-n785256>.

¹⁷⁵ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 126 (citations omitted).

¹⁷⁶ *Id.* at 153–56; NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 79–80, 118; Paul A. Lombardo, *Taking Eugenics Seriously: Three Generations of ??? Are Enough?*, 30 FLA. ST. U. L. REV. 191, 215–16 (2003); Paul A. Lombardo, *Medicine, Eugenics, and the Supreme Court: From Coercive Sterilization to Reproductive Freedom*, 13 J. CONTEMP. HEALTH L. & POL’Y 1, 6 (1996).

¹⁷⁷ NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 82.

¹⁷⁸ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 6; NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at xv.

that “few would lament the elimination of many inherited disease characteristics” which often result in suffering.¹⁷⁹

Germline gene editing combines these eugenics and disability-related concerns with concerns for the ability to prevent certain traits not only in a parent’s child but also in future generations.¹⁸⁰ The significant impact on future generations raises concerns about the direction of the human race and what that might mean for future generations or a future society. Concerns such as these have existed for decades, even before the advent of germline gene editing.

1. Disability-Related Concerns

There is some debate over what traits are deemed “undesirable” and should be targeted for treatment using genetic technologies. This concern regarding the desirability of traits implicates eugenics and disability concerns.¹⁸¹ In the disability context, for example, scholars have noted that many people in the deaf community have not chosen cochlear implants for their children or themselves for various reasons, including the desire to have a child who has the same condition as the parent and the view that deafness is not a disability that needs to be corrected.¹⁸² The same dispute exists among those in various disability communities and the public for other traits, such as dwarfism.¹⁸³

¹⁷⁹ *Id.* at 82.

¹⁸⁰ *See, e.g.*, Roberto Andorno et al., *Geneva Statement on Heritable Human Genome Editing: The Need for Course Correction*, 38 *TRENDS BIOTECH.* 351, 351–54 (2020), <https://www.sciencedirect-com.proxy.wm.edu/science/article/pii/S0167779919303178>; Françoise Baylis, *Counterpoint: The Potential Harms of Human Gene Editing Using CRISPR-Cas9*, 64 *CLINICAL CHEMISTRY* 489, 489–91 (2018).

¹⁸¹ Suter, *supra* note 13, at 955–58.

¹⁸² *ETHICS COMM. OF THE AM. SOC’Y FOR REPROD. MED., Transferring Embryos with Genetic Anomalies Detected in Preimplantation Testing: An Ethics Committee Opinion*, 107 *FERTILITY & STERILITY* 1130, 1131 (2017) (noting that the phenomenon in which parents wish to raise children who have the same genetic conditions as they do is “sometimes referred to as ‘intentional diminishment’ and primarily involves selection for sensory or mobility disorders such as deafness or achondroplasia (dwarfism)” (citation omitted)); Polcz & Lewis, *supra* note 42, at 420–21; *see also* Allegra Ringo, *Understanding Deafness: Not Everyone Wants To Be ‘Fixed’*, *ATLANTIC* (Aug. 9, 2013), <https://www.theatlantic.com/health/archive/2013/08/understanding-deafness-not-everyone-wants-to-be-fixed/278527>.

¹⁸³ Bosley et al., *supra* note 41, at 482 (“[I]n some instance—[like] correction of hearing deficits or enhancement of stature—patient groups have argued that the ‘defect’ is a perfectly acceptable form of human variation that should not be subjected to genetic cleansing.”); Robertson, *supra* note 173, at 441, 460, 480. For both sides of the debate of how dwarfism should be treated, *see* Damian Garde, *A New Treatment Promises To Make Little People Taller. Is It An Insult to ‘Dwarf Pride’?*, *STAT NEWS* (Nov. 18, 2019), <https://www.statnews.com/2019/11/18/a-new-treatment-promises-to-make-little-people-taller-is-it-an-insult-to-dwarf-pride>.

Further, majoritarian views about what society deems disabilities, such as dwarfism or deafness, may lead to a perspective that discourages those with disabilities from choosing embryos that have traits similar to themselves.¹⁸⁴ Physicians who provide PGD tend to oppose the use of PGD to affirmatively select embryos with those traits that society has deemed as disabilities.¹⁸⁵ Nevertheless, the regulatory regime has not instituted additional limitations on these uses of PGD, even though many people find some uses of PGD objectionable.

2. Eugenics Concerns

As a related matter, there is also a concern that gene editing could create an “arms race” of sorts where “parents will feel obligated to engage in pre-birth genetic engineering, because other parents are doing so, just as SAT prep courses have become routine and some athletes feel obligated to use steroids if other athletes are gaining an advantage from them.”¹⁸⁶ This concern already exists with other technologies involving ART, such as PGD.¹⁸⁷ For example, Professor Leon Kass characterizes genetic screening and PGD as “negative eugenic selection.”¹⁸⁸ Enhancement has also been analogized to “positive eugenics.”¹⁸⁹

Applying eugenics concerns to germline gene editing, there is a concern that those who are germline gene edited will be regarded as “superior” to those who have not been changed with germline gene editing before birth.¹⁹⁰ Further, this concern about desirable traits may

¹⁸⁴ See Darshak M. Sanghavi, *Wanting Babies Like Themselves, Some Parents Choose Genetic Defects*, N.Y. TIMES (Dec. 5, 2006), <https://www.nytimes.com/2006/12/05/health/05essa.html> (discussing the efforts of parents to use PGD and donor selection in order to create children who have traits that are viewed as “disabilities” such as deafness and reactions of physicians and others to parental efforts); see also Garde, *supra* note 183.

¹⁸⁵ *Id.*

¹⁸⁶ Robertson, *supra* note 173, at 479; see also NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 81; Michael Sandel, *The Case Against Perfection*, ATLANTIC (Apr. 2004), <https://www.theatlantic.com/magazine/archive/2004/04/the-case-against-perfection/302927> (“The real question is whether we want to live in a society where parents feel compelled to spend a fortune to make perfectly healthy kids a few inches taller.”).

¹⁸⁷ See King, *supra* note 70, at 312.

¹⁸⁸ Leon R. Kass, *The Wisdom of Repugnance*, NEW REPUBLIC, June 2, 1997, at 24.

¹⁸⁹ *Id.* at 25.

¹⁹⁰ See Marcy Darnovsky & Katie Hasson, *CRISPR's Twisted Tales: Clarifying Misconceptions about Heritable Genome Editing*, 63 PERSPS. IN BIOLOGY & MED. 155, 163 (2020); Seema Mohapatra, *Politically Correct Eugenics*, 12 FL. INT'L UNIV. L. REV. 51, 69 (2016) (citing to Rob Stein, *Breaking Taboo, Swedish Scientist Seeks to Edit DNA of Healthy Human Embryos*, NPR (Sept. 22, 2016, 5:07 AM), <http://www.npr.org/sections/>

extend to a concern about whether certain races may be targeted for exclusion within the germline gene editing context. While the term “eugenics,” is often viewed as a loaded term with negative connotations due to historical examples, Professor Sonia Suter has observed that “this alone does not support the implication that eugenics is per se problematic.”¹⁹¹ Nevertheless, in America, the eugenics movement was implicated in the efforts of certain organizations to increase contraceptive usage by certain races, notably African-Americans, under the theory that “this population was unfit to have children.”¹⁹² These same eugenics concerns from the contraceptive context also arise in the context of germline gene editing, although it is expected that the relevant actors will be private actors and not government actors.¹⁹³

Germline gene editing technologies have led to a subset of eugenics concerns, referred to as “neoeugenics” or “liberal eugenics.”¹⁹⁴ Neoeugenics or liberal eugenics, unlike the eugenics of the past, which focused on state action, would arise from private action.¹⁹⁵ Neoeugenics also encompasses a broader effort to select or design children.¹⁹⁶ Because neoeugenics implicates private action instead of state action and “fundamental decisions about parenting[,] . . . some aspects of it arguably fall within a fundamental liberty or privacy interest.”¹⁹⁷ At the same time, because neoeugenics focuses on private actors, it leads to concerns that those with more financial resources will have an advantage over those with fewer resources.¹⁹⁸ To the extent that ART

health-shots/2016/09/22/494591738/breaking-taboo-swedish-scientist-seeks-to-edit-dna-of-healthy-human-embryos).

¹⁹¹ See Suter, *supra* note 13, at 899. For more on eugenics practices that led to a negative connotation of the word, see *id.* at 901–02, 906–16.

¹⁹² See Mohapatra, *supra* note 190, at 55, 57 (discussing the sterilization of minority women “without their knowledge or consent”).

¹⁹³ *Id.* at 55 (“Americans were themselves interested in how to create a perfect child that lacked heritable conditions such as feeble-mindedness or alcoholism.” One could expect that Americans would be interested in preventing the passage of certain heritable conditions that would be viewed as disabilities by the majority but not necessarily as such by those who are affected by those conditions, both directly or indirectly (such as those who have family members with the condition).”); see also *id.* at 73–78 (discussing “ableism” and neglected disability perspectives in medical discussions).

¹⁹⁴ See Nicholas Agar et al., *The Debate over Liberal Eugenics*, 36 HASTINGS CTR. REP. 4, 4–7 (Mar.–Apr. 2006); Nicholas Agar, *Liberal Eugenics*, 12 PUB. AFF. Q. 137, 137 (1998); Suter, *supra* note 13, at 898.

¹⁹⁵ See Agar, *Liberal Eugenics*, *supra* note 194; Suter, *supra* note 13, at 900.

¹⁹⁶ See, e.g., *id.* at 937.

¹⁹⁷ *Id.* at 949; see also Michael Sandel, *The Case Against Perfection*, ATLANTIC (Apr. 2004), <https://www.theatlantic.com/magazine/archive/2004/04/the-case-against-perfection/302927> (discussing “‘privatized’ or ‘free-market’ eugenics”).

¹⁹⁸ Agar, *Liberal Eugenics*, *supra* note 194; Suter, *supra* note 13, at 959.

users tend to be wealthier individuals, a group with fewer minorities in the U.S., these eugenics concerns connect to concerns about access and use of gene editing technologies similar to those related to ART.¹⁹⁹

In addition to concerns about how views on superior or preferred traits (or even races) might impact those who would be seen as undesirable by the majority (or those who would regulate access to gene editing technologies), there is also a concern that some individuals may feel forced to use germline gene editing technologies.²⁰⁰ Under that theory, parents who refused to use germline gene editing technologies to correct genetic disadvantages might be denied access to societal aid “because they could not fairly push the cost of their choices off on other members of the insurance pool” or avail themselves of other common societal measures, such as special education and some forms of public assistance.²⁰¹ This concern also connects to a broader concern about access to healthcare and disparities in access to healthcare, as analyzed through the lenses of race and economics.²⁰²

3. Disparities and Inequality

There are also concerns regarding economic disparities, as well as physical, intellectual, and social disparities, which might arise or broaden with the advent of gene editing technologies. The Nuffield Council on Bioethics, for example, has recommended that heritable genome editing only be used “in circumstances in which it cannot reasonably be expected to produce or exacerbate social division or the unmitigated marginalization or disadvantage of groups within society.”²⁰³ While this is certainly a noble goal, it is hard to see how one could orchestrate such a position. Thus, this concern about disparities and inequality connects to concerns about disability and a hierarchy of disease, which will be discussed *infra*. Concerns about economic disparities are also connected to concerns about racial disparities and eugenics. Additionally, somatic and germline gene editing technologies

¹⁹⁹ See MARSH & RONNER, *supra* note 17, at 5 (discussing the racial shift in ART use); Mohapatra, *supra* note 190, at 69–70.

²⁰⁰ See *id.* at 79.

²⁰¹ Rakowski, *supra* note 11, at 1345, 1353, 1392, 1398.

²⁰² Kimberly M. Mutcherson, *Procreative Pluralism*, 30 BERKELEY J. GENDER L. & JUST. 22, 43 (2015).

²⁰³ NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 87.

are similar to other forms of ART, health care policy, and law in general, insofar as they are accompanied by access-related concerns.²⁰⁴

In addition to concerns about disparities, there are other broader equality concerns. For example, one scholar argues that parents who could transmit genes that would “reduce their children’s life expectancy or greatly impair their quality of life” should have a right to funding for fertility treatments, or else their children would be unequal to other children.²⁰⁵ This argument suggests that gene editing should not only be legally available but subsidized—an argument that has also been made about IVF.²⁰⁶ While the number of states mandating insurance coverage of ART is increasing, generally, polities do not agree that parents have a right to funding for fertility treatment.²⁰⁷ That being said, “genes are not all-determining: [h]eritability and determinism are very different things.”²⁰⁸

More broadly, while certain uses of germline gene editing may ameliorate inequality, such as when parents can give birth to children who do not have devastating conditions, uses of germline gene editing that might lead to enhancement or the idea that some children have “better” traits than others, such as increased intelligence or better athletic ability, could exacerbate inequality.²⁰⁹ In sum, ART and—by extension—germline gene editing, will continue to be accompanied by equality-based concerns related to “equality of access to ARTs (and thus parenthood), equal treatment in the resolution of disputes arising from

²⁰⁴ See, e.g., Jorge L. Contreras & Jacob S. Sherkow, *CRISPR, Surrogate Licensing, and Scientific Discovery*, 355 *SCIENCE* 698 (2017) (discussing litigation related to ownership of and access to gene editing technologies); Arti K. Rai, *Genetic Interventions: (Yet) Another Challenge to Allocating Health Care*, 39 *SAN DIEGO L. REV.* 657, 664–67 (2002) (discussing distributive justice in the context of genetic interventions).

²⁰⁵ Lauren R. Roth, *Reproductive Selection Bias*, 27 *HEALTH MATRIX* 263, 267 (2017).

²⁰⁶ MARSH & RONNER, *supra* note 17, at 206.

²⁰⁷ See, e.g., *State Laws Related to Insurance Coverage for Infertility Treatment*, NAT’L CONF. OF ST. LEGISLATURES (June 12, 2019), <https://www.ncsl.org/research/health/insurance-coverage-for-infertility-laws.aspx>; Maridel Reyes, *New Law in New York Means Most Insurance Plans Will Now Cover IVF*, N.Y. POST (Oct. 7, 2019), <https://nypost.com/2019/10/07/new-law-in-new-york-means-most-insurance-plans-will-now-cover-ivf>.

²⁰⁸ See, e.g., Suter, *supra* note 13, at 940.

