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EDITING HUMANITY: ON THE PRECISE MANIPULATION OF DNA IN HUMAN EMBRYOS*

PAUL ENRÍQUEZ**

Genetically modified humans are among us. Emerging technologies for genome editing have launched humanity into the uncharted territory of modifying the human germline—namely, the reproductive cells and embryos that carry our genetic ancestry. Reports of the first live births of humans with edited genomes in China recently confirmed that the power to manipulate our genes at an embryonic stage is no longer theoretical. In the wake of enormous scientific progress, questions regarding how the law will treat this technological breakthrough abound.

This Article examines the legality of human genome editing, specifically germline genome editing (“GGE”), from administrative and constitutional law perspectives. It argues that the Food and Drug Administration’s (“FDA” or “Agency”) forbearance in claiming jurisdiction over GGE is creating a perilous void for an emerging field of law. At the same time, the contemporary de facto legislative ban on GGE clinical applications, which categorically prohibits the Agency from evaluating the safety and efficacy of any investigational new drug or biological product application derived from the technology, is unnecessary and creates more societal costs than benefits. On a broad scale, the ban embodies poor public policy because it prevents the FDA from exercising jurisdiction over matters that constitute extensions of the Agency’s traditional regulatory scope. An analysis of the law reveals salient regulatory gaps that could be viewed as rendering some types of GGE beyond the FDA’s

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regulatory reach. Notwithstanding those gaps, this Article argues that the FDA can work within the existing statutory framework to cure regulatory deficits and promulgate rules to regulate the technology and, thus, urges the FDA to exercise that jurisdiction. This Article ultimately demonstrates how law and policy converge into a proposed new regulatory paradigm for human GGE that flows from the D.C. Circuit’s ruling in United States v. Regenerative Sciences, LLC, which held that specific stem cell mixtures can be regulated as drugs or biological products within the meaning of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act.

This Article further contends that efforts to ban GGE technologies cannot withstand constitutional scrutiny in the long run because they impinge on a cognizable fundamental right that protects select uses of GGE. This fundamental right flows from jurisprudence in the areas of procreative, parental, and—to some extent—privacy rights, but it is not absolute. The Article presents an interpretive model for this body of jurisprudence in the GGE context, which promotes extrapolation of applicable legal principles that can guide and promote coherent public policy. Launching from this jurisprudential departing point, this Article introduces a novel legal- and science-based normative framework to delineate primary limits for a right to perform GGE based upon four distinct categories: (1) therapeutic uses to remedy disease; (2) prophylactic purposes, which may or may not be therapeutic; (3) cosmetic or enhancement purposes; and (4) uses involving modification of traits that raise concerns of discrimination already prohibited by the law. This conceptual and structural approach outlines a legal blueprint for GGE clinical interventions, but more importantly it circumvents problems that dominate the existing literature, which arise from the conventional tendency to group GGE applications into therapeutic uses on one hand, and enhancements on the other.

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INTRODUCTION

On the eve of the Second International Summit on Human Genome Editing\(^2\) in November 2018, news broke about the first reported live births of human twins whose genomes had been edited.\(^3\) The development follows a stream of recent scientific advances that collectively constitute a revolution concerning “the rational and deliberate manipulation of the genetic composition” of living organisms.

1. The print version of this Article contains only black-and-white figures. Color figures can be found in the online version of this Article, which can be accessed at the North Carolina Law Review’s website, https://www.northcarolinalawreview.org.

2. Genome editing is an umbrella term that refers to “scientific technological advances that enable rational genetic engineering—at a local (gene) or global (genome) level—to facilitate precise insertion, removal, or substitution of fragments of Deoxyribonucleic acid [(“DNA”)] molecules, comprising one or more nucleotides . . . into the cell(s) of an organism’s genome.” Paul Enríquez, Genome Editing and the Jurisprudence of Scientific Empiricism, 19 VAND. J. ENT. & TECH. L. 603, 617 (2017) (footnotes omitted). The term “genome editing” has often been used interchangeably with gene editing, genetic engineering, gene targeting, and other related terms. Id. at 617 n.53.