²⁰⁹ See Mary Crossley, *Dimensions of Equality in Regulating Assisted Reproductive Technologies*, 9 *J. GENDER, RACE, & JUST.* 273, 273–74 (2005) (noting that ART can exacerbate or ameliorate inequality); King, *supra* note 70, at 346–48 (discussing various countries’ regulation of PGD to limit it to “devastating” conditions or those causing “severe impairment” and other terms that establish a hierarchy in diseases and limit the application of PGD to some of the conditions that it could be used to select for); see also *infra* notes 213–20 and accompanying text (discussing efforts to distinguish between various diseases).

the use of ARTs, and equality issues raised by trait-selection practices.”²¹⁰ While many would argue that these disparity-based concerns should prohibit germline gene editing, these concerns have not been sufficient to prohibit many other forms of ART and health care in general.²¹¹

4. Hierarchy of Disease

Not only is there a dispute related to what constitutes a “disease,” there is also a debate as to which “diseases” merit prioritization.²¹² For example, as illuminated by the response to the announcement of the birth of the first “CRISPR babies,” Lulu and Nana in China, many researchers further divide “disease” into categories where some merit interventions or intellectual focus faster or “more than” other diseases.²¹³ For example, part of the opposition to the use of germline gene editing in embryos by Dr. He Jiankui in China, which was purportedly motivated by a desire to confer HIV immunity so that the children would not be affected by their father’s HIV-positive status, was that other methods existed for preventing the transmission of HIV to embryos.²¹⁴ Specifically, ART (without genetic modification) could have achieved prevention of HIV transmission to the offspring or the HIV-negative parent.²¹⁵ Some observers within the medical communities were surprised that germline gene editing was used to target HIV, for which effective methods of avoiding transmission from parent to child

²¹⁰ Crossley, *supra* note 209, at 274.

²¹¹ Darnovsky & Hasson, *supra* note 42, at 164.

²¹² NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 148 (2017) (“Everyone would agree that the manifestation of Tay-Sachs disease is not normal and constitutes a disease, but opinions differ as to whether genetically caused deafness should be considered a disease.”).

²¹³ See, e.g., *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 20 (providing the Prepared Statement of Dr. Jennifer Doudna, which refers to “severe diseases in humans”).

²¹⁴ For more on the opposition to the work of Dr. He Jiankui in the creation of the “first CRISPR babies,” see, for example Greely, *supra* note 54; Kolata & Belluck, *supra* note 55; see also Maryam Zafer et al., *Effectiveness of Semen Washing to Prevent HIV Transmission and Assist Pregnancy in HIV-Discordant Couples: A Systematic Review and Meta-Analysis*, 105 FERTIL STERIL 645 (2016) (showing that there are other ways to prevent transmission of HIV in ART and reproduction, namely “sperm washing”); Pam Belluck, *How to Stop Rogue Gene-Editing of Human Embryos?*, N.Y. TIMES (Jan. 23, 2019), <https://www.nytimes.com/2019/01/23/health/gene-editing-babies-crispr.html>; Sui-Lee Wee & Elsie Chen, *In China Gene-Edited Babies Are the Latest in a String of Ethical Dilemmas*, N.Y. TIMES (Nov. 30, 2018), <https://www.nytimes.com/2018/11/30/world/asia/gene-editing-babies-china.html>.

²¹⁵ *But see id.* (noting difficulties in obtaining access to IVF for those with “sexual diseases,” including HIV, in China).

in ART already exist, instead of other diseases.²¹⁶ When the NAS analyzed the propriety of germline gene editing, for example, it recommended that clinical trials related to gene editing technologies be restricted to “preventing a serious disease or condition.”²¹⁷ The NAS report did not define what would constitute a “serious disease or condition,” but instead noted that different societies would have different interpretations of the concept.²¹⁸ Some professors, like Julian Savulescu and Peter Singer, have argued for a hierarchy that prioritizes “catastrophic single-gene disorders (like Tay-Sachs disease), then severe single-gene disorders (like Huntington’s disease), then reduction in the genetic contribution to common diseases (like diabetes and cardiovascular disease), then enhanced immunity and perhaps even delaying ageing.”²¹⁹

The NAS report also expressed that the criteria for human germline gene editing should include a regulatory system with “reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition.”²²⁰ While the FDA’s definition of “serious disease or condition” was mentioned as a possible starting point for a definition, the experience of the FDA with off-label uses of approved drugs might also show how difficult such a criterion would be to implement in practice.²²¹ Once a product is approved for one use by the FDA, it can be prescribed by doctors for other uses. In such an instance, the FDA has very few options to prevent these uses, other than providing restrictions on the marketing of the drugs for such purposes, in the absence of any adverse events.²²²

²¹⁶ See David Cyranoski, *CRISPR-Baby Scientist Fails to Satisfy Critics* (Nov. 30, 2018), NATURE, <https://www.nature.com/articles/d41586-018-07573-w>; Greely, *supra* note 6, at 139–40, 168 (noting that “HIV infection must be counted as a ‘serious disease or condition,’ although not nearly as serious as it used to be”).

²¹⁷ NAT’L ACADS. SCIS., ENG’G AND MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE, *supra* note 50, at 7.

²¹⁸ *Id.* at 8.

²¹⁹ Julian Savulescu & Peter Singer, *An Ethical Pathway for Gene Editing*, 33 BIOETHICS 221, 222 (2019).

²²⁰ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 8.

²²¹ See, e.g., *id.*

²²² See, e.g., Darnovsky & Hasson, *supra* note 42, at 161; Randall S. Stafford, *Regulating Off-Label Drug Use—Rethinking the Role of the FDA*, 358 N. ENG. J. MED. 1427, 1427 (2008).

Julia Mahoney and Gil Siegal observe that germline gene editing could reduce inequalities by “lead[ing] to the births of fewer humans with serious genetic diseases.”²²³ While this would not minimize access concerns, it would lead to the question of whether parents should feel obligated to use genome editing to prohibit the transmission of harmful genetic traits.²²⁴ At the same time, an often-neglected aspect of the debate is whether those with disabilities or traits that the mainstream public considers “undesirable,” an issue that was discussed earlier in this Part, might decide that this is a trait that they would like to perpetuate in future generations as parents.²²⁵

C. *Morality Concerns Related to the “Moral Status” of Embryos and the Proper Role of Humans*

Abortion is a significant part of the United States debate related to reproductive rights.²²⁶ For many, their opposition to abortion stems from the idea that a fetus is a person and/or that embryos occupy a special or moral status that should disfavor experimentation, the creation of embryos, or the destruction of embryos.²²⁷ As a result, debate over the origin of life and whether techniques that lead to the destruction of embryos or experimentation on embryos (which often leads to their destruction) surfaces in opposition to ART and germline

²²³ Mahoney & Siegal, *supra* note 142, at 210 (discussing “the present generation’s use of PGD and selective termination”); *see also* American Society of Hematology, *Transplant Community & Sickle Cell Disease Advocates Urge Congress to Advance Policies Supporting Sickle Cell Disease Research and Treatment*, PR NEWSWIRE (June 7, 2017), <https://www.prnewswire.com/news-releases/transplant-community--sickle-cell-disease-advocates-urge-congress-to-advance-policies-supporting-sickle-cell-disease-research-and-treatment-300470496.html> (quoting Congresswoman Doris Matsui: “Too often, people with devastating blood disorders like sickle cell disease face significant barriers to treatment. We need to be opening up more options for patients and making the federal investments in research that will accelerate the development of cures.”).

²²⁴ *See* Polcz & Lewis, *supra* note 42, at 419, 425 (discussing disability concerns in the context of somatic (non-germline) use of CRISPR-Cas9).

²²⁵ *See, e.g.,* Pontin, *supra* note 16 (quoting Professor Henry T. Greely of Stanford University) (“What if there are parents who wanted to select for Tay-Sachs disease? There are plenty of people in Silicon Valley who are somewhere on the spectrum, and some of them will want children who are neuro-atypical.”); *see also* Polcz & Lewis, *supra* note 42, at 420, 425.

²²⁶ NUFFIELD COUNCIL ON BIOETHICS, *GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES*, *supra* note 26, at 109.

²²⁷ *See, e.g.,* Dan W. Brock, *Creating Embryos for Use in Stem Cell Research*, J.L. MED. & ETHICS 229, 229–37 (2010); Dan W. Brock, *Is a Consensus Possible on Stem Cell Research? Moral and Political Obstacles*, 32 J. MED. ETHICS 36, 36–42 (2006); Henry T. Greely, *Human Germline Genome Editing: An Assessment*, 2 CRISPR J. 253, 258–59 (2019) (discussing the “moral status” of the embryo).

gene editing.²²⁸ Often these concerns about the status of embryos and the proper role of humans in using scientific and medical innovation to change future outcomes are based on or related to religious views.²²⁹

1. Hubris, Sanctity of Nature, and Religious Concerns

The notion that germline gene editing is not an action that humans should undertake is sometimes grounded in the idea that humans are “playing God” by editing the human germline, which is seen as common to humanity.²³⁰ Concerns about the proper actions of humans in relation to a higher power, the “hubris” of humans, and the idea that they are “playing God” are expressed in varying language including references to the “sanctity of nature.”²³¹

These concerns surface in various sects’ religious views, which also often oppose ART in general, in addition to secular views. For example, the idea of “dignity” is often mentioned in documents issued by the Catholic Church in relation to its condemnation of IVF and the storage and manipulation of embryos.²³² The U.S. Council of Catholic Bishops has noted that IVF is “[o]ne reproductive technology which the Church

²²⁸ NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 109, 174.

²²⁹ *Id.* at 109.

²³⁰ See, e.g., NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 124; Sarah M. Markwood, *Creating a Perfect Human Is Not So Perfect: The Case for Restricting Genetic Enhancement Research*, 110 PENN ST. L. REV. 473, 487–88 (2005); Kelly E. Ormond et al., *Human Germline Genome Editing*, 101 AM. J. HUM. GENETICS 167, 172 (2017); Savulescu, *supra* note 159; Arthur Caplan & Carolyn Plunkett, *Get Out of the Way of Human Genetic Engineering? Unwise and Uncalled For*, FORBES (June 7, 2016), <https://www.forbes.com/sites/arthurcaplan/2016/06/07/get-out-of-the-way-of-human-genetic-engineering-unwise-and-uncalled-for>.

²³¹ See, e.g., NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 112, 124; Caplan & Plunkett, *supra* note 230.

²³² See, e.g., Anna Louie Sussman, *When the Government Seizes Your Embryos*, NEW YORKER (Oct. 22, 2019), <https://www.newyorker.com/tech/annals-of-technology/when-the-government-seizes-your-embryos> (discussing the Vatican’s *Instruction Dignitas Personae on Certain Bioethical Questions*); see also *Congregation for the Doctrine of the Faith: Instruction on Respect for Human Life and in its Origin and on the Dignity of Procreation Replies to Certain Questions of the Day*, HOLY SEE, http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_19870222_respect-for-human-life_en.html (endnote omitted) (citing *Charter of the Rights of the Family, 4b: L’Osservatore Romano*, HOLY SEE (Nov. 25, 1983), http://www.vatican.va/roman_curia/pontifical_councils/family/documents/rc_pc_family_doc_19831022_family-rights_en.html) (“The *Charter of the Rights of the Family* published by the Holy See affirms: ‘Respect for the dignity of the human being excludes all experimental manipulation or exploitation of the human embryo.’”); see also *Congregation for the Doctrine of the Faith: Instruction Dignitas Personae on Certain Bioethical Questions*, HOLY SEE (Dec. 2008), http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_20081208_dignitas-personae_en.html.

has clearly and unequivocally judged to be immoral,” although the Church states that “[l]ike all children, regardless of the circumstances of their conception and birth, they should be loved, cherished and cared for.”²³³ IVF has also been construed as “do[ing] violence to human dignity and to the marriage act.”²³⁴ Despite these views, ARTs, including artificial insemination and IVF, are permissible in many countries, including the United States, and not condemned by all sects of Christianity or by many other religions, with certain complexities.²³⁵

Dignity also arises in discussions of germline modification. Some worry that germline gene editing could result in the possibility of “legally devalu[ing]” or “violat[ing] . . . [the] dignity” of those who are conceived using human germline editing or could be conceived using germline gene editing.²³⁶ Secular views on the possibility that germline gene editing could violate principles of dignity tend to emphasize the lack of autonomy on the part of the germline gene edited person.²³⁷ On the other hand, there is a concern that prohibiting germline gene editing could violate the dignity of future persons by not preventing suffering when possible.

Many observers, including politicians, government employees, and scientists, have expressed opposition to technologies that modify the genetic makeup of humans on various grounds. For example, during the debate over the 2017 Federal Appropriations Bill, Congressman Aderholt, a Republican from Alabama, noted, “The bill also includes a prohibition on gene editing of human embryos. This is a tremendous

²³³ John M. Haas, *Begotten Not Made: A Catholic View of Reproductive Technology*, UNITED STATES COUNCIL OF CATHOLIC BISHOPS (1998), <http://www.usccb.org/issues-and-action/human-life-and-dignity/reproductive-technology/begotten-not-made-a-catholic-view-of-reproductive-technology.cfm>.

²³⁴ *Id.*

²³⁵ See Ariana Eunjung Cha, *Fertility Frontiers: Gifts from God: How Religion is Coming to Terms with Modern Fertility Methods*, WASH. POST (Apr. 27, 2018), <https://www.washingtonpost.com/graphics/2018/national/how-religion-is-coming-to-terms-with-modern-fertility-methods> (discussing Catholic, Islamic, and Jewish views on ART’s acceptability); see also Cynthia B. Cohen, *Protestant Perspectives on the Uses of the New Reproductive Technologies*, 30 FORDHAM URB. L.J. 135, 135–37, 145 (2002); H.N. Sallam & N.H. Sallam, *Religious Aspects of Assisted Reproduction*, 8 FACTS, VIEWS & VISION IN OBGYN 33, 33 (2016).

²³⁶ GERMAN ETHICS COUNCIL, *supra* note 45, at 17. *But see id.* at 26 (“[T]he withholding of a possible germline intervention could be interpreted as a violation of the future child’s dignity, since the child would be unable to benefit from an important therapeutic possibility.”).

²³⁷ Charo, *supra* note 65, at 95.

victory for those who are concerned about life.”²³⁸ At the same time, while Representative Aderholt referred to “life” and how preventing germline gene editing would be a victory, in another statement he did not mention life and instead combined scientific and ethical concerns: “The ethics hadn’t caught up with the science, and . . . the science has not caught up with the science,’ . . . for now, genetically editing embryos had ‘too many unknowns, too many unintended consequences.’”²³⁹ This is one of many statements that represents the tendencies of legislators and regulators to combine safety and ethical concerns when faced with technologies that they find politically and ethically objectionable. Some of the views discussed in this subsection resurface in discussions about the inviolability of the human germline and the shared human identity.²⁴⁰

2. Commodification

Opposition to germline gene editing is often connected to opposition to the commodification of humanity, the human body, human traits more broadly, or opposition to assisted reproduction.²⁴¹ Many of these concerns arise with various forms of assisted reproduction. For example, gestational surrogacy, which also uses IVF, led to predictions that “baby brokers could begin to advertise their babies [similar to how chicken producers advertise their chickens based on superior breeding and feeding]: brand-name, state-of-the-art babies produced from the ‘finest’ of genetic materials and an all-natural vitamin-enriched diet.”²⁴² Surrogacy also raises the specter of exploitation, as many object to it on the theory that richer individuals take advantage of poor women.²⁴³ Those who express commodification-related objections to ART also note that permitting these techniques, which have commercial aspects,

²³⁸ 163 CONG. REC. H3071 (2017); see also Representative Robert B. Aderholt, CONGRESS.GOV, <https://www.congress.gov/member/robert-aderholt/A000055>.