The engine at the core of this molecular revolution is a breakthrough, now commonly known as CRISPR—an acronym that refers to the system of Clustered, Regularly Interspaced, Short, Palindromic Repeats and CRISPR-associated (Cas) proteins.\footnote{Paul Enríquez, \textit{CRISPR GMOs}, 18 N.C. J.L. & TECH. 432, 435 (2017); \textit{see also} Enríquez, supra note 2, at 632 (providing a short list of living organisms that have been modified using CRISPR-based genome-editing technology).}

At the Human Genome Editing Summit, He Jiankui, a researcher from the Southern University of Science and Technology in Shenzhen, China, confirmed reports that he had performed genome editing on viable human embryos using CRISPR–Cas9.\footnote{Enríquez, supra note 2, at 607. CRISPR is an adaptive immunity system that occurs naturally in bacteria and archaea. It has been repurposed for targeted genome editing by scientists. \textit{See id.} at 629–31. For a brief overview of CRISPR–Cas systems, including the popular CRISPR–Cas9 genome-editing platform used to edit the genomes of the first genetically edited humans, see \textit{id.} at 628–33.} The experiments, which led to the birth of the world’s first gene-edited babies, sought to edit a fragment of the \textit{CCR5} locus that encodes a protein receptor involved in HIV resistance in humans.\footnote{Statement, Francis S. Collins, Dir., Nat’l Insts. of Health, \textit{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 [https://perma.cc/RW3Q-BWDV].} He Jiankui performed the clinical trial in virtually complete secrecy, and his subsequent disclosure sent shock waves throughout the world.\footnote{Id.; Cohen, supra note 3; \textit{see also infra} Figure 5.}

To be clear, He Jiankui’s experiments to edit human embryos for clinical use were largely predictable. Another Chinese study published three years earlier amid similar controversy reported the first instance of human embryo editing to correct a genetic mutation.\footnote{See Statement, Francis S. Collins, supra note 6; Cohen, supra note 3.} The distinction between that study and the one conducted by He Jiankui primarily concerns the quality of the embryos used. The former had experimented with embryos incapable of leading to a pregnancy,\footnote{Puping Liang et al., \textit{CRISPR/Cas9-Mediated Gene Editing in Human Triprominal Zygotes}, 6 PROTEIN & CELL 363, 363–64 (2015). For an overview of the results of the study as well as its implications, see Enríquez, supra note 2, at 664–67.} whereas the latter edited healthy embryos that ultimately led to implantation in a woman’s uterus and the live birth of twins.\footnote{See Liang et al., supra note 9, at 364.}

The logical leap between the two Chinese experiments was not large. After all, the same type of experiments had already been
reported in monkeys and numerous other animal species. Indeed, the birth of a genetically edited human had been a forgone conclusion since 2012, following the debut of CRISPR–Cas9 (Figure 1) as a molecular tool repurposed for programmable genome editing. Predictability and inevitability, however, did not soften the blow generated by the realization that it took humans only six years from the advent of an emerging technology to achieve what had been impossible for thousands of years before.

In the aftermath of the births of the first gene-edited babies, calls for permanent or temporary bans on the use of technologies intended for genome editing have surfaced. Critics of the experiments claim that editing the human germline—sperm, eggs, zygotes, and embryos—is immoral, unethical, and will lead humans down a dangerous path. At the same time, gene editing of somatic cells—differentiated cells, not including the germline—is underway to

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13. See Enríquez, supra note 2, at 664 (“Genome editing in human germ cells was largely predictable in light of the successes of germline editing in a plethora of animal and plant species [in recent] years. . . . In principle, manipulation of the human germline is not much different than germline manipulation in other species.”); see also Edward Lanphier et al., Don’t Edit the Human Germline, 519 NATURE 410, 410 (2015) (advocating for a complete ban on human GGE in response to news about the study Liang and colleagues performed on nonviable human embryos in China); Liang et al., supra note 9, at 363–64 (reporting results from the first experiments to edit nonviable human embryos); Lichun Tang et al., CRISPR/Cas9-Mediated Gene Editing in Human Zygotes Using Cas9 Protein, 292 MOLECULAR GENETICS & GENOMICS 525, 525 (2017) (presenting results from experiments to edit viable human embryos).


15. See Enríquez, supra note 2, at 607 (“A quantum leap in genome editing capabilities has led us to the Rubicon of precise, endogenous, genetic manipulation—one originally envisioned decades ago, yet methodologically beyond reach for prior generations of scientists.” (footnote omitted)).


17. Enríquez, supra note 2, at 664.


19. Enríquez, supra note 2, at 633.
address various unmet needs in human therapeutics. But criticisms of
the potential use of human germline genome editing (“GGE”) clinical
applications vastly overlook the advantages of germline modification,
especially when compared to interventions for somatic genome editing.

20. See Damian Garde, FDA Signs Off on Editas CRISPR Study on Patients with a Rare
Genetic Disorder, STAT (Nov. 30, 2018), https://www.statnews.com/2018/11/30/editas-
crispr-trial/ [https://perma.cc/6B92-6AZU].

21. See Enríquez, supra note 2, at 668 (pointing out that human GGE offers “greater
prospects for human health and welfare than somatic” interventions because GGE can be
used to correct genetic aberrations and prevent their transmission to an individual’s
progeny); see also NAT’L ACADS. OF SCI., ENG’G, & MED., HUMAN GENOME EDITING:
SCIENCE, ETHICS, & GOVERNANCE 111, 113–16 (Rona Briere & Helaine Resnick eds.,
2017) [hereinafter NASEM REPORT] (stating that human GGE can potentially alleviate
emotional, financial, and other types of burdens that families experience as a result of the
transmission of serious genetic diseases).
Figure 1. Structural Representation of the CRISPR–Cas9 Enzyme in Complex with Target Double-Stranded DNA and a Single-Guide RNA (sgRNA)\textsuperscript{22}

The x-ray, three-dimensional structure (left) of the CRISPR–Cas9 endonuclease (gray) bound to an sgRNA (orange) and double-stranded DNA (blue) captures the macromolecular complex as it primes for DNA cleavage. The green spheres represent the two active-site residues indispensable for Cas9 catalytic activity (Aspartate 10, on the right; Histidine 840, on the

left). The cartoon representation of the complex is shown on the right.

A panel of the U.S. National Academies of Sciences, Engineering, and Medicine ("NASEM") recently published a report outlining certain recommendations for genome editing in the human germline. The report recommended that human germline editing clinical trials should proceed only if they seek to prevent serious diseases or conditions for which no reasonable alternatives exist and the trials are subject to rigorous oversight and transparency regarding their safety and efficacy.

Although NASEM recommendations outline a potential path forward for translating human GGE technologies to the clinical setting, they are not without potential flaws. And a large void currently exists regarding how the law will treat this emerging technology, particularly given that the technology exists in the context of an increasingly globalized and interconnected world where cultures do not always share the same values.

23. See generally NASEM REPORT, supra note 21 (considering critical questions regarding genome editing in the human germline, providing conclusions on the need for public education and engagement on that issue, and recommending principles for governing human genome editing).

24. Id. at 7–8.

25. For instance, the panel recommended that there should be “ongoing, rigorous oversight during clinical trials of the effects of the procedure on the health and safety of the research participants” as well as “comprehensive plans for long-term, multigenerational follow-up that still respect personal autonomy.” Id. at 8. However, long-term and multigenerational monitoring can be achieved only with the consent of participants, who may wish to revoke consent at any point following the birth of gene-edited offspring. In a recent study involving the birth of a human baby via mitochondrial replacement therapy, which is colloquially known as an intervention involving “three-parent embryos,” see Françoise Baylis, The Ethics of Creating Children with Three Genetic Parents, 26 REPROD. BIOMEDICINE ONLINE 531, 532 (2013), the parents decided not to submit their child for mitochondrial DNA load retesting after the initial testing performed at birth “unless there [would be] a clinical benefit,” John Zhang et al., Live Birth Derived from Oocyte Spindle Transfer to Prevent Mitochondrial Disease, 34 REPROD. BIOMEDICINE ONLINE 361, 367 (2017) (reporting the first live birth of a human baby via mitochondrial replacement therapy—a type of germline intervention—to prevent transmission of mutations in mitochondrial DNA). The researchers’ goals of monitoring the baby every three months in the first year, every six months in the second year, and every year after the third year of age depend largely on the parents’ willingness to permit such monitoring. See id. And the goal of assessing the baby’s “fertility function” after age eighteen will depend on the consent of the adult individual at that point. See id.