²³⁹ Andrew Joseph, *Congress Revives Ban on Altering the DNA of Human Embryos Used for Pregnancies*, SCI. AM. (June 5, 2019), <https://www.scientificamerican.com/article/congress-revives-ban-on-altering-the-dna-of-human-embryos-used-for-pregnancies>.

²⁴⁰ See *supra* Section III.C.1.

²⁴¹ See, e.g., Caplan & Plunkett, *supra* note 230. For more on the imprecision of the term “commodification,” as commonly used, see I. Glenn Cohen, Note, *The Price of Everything, the Value of Nothing: Reframing the Commodification Debate*, 117 HARV. L. REV. 689 (2003).

²⁴² Karen Busby & Delaney Vun, *Revisiting The Handmaid’s Tale: Feminist Theory Meets Empirical Research on Surrogate Mothers*, 26 CAN. J. FAM. L. 13, 42 (2010) (citing BARBARA KATZ ROTHMAN, RECREATING MOTHERHOOD, IDEOLOGY AND TECHNOLOGY IN A PATRIARCHAL SOCIETY 237 (1989)).

²⁴³ Charo, *supra* note 65, at 96.

will lead to parental relationships in which “children [are] commodities rather than subjects of parental love, and that it will lead to the stigmatization of the disabled.”²⁴⁴ Professor Alta Charo has noted that these concerns related to commodification and the stigmatization of disabilities have accompanied “prenatal screening, gamete donation, IVF, surrogacy, PGD, and cloning.”²⁴⁵ Thus, issues related to commodification often implicate other ethical concerns that arise in the context of germline gene editing. So far, these ethical concerns have not prohibited the use of ART or the fertility industry generally: the United States has almost 500 fertility clinics and the revenue of the worldwide fertility market is estimated to be \$25 billion today, with the expectation that “by 2026 the global fertility industry could rake in \$41 [billion] in sales.”²⁴⁶

D. Concerns Related to the Future of the Human Race

Objections to germline gene editing also encompass the idea that humans are interfering with the will of God or nature.²⁴⁷ These objections have also arisen with medicine in general and more specifically, ART and techniques permitting parents to “select” for certain children, both using IVF and PGD, and also using prenatal testing. As noted by the Nuffield Council on Bioethics, many academic sources and international legal documents such as those promulgated by the United Nations have connected the idea of the human genome “and the enjoyment of human rights (or the possession of human dignity)” although, this connection “does not appear necessary.”²⁴⁸ The ideas of human dignity and human rights tend to surface more in non-U.S. traditions.²⁴⁹

²⁴⁴ *Id.* at 95.

²⁴⁵ *Id.*

²⁴⁶ *The Fertility Business is Booming*, ECONOMIST (Aug. 8, 2019), <https://www.economist.com/business/2019/08/08/the-fertility-business-is-booming>; see also Rebecca Robbins, *Investors See Big Money in Infertility. And They're Transforming the Industry*, STAT NEWS (Dec. 4, 2017), <https://www.statnews.com/2017/12/04/infertility-industry-investment>. For more on commodification in relation to the fertility market, see Martha M. Ertman, *What's Wrong with a Parenthood Market? A New and Improved Theory of Commodification*, 82 N.C. L. REV. 1, 3–21 (2003).

²⁴⁷ NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 67.

²⁴⁸ *Id.* at xvii, 93–94 (discussing human dignity in the context of the United Nations' Universal Declaration of Human Rights).

²⁴⁹ *Id.* at xvii–xviii, 114–32. It is worth noting that many international legal frameworks addressed by the Nuffield Council on Bioethics do not apply to the United States. Further, international law includes both “hard law” (binding law) and “soft law” (non-binding documents and norms). For more on international laws related to

1. The Morality of Enhancement

There is also a concern that germline gene editing could be used for human enhancements, to the extent that one could define an enhancement, which then leads to objections to germline gene editing.²⁵⁰ Such a concern is often classified as a “slippery slope” concern.²⁵¹ Applying Professor Eugene Volokh’s analysis of slippery slopes to germline gene editing, one might think that idea A, using germline gene editing to prevent the birth of children with harmful genetic diseases like Tay-Sachs or sickle cell anemia, may sound like a good idea, “or at least not a very bad one. But you’re afraid that A might eventually lead other legislators, voters, or judges to implement policy B, [germline gene editing for enhancement purposes such as above-average intelligence or greater height,] which you strongly oppose.”²⁵² While slippery slopes can be used in support of opposition to germline gene editing, as acknowledged by the National Academies of Sciences, supporters of germline gene editing also invoke arguments related to slippery slopes.²⁵³ These slippery slope arguments are connected to contentions such as those related to hierarchies of disease and an

germline gene editing, see, for example *id.* at 106–09; NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 132–33.

²⁵⁰ Kohn et al., *supra* note 23, at 2554 (“Given that our understanding of the genome is still rudimentary, editing with intent to ‘improve’ is fraught with many caveats, not the least of which is that we do not know, may never know, or nor even be able to define what an ‘improved’ genome would look like.”); Suter, *supra* note 13, at 898, 933–34 (2007); Antonio Regalado, *Engineering the Perfect Baby*, TECH. REV. (Mar. 5, 2015), <https://www.technologyreview.com/s/535661/engineering-the-perfect-baby> [<https://perma.cc/4Z95-N87G>] (archived Jan. 26, 2017); *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 32–33 (providing Testimony of Dr. Jeffrey Khan which highlighted the concern for the use of gene editing for reasons related to selecting “physical or behavioral traits or even enhancements” instead of for disease treatment or avoidance). For more on the debate over the term “enhancement,” see, for example Savulescu, *supra* note 159; see also Wesley W. Chen, *Human Germline Gene Editing: Engineering an Unstoppable Train*, 28 S. CAL. INTERDISC. L.J. 523, 535 (2019) (“[C]ritics might argue that eugenics sits on a slippery slope and if we allow the possibility of ‘breeding out’ negative characteristics, we will eventually find ourselves back in the 1940s alongside the atrocities of the Holocaust . . . [and] even if society does not descend to such depths, the very concept of eugenics is discriminatory because it suggests that some lives are not worth living.”); see, e.g., NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 9 (also noting the difficulty of defining an enhancement).

²⁵¹ Eugene Volokh, *The Mechanisms of the Slippery Slope*, 116 HARV. L. REV. 1026, 1028 (2002); NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 53–55; Baltimore et al., *supra* note 43, at 37.

²⁵² Volokh, *supra* note 251, at 1028; see also *id.* at 1103–04 (discussing “attitude-altering slippery slopes” and “small change tolerance slippery slopes”).

²⁵³ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 128–30.

acknowledgment that germline gene editing can be used for benevolent and potentially malevolent uses (as “enhancement” related uses might be categorized).²⁵⁴ In other words, the continuum that is used to categorize various uses of ART is related to the “slippery slope” style argument discussed above.²⁵⁵

This Article does not argue for a moratorium on germline gene editing because of its potentially malevolent uses. Some scientists, regulators, and observers would ban all uses of germline gene editing so as to avoid the possibility of its use for human enhancement, such as improving intelligence beyond naturally occurring capacities, increasing height, or even changing a child’s eye color or muscle composition.²⁵⁶ Arguments related to the morality of enhancement take varying forms. Some observers are concerned that once enhancement is permitted for “clear” medical or therapeutic purposes, such as specific genetic diseases, that there will be a “slippery slope” to enhancement-related uses such as increased height or intentionally improved intelligence.²⁵⁷ For the purposes of this Article, the debate between the morality of enhancement and medical treatment, as a baseline, will start with the idea that medical treatment “aims to eradicate diseases . . . whereas [enhancement] aims to improve what is ‘normal.’”²⁵⁸ As a result, discussions of germline gene editing involve the same debates about enhancement, eugenics, and “designer babies” that other technologies, such as Recombinant DNA and some forms of ART, have invoked.²⁵⁹

To the extent that germline gene editing would be used for non-disease related purposes, for many, there would be additional opposition or the expectation that genetic “enhancement” should be treated differently than genetic editing to address disease.²⁶⁰ For example, the National Academies of Sciences similarly noted this concern and recommended that germline gene editing be used only to

²⁵⁴ *Id.* See discussion *infra* Section III.B.4. (“Hierarchy of Disease”).

²⁵⁵ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 128.

²⁵⁶ See Lander, *infra* note 284.

²⁵⁷ See, e.g., Caplan & Plunkett, *supra* note 230.

²⁵⁸ Suter, *supra* note 13, at 933.

²⁵⁹ Carolyn P. Neuhaus & Arthur L. Caplan, *Genome Editing: Bioethics Shows the Way*, PLOS ONE (2017), <https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2001934>; Joseph Fletcher, *Ethics and Recombinant DNA Research*, 51 S. CAL. L. REV. 1131, 1133–38 (1978); Robertson, *supra* note 34, at 441; Judith P. Swazey, James R. Sorenson & Cynthia B. Wong, *Risks and Benefits, Rights and Responsibilities: A History of the Recombinant DNA Research Controversy*, 51 S. CAL. L. REV. 1019, 1046–51 (1978).

²⁶⁰ Rai, *supra* note 204, at 665.

prevent disease or disability.²⁶¹ A few public opinion polls exist on the subject of germline gene editing.²⁶² Some polls indicate large-scale public support for “genome editing to prevent genetic disease, if determined to be safe,” but not gene editing for enhancement purposes.²⁶³ At the same time, it is acknowledged that this “largely unenthusiastic” position on enhancement could stem from a number of sources of skepticism, as many commonly accepted phenomena were the subject of skepticism early in their inception.²⁶⁴

Many enhancement-related arguments tend to jump straight to the creation of individuals who would be exponentially superior to existing humans, although there are also concerns about incremental changes. Genetic enhancement for many traits is unlikely. For example, “intelligence,” is a trait that is based on “complex interactions among multiple genes and environments.”²⁶⁵ At the same time, arguments about enhancement tend to ignore how “enhancement” might fit within the purview of the many “unnatural” actions that doctors undertake every day, such as transplanting organs, creating and using vaccines that convey unnatural immunities, and other medical treatments that undo the natural progression of diseases, such as LASIK eye surgery.²⁶⁶

Nevertheless, the above discussion of the difficulty of identifying a “serious disease or condition,” *see supra* Section III.B.4., parallels the difficulty of defining the difference between a therapeutic use and an enhancement-based use.²⁶⁷ These difficulties have not, however, prohibited parents from being permitted to selectively choose reproductive partners or gamete donors based on certain desirable traits, or from selecting certain embryos based on their genetic or sex-based preferences.²⁶⁸ Slippery slope concerns have surfaced not only in

²⁶¹ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 13.

²⁶² *See id.* at 140–43.

²⁶³ Daley et al., *supra* note 49, at 899.

²⁶⁴ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 144.

²⁶⁵ *Id.*; *see also* Savulescu & Singer, *supra* note 219, at 222 (noting that “China is currently funding research that is trying to unravel the genetics of high intelligence”) (citation omitted).

²⁶⁶ *See, e.g.*, Kenan Malik, *The Three-Parent Baby’s First Step*, N.Y. TIMES (Feb. 22, 2015), <http://www.nytimes.com/2015/02/23/opinion/the-three-parent-babys-first-step.html>; *LASIK Eye Surgery* (Nov. 8, 2019), <https://www.mayoclinic.org/tests-procedures/lasik-eye-surgery/about/pac-20384774>

²⁶⁷ *But see* Cohen, *supra* note 170, at 676 (challenging the usefulness of the enhancement distinction).

²⁶⁸ *See, e.g.*, NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 13; Cohen, *supra* note 170, at 678

the context of genetic modification (including a possible slippery slope from research to reproduction) but also in the context of ART and PGD.²⁶⁹ The National Academies of Sciences, for example, noted in its study of genome editing:

IVF, for example, was originally developed to circumvent fallopian tube blockage. It soon was extended, however, to circumventing naturally age-related decline in fertility and even postmenopausal infertility, and later became an enabling technology for PGD. Likewise, PGD was originally designed to select against embryos with serious deleterious mutations but later was expanded to conditions that not all agree are diseases or disabilities, as well as to sex selection.²⁷⁰

Ultimately, as a matter of the potential widespread effects of reproductive technologies, especially those using genetic modification, many members of society have not decided to use arguably enhancement-related options such as using ART instead of sex, sex selection of embryos, or selection of certain gamete donors based on certain enhancement-related traits such as Nobel Prize wins.²⁷¹

2. The “Inviolability” of the Human Germline

Like concerns about the dignity of the human race and whether humans should cross certain lines, many opponents of germline gene editing simply state that the human germline is an inviolable line that “should not be crossed.”²⁷² These arguments assert that there is a significance to the human germline which leads to a determination that interventions affecting the human germline should not occur.²⁷³ Nevertheless, positions on the inviolability of the human germline are changing. In May 2019, the German Ethics Council announced that it unanimously disagrees with the idea that the human germline is

(“[E]specially in terms of enhancing our children, it is important to emphasize that we are already deep into a system of enhancement through our marital and non-marital reproductive mate choices.”).

²⁶⁹ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 129, 156; Kane, *supra* note 38, at 320.

²⁷⁰ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 129.

²⁷¹ Cohen, *supra* note 170, at 679 (“So if enhancement by selection of gamete providers is the main way to enhance our children genetically these days, for many potential parents the costs may outweigh the benefits.”); Jennifer Ludden, *Telling the Full Story of ‘The Genius Factory,’* NPR (June 12, 2005), <https://www.npr.org/templates/story/story.php?storyId=4700156> (discussing the “Nobel Prize sperm bank”).

²⁷² GERMAN ETHICS COUNCIL, *supra* note 45, at 17, 18 (referencing “a ‘dignity of the human species.’”); *see also* Caplan & Plunkett, *supra* note 230.

²⁷³ GERMAN ETHICS COUNCIL, *supra* note 45, at 31.

“categorically inviolable.”²⁷⁴ It disagreed with the assertion that the germline was inviolable based on the inability of the germline to “be the object or the substrate of the protection of dignity or life,” and the fact that “the germline is nonetheless constantly being altered as a consequence of natural processes and human action.”²⁷⁵ For example, germline gene editing would target disease-causing mutations in a manner that would lead to inheritable changes in the human genome.²⁷⁶ Yet mutations occur spontaneously in the human genome, and as such, “the genotoxic risk of the editing process . . . should be put into the context of the natural, ongoing genomic mutations that are occurring in cells all of the time.”²⁷⁷ While some individuals are concerned that changes to the human germline are irreversible, the German Ethics Council has noted that one could theoretically use human germline modification on the children of the genetically modified to reverse the germline gene editing that their genetically modified parent or parents were subjected to.²⁷⁸

3. The “Shared Human Identity”

The idea of the “shared human identity” surfaces, with some objecting to the idea that germline gene editing would lead to inheritable changes and “introduce . . . modified genomes into the human genome pool.”²⁷⁹ For example, discussions of evolution and inheritance often center on the idea of a “Mitochondrial Eve,” a hypothetical common ancestor of all members of the human race.²⁸⁰ In 2019, Senator Dianne Feinstein introduced a resolution noting that “the question of whether to proceed with heritable genome editing touches on all humanity,” as part of a condemnation of the actions of Dr. He

²⁷⁴ *Id.* at 39.

²⁷⁵ *Id.*

²⁷⁶ NAT’L INSTS. OF HEALTH, U.S. NAT’L LIBR. OF MED., *supra* note 49.

²⁷⁷ Kohn et al., *supra* note 23, at 2556–57.

²⁷⁸ GERMAN ETHICS COUNCIL, *supra* note 45, at 10.

²⁷⁹ Kohn et al., *supra* note 23, at 2554.

²⁸⁰ See, e.g., Ewen Callaway, *Genetic Adam and Eve Did Not Live Too Far Apart in Time*, NATURE (Aug. 6, 2013), <https://www.nature.com/news/genetic-adam-and-eve-did-not-live-too-far-apart-in-time-1.13478>; Joshua Rapp Learn, *No, a Mitochondrial “Eve” Is Not the First Female in a Species*, SMITHSONIAN MAG. (June 28, 2016), <https://www.smithsonianmag.com/science-nature/no-mitochondrial-eve-not-first-female-species-180959593/#bM6tveasw3S8mRrj.99>; see also Michael Slezak, *Found: Closest Link to Eve, Our Universal Ancestor*, NEW SCIENTIST (Oct. 8, 2014), <https://www.newscientist.com/article/mg22429904-500-found-closest-link-to-eve-our-universal-ancestor/#ixzz5zcfKvSB>.

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 789

Jiankui who purportedly created the first germline gene-edited babies.²⁸¹

This idea of “damage” to the shared human identity is connected to earlier arguments related to hubris and humanity. Nevertheless, these modified genomes would still be human genomes, which separates gene editing from other extraordinary, non-reproductive technologies that could implicate animal traits, such as those that aim to create human-animal hybrids.²⁸² Some observers, including Professor Hank Greely, note that:

The human germline genome is *not* the holy essence of humanity. For one thing, it doesn’t really exist. There are 7.3 *billion* human germline genomes; each of us has a different one. And those genomes change every generation. . . . The DNA changed, through mutation, during each generation.²⁸³

In some instances, the concern is that these modifications will be introduced into the “gene pool,” and these introduced heritable modifications are said to be irreversible unless the children of germline editing agree not to reproduce or to avail themselves of techniques such that they do not pass on their modifications in reproduction.²⁸⁴ Yet, as noted earlier, gene editing is not necessarily irreversible.²⁸⁵

While there is a reference to the “gene pool,” it is worth noting that human germline modification does not automatically impact all humans.²⁸⁶ As of September 2020, the current world population is 7.68

²⁸¹ *Senate Resolution 275—Calling for International Ethical Standards in Genome Editing* Research, 165 CONG. REC. S4813, S4824 (2019); see also Greely, *supra* note 6, at 111, 151–69 (explaining why the author characterized Dr. Jiankui’s experiment as “criminally reckless . . . grossly premature, and deeply unethical”).

²⁸² See Brock Bastian, *The Uneasy Truth About Human-Animal Hybrids*, BBC NEWS (Feb. 22, 2017), <http://www.bbc.com/future/story/20170222-the-uneasy-truth-about-human-animal-hybrids>; Erin Blackemore, *Human-Pig Hybrid Created in the Lab—Here Are the Facts*, NAT’L GEOGRAPHIC (Jan. 26, 2017), <https://www.nationalgeographic.com/news/2017/01/human-pig-hybrid-embryo-chimera-organs-health-science/#close>; L-M Houdebine, *Use of Transgenic Animals to Improve Human Health and Animal Production*, 40 REPRODUCTION DOMESTIC ANIMALS 269 (2005); see also Rebecca A. Ballard, *Animal/Human Hybrids and Chimeras: What Are They—Why Are They Being Created—And What Attempts Have Been Made to Regulate Them*, 12 MICH. ST. U. J. MED. & L. 297 (2008).

²⁸³ Hank Greely, *Why the Panic Over “Designer Babies” Is the Wrong Worry* (Oct. 30, 2017), <https://leapsmag.com/much-ado-about-nothing-much-crispr-for-human-embryo-editing>; see also Greely, *supra* note 227, at 253, 256–57.

²⁸⁴ See Eric S. Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, 567 NATURE 165 (2019); see also Bosley et al., *supra* note 41, at 481.

²⁸⁵ GERMAN ETHICS COUNCIL, *supra* note 45, at 10.

²⁸⁶ Polcz & Lewis, *supra* note 42, at 423; NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 117–18.

billion people.²⁸⁷ Additionally, current estimates indicate that the “number of [gene editing] users would likely be so small as to have little or no effect on population diversity and distribution of traits.”²⁸⁸ The National Academies of Sciences took a similar position in its 2017 report and noted that, if germline gene editing were approved, there would be a “very small” number of cases and “there is little chance of any significant effects on the gene pool in the foreseeable future.”²⁸⁹

* * *

The foregoing discussion has emphasized bioethical considerations that are the source of opposition to germline gene editing technologies, yet there are competing bioethical concerns that weigh in favor of germline gene editing. This Section has highlighted how much of the bioethical opposition to germline gene editing is the same as opposition to ART, which is legally permissible. Further, claims that are often deemed unique to germline gene editing are similar to those accompanying traditional ART. In light of these similarities, the regulatory system, even when incorporating ethical views into regulatory decisions, should not treat germline gene editing differently than ART. This Part has addressed the concerns related to traditional ART that also accompany germline gene editing, before focusing on some concerns that are specific to gene editing.

Autonomy, for example, is a value that emphasizes the decisions of the individual.²⁹⁰ Procreative autonomy or procreative liberty, more specifically, focuses on the rights of parents within procreation, including their decisions before a future child is born.²⁹¹ This procreative autonomy has been used to justify parents’ selection of embryos with certain traits, which is different from modification, but in some cases has the same effect. These two forms of autonomy can be in tension for many philosophers, and for some philosophers or observers, this tension should be resolved in favor of the future child (and in favor of not modifying, or more specifically, enhancing, the child).²⁹²

²⁸⁷ See *U.S. and World Population Clock*, U.S. CENSUS BUREAU, <https://www.census.gov/popclock>.

²⁸⁸ See also Bosley et al., *supra* note 41, at 481 (providing the statement of R. Alta Charo on population genetics and germline engineering); Greely, *supra* note 283.

²⁸⁹ NAT’L ACADS. SCIS., ENG’G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 118.

²⁹⁰ See Suter, *supra* note 13, at 900, 921.

²⁹¹ Robertson, *supra* note 165, at 953–55.

²⁹² NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 69 (summarizing the views of Michael Sandel, as it relates to the harms of enhancing a future child, and Joel Feinberg as it relates to “anticipatory autonomy rights”).

Concerns related to disability rights and eugenics have also persisted with ART and healthcare innovation in general. Nevertheless, these concerns have not merited federal control over reproduction, or more specifically, ART in the United States. Similarly, while both federal and state debates have centered on morality concerns related to the moral status of embryos, as noted in the longstanding abortion debate in the United States and the broader field of reproductive rights, the fact that embryos can be discarded in ART and experimented on has not prohibited the legality of ART in the United States, although it has corresponded with funding restrictions and some state-based research restrictions as well.²⁹³

Ultimately, many of the bioethical concerns that accompany germline gene editing are the same concerns that have accompanied IVF. Many note that physicians (and society) reject concerns related to hubris and interference with nature by “screen[ing] embryos and fetuses for diseases . . . vaccinat[ing], provid[ing] pain relief to women in labour (despite objections of some earlier Christians that these practices thwarted God’s will)[,] and treat[ing] cancer.”²⁹⁴ Moreover, concerns that have been identified as unique to or possibly exacerbated by germline gene editing still fall within the realm of parental or reproductive autonomy and are similar to the risks imposed by natural reproduction or medicine and pharmaceuticals more generally. In general, the regulatory state has not inquired into parents’ motives in making certain reproductive decisions such as sex selection, using PGD to select for traits that the majority may deem undesirable, or choosing reproductive partners based on physical traits that they would like their children to have. Extending that lack of inquiry to germline gene editing, one could posit that not distinguishing between genetic enhancement and genetic treatment could have some benefits. This Article’s normative argument has emphasized the similarities between currently permitted techniques, federally-regulated products, and germline gene editing.

²⁹³ See, e.g., Sheryl Gay Stolberg, *States Pursue Cloning Laws as Congress Debates*, N.Y. TIMES (May 26, 2002), <https://www.nytimes.com/2002/05/26/us/states-pursue-cloning-laws-as-congress-debates.html>.

²⁹⁴ Savulescu, *supra* note 159; see also Associated Press, *First Use of CRISPR Against Cancer in Patients Clears Early Safety Hurdles*, STAT NEWS (Nov. 6, 2019), <https://www.statnews.com/2019/11/06/first-use-of-crispr-against-cancer-in-patients-clears-early-safety-hurdles> (discussing trials using gene editing in cancer patients in order to “remove, alter and give back to the patient cells that are super-powered to fight their cancer—a form of immunotherapy,” not change a person’s DNA).

Additionally, regulating germline gene editing like IVF could reduce the need to differentiate between therapy and enhancement. First, scholars have acknowledged the difficulty in differentiating between curing diseases and augmenting humans.²⁹⁵ Some have asked whether vaccines are enhancements, as they enhance the immune system so that it can ward off disease.²⁹⁶ George Church, an innovator in the field of genetics, has noted that gene therapies, which are FDA approved, constitute modifications.²⁹⁷ Others have noted that doctors “play God” every day, so efforts at genetic modification fall within the realm of what is expected of medical professionals.²⁹⁸ The idea that gene editing is another part of medical treatment renders it more similar to natural reproduction, which tends to fall within the “standard” medical regulatory regime, such as through malpractice regulation. Concerns related to commodification and the role of “baby brokers” offering “state-of-the-art babies produced from the ‘finest’ of genetic materials and . . . diet,” due to the use of gestational surrogacy, have also proven to be unfounded.²⁹⁹ That being said, many scholars continue to think that surrogacy, which is permitted in many American states, possibly exploits women and is accompanied by “serious issues of commodification—of sex, of childbirth, of birthmothers, and of children—by allowing contracts, sales, and money to govern these once noncommercialized areas of life.”³⁰⁰ Nevertheless, access to surrogacy is broadly permitted within the United States and around the world.³⁰¹

²⁹⁵ See, e.g., Savulescu, *supra* note 159, at 38 (“Enhancement is a misnomer. It suggests luxury. But enhancement is no luxury. In so far as it promotes well-being, it is the very essence of what is necessary for a good human life.”).

²⁹⁶ See Mohapatra, *supra* note 190, at 63 (citation omitted).

²⁹⁷ See David Cyranoski, *Ethics of Embryo Editing Divides Scientists*, NATURE (Mar. 18, 2015), <https://www.nature.com/news/ethics-of-embryo-editing-divides-scientists-1.17131>; George Church, Ph.D., WYSS INSTITUTE, <https://wyss.harvard.edu/team/core-faculty/george-church>; see also *infra* Section IV.A. (discussing FDA-approved gene therapies which modify somatic cells, but do not result in heritable modifications).

²⁹⁸ See Malik, *supra* note 266.

²⁹⁹ Busby & Vun, *supra* note 242, at 42 (citing to BARBARA KATZ ROTHMAN, RECREATING MOTHERHOOD, IDEOLOGY AND TECHNOLOGY IN A PATRIARCHAL SOCIETY 237 (1989)).

³⁰⁰ See, e.g., Field, *supra* note 67, at 1155; see *id.* at 1158–59, 1161, 1164–65.

³⁰¹ For an overview of surrogacy law in the United States and access to surrogacy worldwide, see COLUM. L. SCH. SEXUALITY & GENDER L. CLINIC, SURROGACY LAW AND POLICY IN THE U.S.: A NATIONAL CONVERSATION INFORMED BY GLOBAL LAWMAKING 8–17 (2016), https://web.law.columbia.edu/sites/default/files/microsites/gender-sexuality/files/columbia_sexuality_and_gender_law_clinic_-_surrogacy_law_and_policy_report_-_june_2016.pdf; see also Michael Alison Chandler, *With New Surrogacy Law, D.C. Joins Jurisdictions That Are Making It Easier for Gay and Infertile Couples to Start Families*, Social Issues, WASH. POST (June 3, 2017), <https://www.washingtonpost.com/local/social-issues/with-new-surrogacy-law-dc-joins-jurisdictions-that-are-making-it->

Further, the regulatory regime for ART (or lack thereof, as many characterize it), recognizes that ART generally has the same goals as traditional reproduction and attempts to treat it in that manner.

Germline gene editing is accompanied by some technique-specific moral concerns, including those related to the “inviolability” of the human germline and the idea that some “shared human identity” would be destroyed if the technique were to go forward. Yet, as discussed above in Section III.D.3., the idea of a “shared human identity” is speculative. Some scientists, government officials, and members of the public have called for moratoria on the clinical use of gene editing; moratoria on research related to human gene editing; limiting the use of gene editing to certain situations; international frameworks; and/or combinations of some of the aforementioned options.³⁰² Some individuals oppose germline gene editing for various reasons, including that they do not want the technology to exist due to its possible use for human enhancements like improving intelligence beyond naturally occurring capacities, increasing height, or even changing a child’s eye color or muscle composition.³⁰³ Others believe that further deliberation is required and that halting research and public deliberation would be “unwise.”³⁰⁴

Ultimately, treating germline gene editing in the same manner as traditional ART means placing the majority of regulation under state rather than federal control. Some would argue that the possibility that germline gene editing could affect the gene pool renders it a “classic area for federal regulation”; however, natural reproduction has the same effect and is not subject to federal regulation.³⁰⁵ Others note that at least

easier-for-gay-and-infertile-couples-to-start-families/2017/06/03/845c90d4-3c99-11e7-8854-21f359183e8c_story.html.

³⁰² See generally Baltimore et al., *supra* note 43, at 37; Bosley et al., *supra* note 41, at 484–86 (providing the perspectives of various legal scholars and scientists ethicists and scientists on the practical effects of a moratorium on gene editing and the likelihood of success); Russell A. Spivak et al., *Moratoria and Innovation in the Reproductive Sciences: Of Pretext, Permanence, Transparency, and Time-Limits*, 14 J. HEALTH & BIOMEDICAL L. 5, 6–7 (2018); see also Lander et al., *supra* note 89, at 165. When scientists use the term “moratorium,” their use of the term sometimes refers to a pause on research or clinical use as opposed to a “ban,” which is the usual meaning of the term. See also Editorial, *Germline Gene-Editing Research Needs Rules*, NATURE (Mar. 13, 2019), <https://www.nature.com/articles/d41586-019-00788-5>; Wolinetz & Collins, *supra* note 89.

³⁰³ See Lander, *supra* note 284, at 166.

³⁰⁴ See, e.g., Daley et al., *supra* note 49, at 897. See generally Bosley et al., *supra* note 41, at 483–84.

³⁰⁵ See, e.g., Jack M. Balkin, *Commerce*, 109 MICH. L. REV. 1, 6 (2010); Brian Galle & Mark Seidenfeld, *Administrative Law’s Federalism: Preemption, Delegation, and Agencies at the*

the federal government has a clear structure for the testing of products; however, other aspects of medicine flourish without the FDA's oversight.³⁰⁶ Surgical techniques, for example, are, as a part of the practice of medicine, unregulated by the FDA, and many surgical innovations have surfaced (and become widespread) over the years, such as heart surgery and organ transplantation.³⁰⁷ Further, ART, namely IVF, has flourished around the world and was the basis for the 2010 Nobel Prize in Physiology or Medicine.³⁰⁸ Siting authority in states instead of the federal government could minimize the role of public deliberation, which was not a part of the human clinical use of IVF in the United States.³⁰⁹

IV. APPLYING TRADITIONAL ASSISTED REPRODUCTIVE TECHNOLOGY REGULATION TO EMERGING GERMLINE GENE EDITING TECHNOLOGIES

As outlined *supra* in Part III, there are many reasons why individuals are opposed to germline gene editing. That opposition, however, should not prevent the use of germline gene editing in the United States. While scholars and practitioners have acknowledged that the current FDA regime can regulate gene therapy (and little debate has ensued over that jurisdictional assertion), some think that germline gene editing requires a new regulatory regime. This Article argues that it does not because the tools to regulate gene editing in the United States already exist, although the emphasis on federal regulation is misplaced.³¹⁰ Instead, past examples of FDA action related to medical

Edge of Federal Power, 57 DUKE L.J. 1933, 1987 (2008) (noting, regarding spillovers: "Lax regulations in one state—be they on handguns, fireworks, or abortions—can make restrictions in nearby states largely fruitless") (citations omitted); Heather K. Gerken & Ari Holtzblatt, *The Political Safeguards of Horizontal Federalism*, 113 MICH. L. REV. 57, 69–73, 101 (2014) (discussing spillover effects and federalism); Richard F. Storrow, *The Bioethics of Prospective Parenthood: In Pursuit of the Proper Standard for Gatekeeping in Infertility Clinics*, 28 CARDOZO L. REV. 2283, 2299 (2007).

³⁰⁶ See *supra* Section II.B.

³⁰⁷ *Id.*

³⁰⁸ Press Release, The Nobel Prize in Physiology or Medicine 2010, Nobel Prize (Oct. 4, 2010), <https://www.nobelprize.org/prizes/medicine/2010/press-release> [<https://perma.cc/CK2M-NNJE>].

³⁰⁹ NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 193–95 (recommending societal deliberation related to genome editing).

³¹⁰ See, e.g., NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 110 ("RECOMMENDATION 4-1. Existing regulatory infrastructure and processes for reviewing and evaluating somatic gene therapy to treat or prevent disease and disability should be used to evaluate somatic gene therapy that uses genome editing."); Bosley et al., *supra* note 41, at 478, 483, 486; Kane, *supra* note 38,

techniques involving genetic modification or assisted reproduction indicates that federal involvement will likely stymie innovation in this area.³¹¹ Thus, this Article argues for a regulatory treatment of germline gene editing similar to that of traditional ART.

A. *The Similarities Between Germline Gene Editing and Drugs/Biologics*

While this Article does not advocate for the federal regulatory treatment of gene editing, the FDA has simultaneously declared jurisdiction over gene editing and implied that it is distinct from other “products” as has the NIH in funding decisions, which merits an argument as to why gene editing is not exceptional.³¹² This

at 319 (2017) (arguing that germline gene editing has a “more complex regulatory profile” than mitochondrial transfer or human reproductive cloning).

³¹¹ See, e.g., *supra* note 8 and accompanying text; see also Carbone, *supra* note 135, at 354 (noting the impact of federal policy on the funding of embryo research). *Id.* (“Given the lack of consensus on a basis for substantive regulation and the interaction of safety requirements with deep-seated religious opposition to assisted reproduction, substantive regulation is likely to shut down promising innovations rather than provide a safer way to test their impact. The industry lobbying that subverts safety regulation (but also overcomes obstructionist regulation) depends on powerful advocates for the procedures at issue, something that does not exist for techniques still on the drawing board.”).

³¹² See, e.g., *Information About Self-Administration of Gene Therapy*, U.S. FOOD & DRUG ADMIN. (Nov. 21, 2017), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy>; *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT’L INSTS. OF HEALTH (Apr. 28, 2015), <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos> (“NIH will not fund any use of gene editing technologies in human embryos.”); *Therapeutic Cloning and Genome Modification*, U.S. FOOD & DRUG ADMIN. (Mar. 16, 2018), <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/therapeutic-cloning-and-genome-modification> (stating that “FDA has regulatory authority over genetically manipulated cells” and therefore, investigational new drug applications must be submitted before researchers use them); see Robert M. Califf & Ritu Nalubola, *FDA’s Science-Based Approach to Genome Edited Products*, FDA VOICE (Jan. 18, 2017), <http://blogs.fda.gov/fdavoices/index.php/2017/01/fdas-science-based-approach-to-genome-edited-products> [<https://perma.cc/X936-U9JJ>] (“[FDA oversight] is one aspect of broader governance necessary for safe and responsible research and development of genome editing applications. Moreover, the expansive scope of [gene editing] has triggered debate on fundamental ethical and social issues Even as FDA implements necessary steps for effective regulation to ensure the safety of products, the role of broader, inclusive public discussion involving multiple constituencies . . . to address the larger societal considerations should not be overlooked.”); *Id.* (“Human medical products that apply gene editing to exert their therapeutic effect are regulated under our existing framework for biological products, which include gene therapy products. ‘Gene editing’ here refers to non-heritable situations somatic cell gene therapy only, and not to heritable conditions (germ line gene therapy). The FY16 [Congressional] appropriations bill restricted use of federal funds ‘in research in which

exceptionality should be analyzed because, while the FDA purports to fit germline gene editing into its framework for biologics and drugs, the FDA's categorization of certain techniques into that framework has led to the FDA essentially treating those reproductive techniques differently than its other approved products.³¹³ Further, due to the budget rider that has been renewed every year since 2015, the FDA cannot even consider approving gene editing techniques that would lead to heritable changes.³¹⁴ This also serves to stymie progress under a federally-focused regime.

While the FDA is known for its regulatory baseline of "safety and efficacy," which must be achieved before a product obtains marketing approval, this standard also exists within science and the practice of medicine generally.³¹⁵ For example, after the birth of Louise Brown

a human embryo is intentionally created or modified to include a heritable genetic modification.""); see also Francis S. Collins, *NIH Supports International Moratorium on Clinical Application of Germline Editing*, NAT'L INSTS. OF HEALTH (Mar. 13, 2019), <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-supports-international-moratorium-clinical-application-germline-editing> ("Research on the potential to alter the very biological essence of humanity raises profound safety, ethical, and philosophical issues Until nations can commit to international guiding principles to help determine whether and under what conditions such research should ever proceed, NIH strongly agrees that an international moratorium [on clinical application of germline editing] should be put into effect immediately."); Francis S. Collins, M.D., Ph.D., Director, *Statement on Claim of First Gene-Edited Babies by Chinese Researcher*, NAT'L INSTS. OF HEALTH (Nov. 28, 2018) <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-claim-first-gene-edited-babies-chinese-researcher> ("NIH does not support the use of gene-editing technologies in human embryos."); *Gene Therapy for Rare Disorders*, MOLECULAR MED. TRI-CON., <https://www.triconference.com/transcripts/peter-marks-transcript> (last visited July 28, 2020) (providing the statement of Peter Marks, the Director of the FDA's Center for Biologics Evaluation and Research, characterizing the area of "heritable genetic modifications" as "a tremendously controversial area").

³¹³ See *supra* Part II; see also NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE, *supra* note 50, at 136 (discussing the Congressional budget rider that would apply to germline gene editing). While the actions of the FDA and Congress are separate, the combined history of the FDA's regulatory treatment of techniques involving genetic modification and Congress' budget rider, indicate that the regulatory system is treating germline genetic modification differently than similar techniques.

³¹⁴ See NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE *supra* note 50, at 136.

³¹⁵ For more on the phases of testing required to obtain marketing approval in the United States for a drug or biologic, see Abigail All. for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 698 (D.C. Cir. 2007) (citing 21 C.F.R. § 312.21); see also *Investigational New Drug (IND) or Device Exemption (IDE) Process (CBER)*, U.S. FOOD & DRUG ADMIN. (May 14, 2019), <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/investigational-new-drug-ind-or-device-exemption-ide-process-cber> (explaining the investigational new drug applications

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 797

resulting from IVF in the U.K. (but before the first American birth due to IVF), a report from the precursor to the U.S. Department of Health and Human Services' Ethics Advisory Board noted that research related to IVF in the U.S. would be ethically acceptable as long as "the studies were designed to 'establish the safety and efficacy of [IVF,] and to obtain important scientific information toward that end not reasonably obtainable by other means.'"³¹⁶ That same report also "recommended that only 'married couples' should be eligible for IVF procedures," illustrating the moral views that can impact federal regulation and research in general.³¹⁷

By emphasizing the unknown long-term effects of germline gene editing as a reason not to permit the use of the technique, those who wish to prohibit germline gene editing neglect the current treatment of the unknown long-term effects of many approved pharmaceuticals.³¹⁸ There is significant literature in the health law context, and specifically in the food and drug law and tort law areas, surrounding risk, "side effects" or "adverse drug reactions,"³¹⁹ and the response of the pharmaceutical law and tort law regimes to the side effects of pharmaceuticals.³²⁰ While the Food, Drug, and Cosmetic Act leads to the characterization that the FDA regulates products for "safety and effectiveness," pharmaceutical commercials and adverse event reports remind the public that FDA-approved products are not completely

apply to drugs and biologics). *But see* Timothy Brewer & Graham A. Colditz, *Postmarketing Surveillance and Adverse Drug Reactions: Current Perspectives and Future Needs*, 281 J. AM. MED. ASSOC. 824, 824 (1999) (noting that premarket clinical trials, "frequently do not have sufficient power to reliably detect important [adverse drug reactions (ADRs),] . . . lack the follow-up necessary to detect [adverse drug reactions] widely separated in time from the original use of the drug or delayed consequences associated with long-term drug administration[,] . . . [and] often do not include special populations such as pregnant women or children who may be at risk for unique ADRs or for an increased frequency of ADRs compared with the general population"). For more on "safety and efficacy" in the context of germline gene editing, *see* NAT'L ACADS. SCIS., *HERITABLE HUMAN GENOME EDITING*, *supra* note 52, at 31 ("Many scientific and medical questions about the procedures remain to be answered, and determining the safety and efficacy of germline genome editing will be necessary but not sufficient conditions for future clinical usage.").

³¹⁶ MARSH & RONNER, *supra* note 17, at 63–64.

³¹⁷ *Id.* at 64.

³¹⁸ *See supra* Section III.A.

³¹⁹ *See* Brewer & Colditz, *supra* note 315, at 824.

³²⁰ *See* Brief of New England Journal of Medicine Editors and Authors as Amici Curiae in Support of Respondent, *Wyeth v. Levine*, 555 U.S. 555 (2008) (No. 06-1249), 2008 WL 3851616, at *11–30. For more information on harmful products that were approved by the FDA, *see also* Sue McGrath, *Only A Matter of Time: Lessons Unlearned at the Food and Drug Administration Keep Americans at Risk*, 60 FOOD & DRUG L.J. 603 (2005).

“safe.”³²¹ Instead, the FDA’s regulatory regime emphasizes disclosure of risk and balancing of benefits and harms as opposed to complete safety.³²² The same inability to guarantee safety that exists with pharmaceuticals, whether prescription or over-the-counter, also exists with gene editing and other medical techniques.³²³ Further, as noted above, approved drugs, such as diethylstilbestrol, and environmental harms that can be exacerbated by humans, like air pollution and radiation, can have deleterious effects on fetuses, including germline effects and increased incidences of cancer.³²⁴

Science and medicine have been moving toward more tailored medical treatments, as emphasized by various initiatives related to precision medicine, gene editing, and even gene therapy. In this way, these treatments have moved closer to the state-regulated practice of medicine.³²⁵ Gene therapy offers individualized treatments.³²⁶ For example, a *New York Times* article on the recently approved gene therapy, Kymriah (then referred to as “CTL019” or tisagenlecleucel),

³²¹ See 21 U.S.C. § 355(b); Brewer & Colditz, *supra* note 315, at 824 (“Safety is not an absolute concept.”).

³²² *Id.* (“For example, the toxic effects of many available chemotherapeutic agents would be unacceptable in drugs marketed for uncomplicated urinary tract infections.”); see also Stephen F. Amato, *Regulatory Strategies for Biomaterials and Medical Devices in the USA: Classification, Design, and Risk Analysis*, in REGULATORY AFFAIRS FOR BIOMATERIALS AND MEDICAL DEVICES 31–33 (Stephen F. Amato & Robert M. Ezzell, Jr. eds., 2015).

³²³ See, e.g., Pontin, *supra* note 16 (“There are always unknowns. No innovative therapy, whether it is a drug for a disease or something so bold and disruptive as germ line intervention, can ever remove all possible risk. Fear of the unknown and unquantifiable risks shouldn’t absolutely prohibit us from making interventions that could have great benefits. The risks of a genetic, inherited disease are quantifiable, known, and in many cases devastating. So we go forward, accepting the risks.” (quoting George Q. Daley, Dean of Harvard Medical School)); *DES History*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/des/consumers/about/history.html> (providing the history of diethylstilbestrol, a drug that was prescribed to pregnant women until the FDA warned against prescribing it to them due to its deleterious effects on children exposed to DES in the womb); *About DES*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/des/consumers/about/index.html>. For more on the “unknowns” that might exist with germline gene-editing technologies, see NAT’L ACADS. SCIS., HERITABLE HUMAN GENOME EDITING, *supra* note 52, at 92–93.

³²⁴ See Vulimiri & Olivero, *supra* note 98, at 392–93.

³²⁵ See, e.g., Robertson, *supra* note 34, at 440 (referring to pharmacogenomics which “may enable physicians to prescribe drugs tailored to a patient’s genotype”). For more on precision medicine and pharmacogenomics, see *All of Us Research Program Overview*, NAT’L INSTS. OF HEALTH, <https://allofus.nih.gov/about/all-us-research-program-overview>; *What Is Precision Medicine?* MEDLINEPLUS, <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition> (last updated Sept. 22, 2020).

³²⁶ See, e.g., Denise Grady, *F.D.A. Panel Recommends Approval for Gene-Altering Leukemia Treatment*, N.Y. TIMES (July 12, 2017), <https://www.nytimes.com/2017/07/12/health/fda-novartis-leukemia-gene-medicine.html>.

emphasized a number of adverse reactions that resulted from the use of the drug.³²⁷ The patient highlighted in the article successfully completed the treatment, which was accompanied by “severe side effects” that nearly killed her, but that ultimately led to her remission for leukemia.³²⁸ While the patient highlighted in the *New York Times* article did not die, several other patients died during pre-market clinical trials.³²⁹ Nevertheless, these deaths were not sufficient to prevent FDA approval of the pharmaceutical.³³⁰

Many FDA-approved drugs have known side effects that could parallel the possible side effects of germline gene editing.³³¹ Similarly, many of the concerns related to gene therapy are similar to those related to germline gene editing, including that germline gene editing may have deleterious effects on patients later in life, which may also occur with gene therapy patients.³³² For instance, in the FDA-created Briefing Document for the Oncologic Drugs Advisory Committee Meeting discussing Kymriah, the FDA noted that “careful attention should be given to antibody selection to minimize possible risks from nonspecific or off-target effects.”³³³ Off-target effects are an often-cited objection (and safety concern) that accompany germline gene editing and gene therapy.³³⁴

FDA advisory committee documents provide useful insights into the approval process, as they are one of the few sources of public information available related to the FDA’s notoriously obscure approval process.³³⁵ Yescarta, another gene therapy product that was approved

³²⁷ *Id.*; see also U.S. FOOD & DRUG ADMIN., FDA BRIEFING DOCUMENT: ONCOLOGIC DRUGS ADVISORY COMM. MEETING, BLA 125646, TISAGENLECLEUCEL, NOVARTIS PHARM. CORP. (2017), <https://www.fda.gov/media/106081/download> [hereinafter FDA BRIEFING DOCUMENT]; Press Release, Novartis, Novartis Receives First Ever FDA Approval for a CAR-T Cell Therapy, Kymriah (TM) (tisagenlecleucel, CTL019), for Children and Young Adults with B-cell ALL that is Refractory or has Relapsed at Least Twice (Aug. 30, 2017), <https://www.novartis.com/news/media-releases/novartis-receives-first-ever-fda-approval-car-t-cell-therapy-kymriahtm-ctl019>.

³²⁸ Grady, *supra* note 326.

³²⁹ *Id.*

³³⁰ *Id.*; Novartis, *supra* note 327.

³³¹ See *supra* notes 59–61; *infra* note 333 (discussing the harms of FDA-approved gene therapy products).

³³² See Bosley et al., *supra* note 41, at 480; see also *infra* notes 350–51.

³³³ FDA BRIEFING DOCUMENT, *supra* note 327, at 16. In many regulatory documents such as this, Kymriah is referred to as “tisagenlecleucel” as opposed to its commercial name.

³³⁴ See *supra* notes 59–61, 333.

³³⁵ See, e.g., Patti Zettler, *FDA Advisory Committees and Industry-Funded Patient Advocacy*, STAN. L. SCH.: STAN. L. & BIOSCIENCES BLOG (June 23, 2017),

after Kymriah, was not subject to an FDA advisory committee meeting “because Y[escarta] is not the first biologic in its class, and there were no critical review issues that required input from an Advisory Committee.”³³⁶

The advisory committee that was consulted on the approval of Kymriah expressed concerns about the possibility of secondary cancers and other long-term side effects that could not be known at the time of treatment.³³⁷ Despite these concerns, the FDA still approved the therapy.³³⁸ While off-target effects exist with gene therapies such as Kymriah, those off-target effects were not enough to prevent FDA approval of Kymriah. A recent article in *Science* magazine covered the possibility that the viral vectors used in approved gene therapy products may pose cancer risks, a concern that has persisted for “nearly 20 years.”³³⁹

Serious adverse effects can result from the use of Kymriah and other approved gene therapies like Yescarta.³⁴⁰ Kymriah and Yescarta

<https://law.stanford.edu/2017/06/23/fda-advisory-committees-and-industry-funded-patient-advocacy> (citing Matthew Herper, *The FDA Ignores Its Advisors A Quarter of The Time*, FORBES (Oct. 12, 2010), <https://www.forbes.com/sites/matthewherper/2010/10/12/the-fda-ignores-its-advisors-a-quarter-of-the-time/#474ed23c3b97>) (“Partly because advisory committee meetings may be the first public airing of the agency’s questions about an unapproved drug and partly because the agency follows advisory committee recommendations roughly 75% of the time, . . . these meetings and recommendations frequently are closely watched.”).

³³⁶ Michael Havert, *Summary Basis for Regulatory Action*, U.S. FOOD & DRUG ADMIN. 17 (Oct. 18, 2017), <https://www.fda.gov/media/108788/download>.

³³⁷ Grady, *supra* note 326.

³³⁸ Press Release, U.S. Food & Drug Admin., FDA Approval Brings First Gene Therapy to the United States (Aug. 30, 2017), <https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states>.

³³⁹ Jocelyn Kaiser, *Virus Used in Gene Therapies May Pose Cancer Risk, Dog Study Hints*, SCI. (Jan. 6, 2020), <https://www.sciencemag.org/news/2020/01/virus-used-gene-therapies-may-pose-cancer-risk-dog-study-hints>.

³⁴⁰ For the documents providing the approvals of various gene therapy products, see BLA Approval Letter from Wilson W. Bryan, M.D., Dir., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Dr. Manisha Patel, PharmD, Novartis Pharm. Corp. (Aug. 30, 2017), <http://www.fda.gov/media/106989/download> [<https://perma.cc/Q9GS-BLVD>] (granting BLA approval for Kymriah); BLA Approval Letter from Mary A. Malarkey & Wilson W. Bryan, M.D., Dirs., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Rizwana F. Sproule, Ph.D., Vice President, Kite Pharma, Inc. (Oct. 18, 2017), <http://www.fda.gov/media/108458/download> [<https://perma.cc/7V6P-CZJP>] (granting BLA approval for Yescarta); BLA Approval Letter from Mary A. Malarkey & Wilson W. Bryan, M.D., Dirs., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Jim Wang, Ph.D., MBA, Spark Therapeutics, Inc. (Dec. 19, 2017), <http://www.fda.gov/media/109487/download> [<https://perma.cc/4SH4-ABJM>] (granting BLA approval for Luxturna); *see also Cytokine Release Syndrome*, NCI

can both cause Cytokine Release Syndrome, which is an adverse event that is closely monitored by physicians.³⁴¹ While some patients recover from “[l]ife-threatening Cytokine Release Syndrome” and subsequently are in remission from the underlying disease, others do not.³⁴² During Kymriah’s clinical trial, several subjects developed infections after infusion that included encephalitis, clostridium difficile, and fungal sepsis, some of which were fatal.³⁴³ Other potential risks (which did not preclude approval) include “secondary malignancy, new/exacerbated neurological event, new/exacerbated autoimmune disorder, new hematological disorder, [and] vector virus replication.”³⁴⁴

Further, at least three deaths out of 123 patients were “suspected” to be related to the infusion of Kymriah.³⁴⁵ Similarly, “four deaths were attributed to [Yescarta] as per FDA analysis. . . . Fatal cases of CRS and neurologic toxicity have occurred after receiving Y[escarta].”³⁴⁶ Additionally, during the Kymriah advisory committee meeting, an FDA employee expressed concern about the “possibility of long term mutagenesis,” in which the DNA of the patient could be affected and even lead to leukemia.³⁴⁷

Dictionary of Cancer Terms, NAT’L CANCER INST., <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cytokine-release-syndrome>.

³⁴¹ FDA BRIEFING DOCUMENT, *supra* note 327, at 47, 55; Havert, *supra* note 336, at 3, 13, 18.

³⁴² FDA BRIEFING DOCUMENT, *supra* note 327, at 47, 55; *see also* NOVARTIS, ONCOLOGIC DRUGS ADVISORY COMM. BRIEFING DOCUMENT, TISAGENLECLEUCEL (CTL019) FOR THE TREATMENT OF PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA 18–19 (2017) [hereinafter NOVARTIS BRIEFING DOCUMENT], <https://www.fda.gov/media/106093/download> (noting that Cytokine Release Syndrome is classified as an “expected on-target toxicity,” and explaining and identifying deaths due to disease progression after the infusion of Tisagenlecleucel).

³⁴³ FDA BRIEFING DOCUMENT, *supra* note 327, at 48–51.

³⁴⁴ *Id.* at 52.

³⁴⁵ NOVARTIS BRIEFING DOCUMENT, *supra* note 342, at 76 (showing Table 6-10 “Deaths attributed to adverse events—Studies B2202 and B2205J”); *id.* at 66 (stating 123 as the number of “patients enrolled in Studies B2202 and B2205J.”); *id.* at 83 (“Three patients developed infections that proved to be fatal (Table 6-10).”); *id.* at 84.

³⁴⁶ Havert, *supra* note 336, at 15.

³⁴⁷ U.S. Food & Drug Admin., Summary Minutes of the Oncologic Drugs Advisory Committee, Ctr. for Drug Evaluation and Research (July 12, 2017), at 5 (transcript available at <https://www.fda.gov/media/107129/download>) [hereinafter *Summary Minutes of the Oncologic Drugs Advisory Committee*]; *see also* *Mutagen*, NCI Dictionary of Cancer Terms, NAT’L CANCER INST., <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mutagen>; Transcript, U.S. Food & Drug Admin., Ctr. for Drug Evaluation and Research Oncologic Drugs Advisory Comm., Morning Session, Wednesday, July 12, 2017, 7:59 am to 11:00 am, at 67–68 (transcript available at <https://www.fda.gov/media/107138/download>) [hereinafter Transcript, CDER Morning Session].

Other uncertainties related to Kymriah, including those related to manufacturing consistency, the safety and efficacy of the product outside of the clinical trial context, and secondary malignancy, also merited the expression of concern but not the prevention of approval.³⁴⁸ Similarly, the possibility of secondary malignancy due to insertional mutagenesis did not prohibit the approval of Yescarta.³⁴⁹ Further, Novartis, the sponsor of Kymriah's BLA, plans to monitor clinical trial patients "for 15 years per the FDA guidance."³⁵⁰ Kite Pharma Incorporated, the sponsor of Yescarta, will also follow members of a safety study for 15 years; the post-marketing study would thus be completed in December 2037, with a final report submitted in 2038.³⁵¹

The current federal regulatory framework, in which side effects are discovered both before and after approval for pharmaceuticals, is another similarity between gene editing technologies and products currently regulated by the FDA.³⁵² For example, many have noted that "present technology cannot assure us that unintended modifications created through an editing procedure would not result in a devastating long-term outcome such as cancer or adverse developmental effects if one were to modify a zygote."³⁵³ Yet this same concern that accompanies germline gene editing also exists with approved gene therapy products.³⁵⁴

³⁴⁸ Transcript, CDER Morning Session, *supra* note 347, at 18–21 (providing "FDA Introductory Remarks" by Wilson Bryan, M.D.); *see also id.* at 61 ("Unlike traditional pharmaceutical drugs, tisagenlecleucel is a dynamic living biologic.").

³⁴⁹ Havert, *supra* note 336, at 5.

³⁵⁰ Transcript, CDER Morning Session, *supra* note 347, at 93.

³⁵¹ Havert, *supra* note 336, 16–17.

³⁵² *See, e.g.*, 21 C.F.R. §§ 201.80(e)–(g) (2020); 21 U.S.C. § 355(k) (2020); 21 C.F.R. § 314.98 (2020); 21 C.F.R. § 314.80 (2020); 21 C.F.R. § 201.57(a)(11) (2020); Evans, *supra* note 149, at 446, 457 n.253 (2010); FDA BRIEFING DOCUMENT, *supra* note 327, at 25 ("In 2006, FDA published recommendations for the long-term follow-up monitoring of gene therapy recipients for delayed adverse events (FDA Guidance for Industry: *Gene Therapy Clinical Trials—Observing Subjects for Delayed Adverse Events*, 2006)."); *Summary Minutes of the Oncologic Drugs Advisory Committee*, *supra* note 347, at 6 ("A committee member stated concern over unknown late toxicities, but that long term survival outweighs that potential risk.").

³⁵³ Kohn et al., *supra* note 23, at 2554; *see also* Bosley et al., *supra* note 41, at 480 (providing the statement of Dr. Jennifer Doudna on the possible "unintended long-term consequences of germline editing."); *id.* at 482 (providing the statement of Martin Pera where he referred to the "risk[] ... [of] unanticipated consequences of genetic intervention (variant alleles may have important advantages in some situations that we cannot anticipate)").

³⁵⁴ *See supra* Section III.B.

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 803

Currently, state and federal regimes address the adverse effects of pharmaceuticals post-approval.³⁵⁵ Within that literature, there is a larger debate regarding which of the regimes is more helpful or which polity should take the lead on regulating pharmaceuticals.³⁵⁶ The FDA has expressed its views regarding its primacy as “the expert Federal agency responsible for evaluating and regulating drugs.”³⁵⁷ Nonetheless, many well-publicized stories of drugs that were withdrawn from the market after FDA approval emphasize the limitations of this regime.³⁵⁸ The FDA has spent decades regulating innovative therapies similar to more traditional areas of regulated products, such as drugs and biologics.³⁵⁹ This Article argues that the consequences of the use of germline gene editing, as examined from a regulatory perspective, are not substantially different from the consequences of using gene therapy. Accordingly, germline gene editing should be minimally regulated, like traditional ART, which involves the use of IVF (without genetic modification).³⁶⁰

There are of course limitations to this analogy. Some would draw distinctions and note that pharmaceutical products can be removed from the market. While this is a rarely exercised regulatory tool that would not be available to the FDA if gene editing is regulated like IVF, most pharmaceuticals that are withdrawn from the market are withdrawn by the manufacturers and not the FDA.³⁶¹ Further, there are

³⁵⁵ See *Wyeth v. Levine*, 555 U.S. 555 (2009). *But see* *Mutual Pharm. Co. v. Bartlett*, 570 U.S. 472 (2013).

³⁵⁶ Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 1–27 (2016); Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 845 (2017).

³⁵⁷ Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3935 (Jan. 24, 2006) (to be codified at 21 C.F.R. § 201.56(d)).

³⁵⁸ See Brief of New England Journal of Medicine Editors and Authors as Amicus Curiae in Support of Respondent, *Wyeth v. Levine*, 555 U.S. 555 (2008) (No. 06-1249), 2008 WL 3851616, at *11–30. For more information on harmful products that were approved by the FDA, see Sue McGrath, *Only A Matter of Time: Lessons Unlearned at the Food and Drug Administration Keep Americans at Risk*, 60 FOOD & DRUG L.J. 603 (2005).

³⁵⁹ See Lewis, *Halted Innovation*, *supra* note 122, at 1100–01.

³⁶⁰ See *supra* note 82 and accompanying text (describing ART as “minimally regulated”). Traditional ART, which does not involve genetic modification, is minimally regulated, whereas forms of ART involving genetic modification are highly regulated. See *supra* Part III.

³⁶¹ See 21 C.F.R. § 7.3 (2012); 21 C.F.R. § 216.24 (2018); see also Cassie Frank et al., *Era of Faster FDA Drug Approval Has Also Seen Increased Black-Box Warnings and Market Withdrawals*, 33 HEALTH AFF. 1453, 1455 (2014) (stating there is “no comprehensive source of information on black-box warnings or withdrawals available to clinicians, researchers, or the public”); Aaron S. Kesselheim et al., *Pharmaceutical Policy in the*

medical procedures that do not work as intended; physicians stop providing these techniques (if they are wholly ineffective) or accept the failure (such as surgeries in which the patient dies or where a surgical intervention failed). The same could be done for harmful forms of gene editing, depending on the degree of failure.³⁶² Notably, somatic cell gene editing is currently viewed as “much closer to being shown safe and effective” than germline gene editing.³⁶³

B. *Regulating Gene Editing Like Assisted Reproductive Technology*

Many of the scientific and ethical concerns related to ART, such as those related to the ability of children to consent, the hubris of humans, and the long-term medical effects of these techniques are the same as

United States in 2019: An Overview of the Landscape and Avenues for Improvement, 30 STAN. L. & POL'Y REV. 421, 452 (2019); Pierre La Rochelle, et al., *Analysis of the Drugs Withdrawn from the U.S. Market from 1976 to 2010 for Safety Reasons*, 30 PHARM. MED. 277, 278, 286 (2016) (explaining “the FDA website does not contain . . . a consolidated list [of withdrawals]” and that “[t]he first limitation of [the] study [was] the inability to completely access the evidence justifying withdrawals ordered by the FDA or voluntarily undertaken by drug companies”); W. Nicholson Price II, *Drug Approval in a Learning Health System*, 102 MINN. L. REV. 2413, 2428–29 (2018). The FDA maintains information on recalls and withdrawals on its website (subject to limitations noted by commentators). See, e.g., *FDA's Role in Drug Recalls*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/drug-recalls/fdas-role-drug-recalls> (last updated July 3, 2018); *Recalls*, U.S. FOOD & DRUG ADMIN., <https://datadashboard.fda.gov/ora/cd/recalls.htm> (last visited May 28, 2020); *Recalls, Market Withdrawals, & Safety Alerts*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts> (last updated May 28, 2020). Many of these recalls are voluntarily made by the drug manufacturer. For a list of such recalls, see *Drug Recalls*, U.S. FOOD & DRUG ADMIN. (June 29, 2020), <https://www.fda.gov/drugs/drug-safety-and-availability/drug-recalls> (“A drug recall is the most effective way to protect the public from a defective or potentially harmful product. A recall is a voluntary action taken by a company at any time to remove a defective drug product from the market.”).

³⁶² But see David Epstein, *When Evidence Says No, But Doctors Say Yes*, ATLANTIC (Feb. 22, 2017), <https://www.propublica.org/article/when-evidence-says-no-but-doctors-say-yes> (noting that some physicians still continue to prescribe approved drugs and use them in spite of a lack of clinical effectiveness); Frank Pasquale, *The Hidden Costs of Health Care Cost-Cutting: Toward a Post-Neoliberal Health-Reform Agenda*, 77 L. & CONTEMP. PROBS. 171, 173–74 (2014).

³⁶³ Greely, *supra* note 227, at 253, 258–60 (discussing the “moral status” of the embryo); see also Emily Mullin, *Gene Editing Study in Human Embryos Points Toward Clinical Trials*, MIT TECH. REV. (Aug. 2, 2017), <https://www.technologyreview.com/2017/08/02/242242/gene-editing-study-in-human-embryos-points-toward-clinical-trials>; Antonio Regalado, *US Scientist Who Edited Human Embryos With CRISPR Responds to Critics*, MIT TECH. REV. (Aug. 8, 2018), <https://www.technologyreview.com/2018/08/08/1411119/us-scientist-who-edited-human-embryos-with-crispr-responds-to-critics>.

those that accompany germline gene editing.³⁶⁴ Further, they are the same as those that accompany natural reproduction, as genes are inheritable (without consent), as evidenced by the rules of reproduction and also recent coverage of the impact of donating a sample to a genetic database.³⁶⁵ These concerns were analyzed in Part III. The FDA's assertion of jurisdiction over gene editing and forms of ART involving genetic modification does not mean that the FDA is the best regulator of these innovative therapies. Scholars like Jane Bambauer have asked, "what would happen if medical AI were regulated like their closest substitutes—doctors—instead of like devices?"³⁶⁶ This Article argues for leaving the regulation of ART to the physician-patient relationship.³⁶⁷ State medical boards and tort law regulate doctors; this regulatory system treats other techniques like surgery and IVF.³⁶⁸

While some characterize the field of ART as unregulated, there is a robust literature on regulation within the medical field.³⁶⁹ At the same time, some argue that doctors are incapable of self-policing.³⁷⁰

³⁶⁴ For more on the safety concerns that accompany germline gene editing and ART see Sections II.A.3.–4. For more on the ethical concerns that accompany ART and germline gene editing, see Sections III.A.–C.

³⁶⁵ See Natalie Ram, *DNA by the Entirety*, 115 COLUM. L. REV. 873, 873–78, 898–900 (2015).

³⁶⁶ Bambauer, *supra* note 14, at 391.

³⁶⁷ For a discussion of the physician-patient relationship, see Ezekiel J. Emanuel & Linda L. Emanuel, *Four Models of the Physician-Patient Relationship*, 267 JAMA 2221, 2221–26 (1992); Mark A. Hall, *The Legal and Historical Foundations of Patients as Medical Consumers*, 96 GEO. L.J. 583, 593–94 (2008); Code of Medical Ethics Opinion 1.1.1, AMA, <https://www.ama-assn.org/delivering-care/ethics/patient-physician-relationships>.

³⁶⁸ *But see* George J. Annas, *Human Cloning: A Choice or an Echo?*, 23 U. DAYTON L. REV. 247, 263–66 (1998) ("Professional-organization ethics committees composed primarily of practitioners are simply too narrow to be anything but self-serving in their outlook and actions. A similar observation can be made concerning IRBs and state licensing boards.").

³⁶⁹ See Sandra Johnson, *Structure of Governmental Oversight of Quality in Healthcare*, in THE OXFORD HANDBOOK OF U.S. HEALTH LAW 490–510 (I. Glenn Cohen, Allison K. Hoffman & William M. Sage eds., 2017); Kristen Madison & Mark Hall, *Quality Regulation in the Information Age: Challenges for Medical Professionalism*, in MEDICAL PROFESSIONALISM IN THE NEW INFORMATION AGE 23–24 (David J. Rothman & David Blumenthal eds. 2010); Robert I. Field, *Regulation of Health Care in the United States: Complexity, Confrontation and Compromise*, 16 AN INST HIGH MED TROP, S61, S61–S62, S65 (2017); Robert I. Field, *Why is Health Care Regulation so Complex?*, 33 HEALTH CARE & L. 607, 607–08 (2008); Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 164 (2004); William M. Sage, *Relational Duties, Regulatory Duties, and the Widening Gap Between Individual Health Law and Collective Health Policy*, 96 GEO. L.J. 497, 497–501 (2008);

³⁷⁰ See, e.g., Annas, *supra* note 368, at 263–66 (criticizing professional societies in reproductive medicine); Goodwin, *supra* note 20, at 1079 (noting "compelling evidence

Malpractice regimes and physician discipline also exist. Furthermore, the field of ART is populated by a number of professional, though voluntary, societies, including the American Society for Reproductive Medicine, American College of Obstetricians Gynecologists (which is broader than the field of ART), and the Society for Assisted Reproductive Technology. These organizations provide specific guidance for physicians in the field on a number of topics, including medical practice and nondiscrimination.³⁷¹ While these professional societies are criticized by some commentators because their guidelines are voluntary, they are nonetheless a source of useful guidelines and professional norms.³⁷²

Instead of treating germline gene editing as a medical product, treating it as a medical procedure, like ART, could maximize innovation and parental autonomy.³⁷³ In other words, the FDA should withdraw previous assertions of jurisdiction over germline gene editing and instead employ the same hands-off approach to germline gene editing that it has applied to ART that does not involve genetic modification. This hands-off approach includes, for example, the application of laboratory safety standards to prevent cross-contamination and the applicability of regulations related to disease transmission that apply to laboratories and fertility treatment centers that conduct IVF.³⁷⁴ It would not, however, require pre-market approval by the federal government.

that the [fertility] industry self-regulates quite poorly (doctors are not reprimanded or censured for implanting embryos in women over sixty years old or for implanting too many embryos in women in their thirties)"); Yaniv Heled, *The Regulation of Genetic Aspects of Donated Reproductive Tissue—The Need for Federal Regulation*, 11 COLUM. SCI. & TECH. L. REV. 243, 276–77 (2010) (discussing the insufficiency of self-regulation in the ART field); Maxwell J. Mehlman, *Professional Power and the Standard of Care in Medicine*, 44 ARIZ. ST. L.J. 1165, 1229 (2012) ("Numerous critics complain, for example, about the profession's unwillingness to sanction incompetent colleagues.") (citation omitted).

³⁷¹ Moses, *supra* note 26, at 542–45 (2005); Richard F. Storrow, *Medical Conscience and the Policing of Parenthood*, 16 WM. & MARY J. WOMEN & L. 369, 390–91 (2010).

³⁷² *Code of Medical Ethics: Genetics & Reproductive Medicine*, AMA, at 4 (2016), <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/code-of-medical-ethics-chapter-4.pdf>; Anne Drapkin Lyerly, *Marking the Fine Line: Ethics and the Regulations of Innovative Technologies in Human Reproduction*, 11 MINN. J.L. SCI. & TECH. 685, 702–10 (2010); Brenda Reddix-Smalls, *Assessing the Market for Human Reproductive Tissue Alienability: Why Can We Sell Our Eggs But Not Our Livers?*, 10 VAND. J. ENT. & TECH. L. 643, 676, 685–86 (2008); Jennifer L. Rosato, *The Children of ART: Should the Law Protect Them from Harm?*, 2014 UTAH L. REV. 57, 66–71 (2014).

³⁷³ NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 120 ("The possible benefits of heritable genome editing accrue most immediately to individuals: the prospective parents who want to have an unaffected genetically related child (and that child) but fear passing along a disease.").

³⁷⁴ See *supra* note 83 (providing federal regulations applicable to laboratories that provide ART services).

The FDA requires that “sponsors” (also referred to as “sponsor-investigators”) have an active IND application to continue their human clinical investigations.³⁷⁵ This Article disagrees with the application of the federal IND requirements to a technique that should be the subject of state jurisdiction.³⁷⁶

Beyond the jurisdictional debate, the FDA’s IND requirements have been critiqued from a number of perspectives, including their operation as an obstacle to innovation and unsuitability for non-traditional medical products.³⁷⁷ Many researchers find the FDA’s IND requirement burdensome when applied to “everyday uses” of foods and routine medical treatments. For example, probiotics research in the United States requires an IND application, the approval of which many view as the cause of research delays.³⁷⁸ Similarly, the IND requirements, as noted through Untitled Letters to physician-researchers, had a “chilling effect” on innovation, and have stymied the use of ART techniques that involve genetic modification.³⁷⁹ Additional critiques have focused on the structural limitations of the FDA’s regime.³⁸⁰

It is unclear why the FDA, which continues to maintain that it does not regulate the practice of medicine, would treat germline gene editing, a medical technique similar to IVF or heart surgery, as a product. In fact,

³⁷⁵ See *Drug Approval Process*, U.S. FOOD AND DRUG ADMIN., <https://www.fda.gov/media/82381/download>; *Information for Sponsor-Investigators Submitting Investigational New Drug Applications (INDs)*, U.S. FOOD AND DRUG ADMIN. (June 27, 2017), <https://www.fda.gov/drugs/investigational-new-drug-ind-application/information-sponsor-investigators-submitting-investigational-new-drug-applications-ind>.

³⁷⁶ See *supra* Section II.B. and accompanying text (discussing the practice-products divide).

³⁷⁷ See, e.g., Lewis, *Halted Innovation*, *supra* note 122, at 1110 (criticizing the application of investigational new drug application requirements to innovative medical therapies); Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 HOUS. J. HEALTH L. & POL’Y 1, 53–56 (2002) (explaining how the FDA’s use of investigational new drug requirements led to a “theoretical legal moratorium” on cloning in the late 1990s); Merrill & Rose, *supra* note 123, at 102 (noting that the lack of clarity and “casual” nature of the FDA’s regulation of cloning research put researchers at legal risk if they “failed to seek and secure agency approval”); Pilar N. Ossorio & Yao Zhou, *FMT and Microbial Medical Products: Generating High-Quality Evidence Through Good Governance*, 47 J.L., MED., & ETHICS 505, 511–13 (2019) (providing commentators’ arguments that the FDA should not regulate stool and stool-derived products as drugs, which require investigational new drug applications).

³⁷⁸ See, e.g., Mary Ellen Sanders et al., *Advancing Probiotic Research in Humans in the United States: Challenges and Strategies*, 7 GUT MICROBES 97, 97–98 (2016) (positing that the reason for the small number of probiotics research trials conducted in the United States as compared to other countries is the FDA’s treatment of probiotics as “drugs” requiring investigational new drug application approval).

³⁷⁹ Lewis, *How Subterranean*, *supra* note 8, at 1256.

³⁸⁰ *Id.* at 1241; Sanders et al., *supra* note 378 at 97–98.

the now-disgraced Dr. Jiankui routinely referred to his use of CRISPR technology in embryos as “gene surgery.”³⁸¹ Academics examining the obligations of parents to address genetic disparities have employed the same analogy.³⁸² Using that analogy, one could see that gene surgery or gene editing, in which defective genes are replaced or corrected, could be similar to the forms of surgery in which defective organs are replaced or corrected.

The regulation of ART has been criticized by many, including those who would prefer (or advocate for) additional governmental regulation. Nevertheless, in the absence of a strict regulatory regime, a number of norms of self-regulation have developed in ART, in addition to the requirements imposed by state and federal statistical reporting requirements.³⁸³ These norms are in addition to the fact that providers of ART are physicians who are licensed by the state, as are the facilities where ART would take place.³⁸⁴ Germline gene editing allows parents a chance to improve their children’s health, a normative goal that is supported by laws related to child welfare and the practice of medicine.³⁸⁵ The Nuffield Council on Bioethics has recommended that germline genome editing only be used for purposes intended to “secure the welfare . . . of a person who may be born as a consequence of” the genome editing treatment, a recommendation that this Article supports.³⁸⁶

³⁸¹ Greely, *supra* note 6, at 134 (2019) (“In short: germline editing creates changes that a person’s descendants can inherit, as opposed to changes that could not be passed on to future generations.”).

³⁸² See, e.g., Rakowski, *supra* note 11, at 1384 (“[S]uppose that a surgeon modifies a fetus’s genes in utero so that it is born and later lives a self-conscious individual with normal sensory capacities. Further suppose that had the surgeon done nothing, the person would have been born and remained deaf, dumb, and blind.”).

³⁸³ See, e.g., *Code of Medical Ethics Overview*, AMA, <https://www.ama-assn.org/delivering-care/ethics/code-medical-ethics-overview> (Chapter 4 is entitled “Ethics of Genetics & Reproductive Medicine”); *Oversight of Assisted Reproductive Technology*, AM. SOC. REPROD. MED. 1, 7–11 (2010), <https://www.asrm.org/about-us/media-and-public-affairs/public-affairs/oversight-of-assisted-reproductive-technology>; *supra* note 91 (discussing the Fertility Clinic Success Rate Act).

³⁸⁴ See David Adamson, *Regulation of Assisted Reproductive Technologies in the United States*, 78 FERTILITY & STERILITY 932, 932–33 (2002).

³⁸⁵ See, e.g., Vermette, *supra* note 158, at 32.

³⁸⁶ NUFFIELD COUNCIL ON BIOETHICS, *GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES*, *supra* note 26, at xvii, 77, 96.

Thus, while there are limits on parental autonomy, those limits on parental autonomy tend to focus on prohibiting harms to children, like those associated with child cruelty.³⁸⁷ Following through on the lack of regulation of traditional ART and the tendency of family law to treat the children of ART in a manner that parallels that of children conceived through natural reproduction, the less germline gene editing is regulated by the federal government, the more it (and the children conceived with its assistance) will be treated in the same way as natural reproduction.

Somatic and germline gene editing technologies are not different in a legally significant manner from existing technologies in other areas. For example, other technologies, such as nuclear energy and radiation (which can accompany nuclear energy and medical treatment), can impact existing and future humans in negative ways, yet they remain legal.³⁸⁸ This legality (and associated availability) continues, although the field of epigenetics focuses on the impacts of the environment on the epigenome and genetic expression; thus, even though many environmental factors, including radiation, can affect genetic expression, those environmental factors continue to exist and sometimes negatively impact reproduction.³⁸⁹ In this regard, germline

³⁸⁷ *Id.* at 96; Coleman, Dodge & Campbell, *supra* note 158, at 120; *see also* NAT'L ACADS. SCIS., ENG'G & MED., HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE, *supra* note 50, at 121.

³⁸⁸ *See* Ashley Hardy & Dontan Hart, *Policy Meltdown: How Climate Change Is Driving Excessive Nuclear Energy Investment*, 24 BUFF. ENVTL. L.J. 137, 190 (2016–18); *cf.* Sandra E. Black et al., *This is Only a Test? Long-Run and Intergenerational Impacts of Prenatal Exposure to Radioactive Fallout*, 101 REV. ECON. & STAT. 531, 543–44 (2019). For more on nuclear medicine, *see Nuclear Medicine*, HOPKINS MED., <https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/nuclear-medicine> (last visited Nov. 1, 2020) and NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, *supra* note 26, at 89.

³⁸⁹ *What is Epigenetics?*, NAT'L INSTS. HEALTH, <https://ghr.nlm.nih.gov/primer/howgeneswork/epigenome> (last updated Sept. 21, 2020) (“Environmental influences, such as a person’s diet and exposure to pollutants, can also impact the epigenome. Epigenetic changes can help determine whether genes are turned on or off and can influence the production of proteins in certain cells, ensuring that only necessary proteins are produced.”); *see also* Black et al., *supra* note 388, at 543–44; Savulescu, *supra* note 173, at 38 (noting that “the environment only acts to affect our biology. If we accept environmental manipulations, by force of consistency, we must accept genetic or other biological manipulations that are safe and have the same effects”); Andrew Curry, *Parents’ Emotional Trauma May Change Their Children’s Biology. Studies in Mice Show How*, SCI. (July 18, 2019, 2:05 PM), <https://www.sciencemag.org/news/2019/07/parents-emotional-trauma-may-change-their-children-s-biology-studies-mice-show-how> (exploring the hypothesis that emotional trauma can lead to inheritable changes in DNA); *Birth Defects Research*, MARCH OF DIMES, <https://www.marchofdimes.org/research/birth-defects-research.aspx> (last visited Oct. 19, 2020).

gene editing is not necessarily as exceptional as commentators note because it is one of many technologies or factors that impact genetic expression.

C. *Lessons from Assisted Reproductive Technology*

Germline gene editing implicates multiple areas of controversy, including controversy related to the use of embryos in research and clinical use, heritable changes, and ART in general.³⁹⁰ The fact that germline gene editing involves reproduction, unlike somatic cell gene editing, warrants particular scrutiny of federal involvement in light of the particularly complicated nature of reproduction in the American legal and political sphere. The regulation of ART provides an option for the regulation of gene editing. Traditional ART does not come without risks, including risks related to the drugs used in ART (which are regulated by the FDA). There are also risks related to maternal-fetal outcomes and the connections between ART and certain adverse birth outcomes, such as “low birth weight[] and congenital malformations, even among singleton pregnancies.”³⁹¹ Even with its continued use and acceptance, the long-term effects of ART on offspring and the women involved in the creation of those offspring remain unknown.³⁹²

These long-term effects have not hindered the legality of non-gene modifying or traditional ART in the United States. The idea of regulating gene editing more like other products or techniques instead of federally-regulated products has arisen before. Jennifer Doudna, one of the American developers of CRISPR-Cas9, has described it as “analogous to software that is easily reprogrammable for a wide variety of experiments and functions across a broad range of plant and animal systems.”³⁹³ Further, gene editing, at least for embryos, still has to be

³⁹⁰ See *supra* Parts II and III.

³⁹¹ Maria Velez et al., *Care Plans for Women Pregnant Using Assisted Reproductive Technologies: A Systematic Review*, 16 REPROD. HEALTH at 1, 2 (2019), <https://reproductive-health-journal.biomedcentral.com/articles/10.1186/s12978-019-0667-z>. See also *id.* at 10; Goodwin, *supra* note 20, at 1058–60 (2010); King, *supra* note 70, at 304–05, 308; *Good Clinical Treatment in Assisted Reproduction—An ESHRE Position Paper*, EUR. SOC’Y HUM. REPROD. & EMBRYOLOGY at 1, 4 (June 2008), <https://www.eshre.eu/-/media/sitecore-files/Guidelines/Guidelines/Position-Papers/GCT-in-ART.pdf>.

³⁹² See, e.g., Baruch, *supra* note 70, at 249.

³⁹³ *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 20 (providing the Prepared Statement of Dr. Jennifer Doudna).

2021] *IS GERMLINE GENE EDITING EXCEPTIONAL?* 811

combined with “medical procedures to successfully deliver modified gametes or embryos into the human reproductive cycle.”³⁹⁴

Some would argue that the current lack of regulation of traditional IVF is due to path dependence, not a reasoned inquiry.³⁹⁵ While attempts to federally regulate IVF and ART occurred, they never succeeded.³⁹⁶ In the realm of gene editing, human germline gene editing has so far been the subject of regulation via federal research funding restrictions and the ban on the FDA’s consideration of any such applications.³⁹⁷

ART has addressed many of the issues that germline gene editing will need to address as it moves toward human clinical use. As noted in Section II.B., in the late 1990s and early 2000s, the FDA targeted cytoplasmic transfer, a form of ART involving genetic modification, for regulation.³⁹⁸ During an advisory committee meeting after the FDA’s issuance of letters to those providing cytoplasmic transfer, physicians noted the difficulty of long-term studies in the context of ART.³⁹⁹ Often, parents have no interest in including their children in follow-up studies following the excitement of a presumably healthy birth. It is also difficult for physicians to keep track of patients in light of the transience of patients in general.⁴⁰⁰ Those same difficulties could likely arise in the from gene editing context. As patients grow older, move, and change physicians, it is likely harder to keep track of them and the long-term effects of certain medical treatments.⁴⁰¹ Further, parents may not wish to subject their children to a physician’s intrusive tests by virtue of their conception using new technologies. Additionally, those conceived using ART might object to continued long-term studies. But various bodies, including the National Academies of Sciences, have emphasized the

³⁹⁴ See also Bosley et al., *supra* note 41, at 485 (providing the statement of Martin Pera, Department of Anatomy and Neuroscience at the University of Melbourne).

³⁹⁵ Volokh, *supra* note 251, at 1035–36 (discussing path dependence in the context of slippery slope arguments).

³⁹⁶ MARSH & RONNER, *supra* note 17, at 108.

³⁹⁷ See *supra* Section II.B.

³⁹⁸ See Lewis, *How Subterranean*, *supra* note 8, at 1250, 1254–61.

³⁹⁹ See, e.g., Transcript, Center for Biologics Evaluation and Research, Food and Drug Administration, Biological Response Modifiers Advisory Committee Open Session, Meeting #32, 375 (May 9, 2002, 8:00 AM), <https://www.fda.gov/OHRMS/DOCKETS/ac/02/transcripts/3855t1-01.pdf> [<https://wayback.archive-it.org/7993/20170404082240/https://www.fda.gov/OHRMS/DOCKETS/ac/02/transcripts/3855t1.htm>].

⁴⁰⁰ *Id.* at 123–24.

⁴⁰¹ *Id.*

need for follow-up studies in the realm of germline gene editing.⁴⁰² The National Academies of Sciences has also emphasized the usefulness of developing ethical norms and the existing regulatory regimes that accompany “human clinical research, gene transfer research, and existing somatic cell therapy” with heritable genome editing.⁴⁰³ This Article argues that the norms of ART and its accompanying regulatory framework would be better than treating germline genome editing like a medical product.

Federal regulation adds an additional hurdle to access because it tends to lengthen the time between access and innovation. It also arguably increases prices for consumers, as regulatory compliance increases costs for developers who must pay for the approval process, and who eventually pass those costs on to consumers. Federal regulation can contribute to reproductive or medical tourism, which increases barriers to access. Minimizing regulation would reduce barriers to access because, at the very least, those with financial means would be able to access germline gene editing in the United States, similar to other medical techniques, as opposed to having to face burdensome federal regulation or hurdles that hinder even research.⁴⁰⁴

Instead of regulating germline gene editing as an exceptional technology or product, regulating it like IVF, a traditional form of ART, could have many benefits. It would help to prevent the stigmatization of those who are produced as a result of gene editing by not treating them differently than children who are conceived through sex or traditional ART.⁴⁰⁵ Many of the bioethical concerns explored in Part III indicate a concern by the public or bioethicists that those who are

⁴⁰² NAT'L ACADS. SCIS., HERITABLE HUMAN GENOME EDITING, *supra* note 52, at 84–85; NAT'L ACADS. SCIS., ENG'G & AND MED, HUMAN GENOME EDITING: SCI., ETHICS, AND GOVERNANCE *supra* note 50, at 104, 135.

⁴⁰³ *Id.* at 6.

⁴⁰⁴ For examples of scholars asking for more regulation of ART, see NAOMI R. CAHN, TEST TUBE FAMILIES: WHY THE FERTILITY MARKET NEEDS LEGAL REGULATION (2009); *see also* Steve P. Calandrillo & Chryssa V. Deliganis, *In Vitro Fertilization and the Law: How Legal and Regulatory Neglect Compromised a Medical Breakthrough*, 57 ARIZ. L. REV. 311, 336–41 (2015). This Article is particularly America-centric and focuses on how germline gene editing fits within the American legal system. Other countries, notably the UK, have a robust governmental framework for using ART that imposes governmental limitations on ART access. *See, e.g.*, Judith Daar, *Federalizing Embryo Transfers: Taming the Wild West of Reproductive Medicine?*, 23 COLUM. J. GENDER & L. 257, 297 (2012); Alicia Ouellette et al., *Lessons Across the Pond: Assisted Reproductive Technology in the United Kingdom and the United States*, 31 AM. J.L. & MED. 419, 419–21 (2005).

⁴⁰⁵ Courtney Megan Cahill, *Reproduction Reconceived*, 101 MINN. L. REV. 617, 671 (2016) (discussing the separate legal treatment of sexual and alternate reproduction).

“created” with the use of gene editing will be different from the general population. Reducing regulation, with an emphasis on reducing the federal government’s involvement in their lives, reduces the likelihood that they will be deemed different from the “naturally occurring” population.

V. CONCLUSION

Gene editing presents a number of unique opportunities. Scientifically, improving gene editing will correspond with an increase in scientific knowledge, as scientists will gain an increased understanding of a number of issues, including the role of genetics in disease and human development. Medically, gene editing offers the possibility of eradicating a number of diseases.⁴⁰⁶

ART, which has existed since at least 1978, is accompanied by safety concerns—as are germline gene editing, gene therapy, and most medical treatments. Treating germline gene editing like ART, namely IVF, a technology that must be used in any gene editing of the embryo that would result in the birth of the child, not only serves to reduce stigmatization of those who might be born as a result of the technique but also removes the federal government from the regulation of reproductive rights. Treating germline gene editing like IVF also minimizes the federal government’s ability to introduce social and political concerns into the regulatory process, to the advantage of innovation that would allow parents to give birth to children that are not affected by their family members’ genetic conditions. Additionally, estimates indicate that somatic and reproductive gene editing might be ready for widespread human clinical use in the next five years. As such, germline gene editing (at least in the United States) is one of the few opportunities for the law to develop at the same time as scientific innovation, or to precede scientific application instead of lagging behind science, as it often does.

⁴⁰⁶ *The Science and Ethics of Genetically Engineered Human DNA*, *supra* note 22, at 23 (providing the testimony of Dr. Elizabeth McNally).