Much has been written about human cloning and somatic cell gene therapy from diverse perspectives in the last three decades.

human germline are permissive in Mexico, Japan, and China and slightly more restrictive in the United States and the United Kingdom. See, e.g., R. Isasi, E. Kleiderman & B.M. Knoppers, Editing Policy to Fit the Genome?, 351 SCIENCE 337, 337–38 (2016); Cohen, supra note 3; David Cyranoski, Japan Set to Allow Gene Editing in Human Embryos, NATURE (Oct. 3, 2018), https://www.nature.com/articles/d41586-018-06847-7 [https://perma.cc/UA9Y-BYJ2]. Meanwhile, other countries like Canada and Germany have instituted broad bans on human germline manipulations. Isasi et al., supra, at 337.

recently, a body of ethics-based scholarship has focused on germline genetic modification from moral, egalitarian, and other societal perspectives, primarily in the context of whether it is appropriate for humans to modify the genome of future generations. However, the legal scholarship on the implications of modern methods to perform genome editing in the human germline—namely, (1) the extent to which existing laws address GGE regulatory issues; (2) whether any constitutional rights as to GGE may exist; and (3) what specific legal- and science-based structural schemes, if any, should be implemented at this point in time to promote or hinder GGE technological development—is remarkably thin.

In panoramic scope, this Article examines the legality of human genome editing and, more specifically, GGE with the overarching goal of closing salient gaps in this emerging field of legal scholarship. To that end, this Article makes three distinct contributions that, collectively, outline a legal- and science-based blueprint that deconstructs the nuances inherent in various uses of genome editing for targeted manipulation of the genetic composition of the human germline. Above all, the Article outlines an approach that ameliorates intractable problems that often arise from the conventional tendency about human cloning as immaterial because married couples purportedly have a constitutional right to use the technology for reproductive purposes).

to group GGE applications into therapeutic uses on one hand and enhancements on the other. That outdated model is inefficient and susceptible to analytical derailments stemming from awkward attempts to fit therapeutic, eugenical, and so-called “designer baby” enhancements into a single doctrinal model. Positing a “therapeutic” and “enhancement” dichotomy also perpetuates a basic misunderstanding of reproductive technologies and breeds an environment for “deceptive simplicity.”

The first contribution centers on the intersection of GGE and administrative law, particularly in the context of executive authority under existing law to regulate GGE technological advances. Specifically, the Article focuses on the FDA’s jurisdictional powers as the agency in charge of “protecting the public health by ensuring the safety, efficacy, and security of human . . . drugs, biological products, and medical devices,” and its current role in shepherding scientific discoveries into the clinical realm. However, GGE research involving human embryos is also currently susceptible to regulation pursuant to the Dickey-Wicker Amendment, the oversight of the National

29. The term “designer baby” has taken root in popular culture, but it is far from helpful in the context of discussing assisted reproductive technologies and their societal implications. This inapplicability is due primarily to the fact that the term is frequently and sensationally associated with phenotypic preferences that are technologically impracticable. See Enríquez, supra note 2, at 676, 678 nn.504 & 506. A common scientific misperception concerns the notion that technological advances bestow upon humankind the ability to engineer humans in a petri dish who exhibit superior beauty, athletic prowess, tall stature, enhanced musical ability and intelligence, etc.—none of which are practicable with the use of current technology. See id.

30. The term “deceptive simplicity” refers to “preposterous, impractical, or sensationalist claims . . . concerning issues raised by technological advances.” Id. at 672.


32. The Dickey-Wicker Amendment prohibits the Department of Health and Human Services (“DHHS”) from using appropriated funds on “research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero.” Balanced Budget Downpayment Act, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996). The Amendment was passed by Congress in 1996 and signed into law by President Clinton. It has exerted a significant inhibitory effect on the generation of new stem cell lines despite continuous funding for research on already-existing cell lines. See Russell A. Spivak, I. Glenn Cohen & Eli Y. Adashi, 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, 30 (2017).
Institutes of Health (the “NIH”), and other regulations related to assisted reproductive technologies.

At its core, the Article’s first contribution proposes a new regulatory path for GGE that flows from the D.C. Circuit’s ruling in United States v. Regenerative Sciences, LLC, which held that specific stem cell mixtures can be regulated as drugs or biological products within the meaning of the Federal Food, Drug, and Cosmetic Act (“FDCA”) and the Public Health Service Act (“PHSA”). The approach reinforces FDA jurisdiction over GGE products and therapies.

The second contribution focuses on GGE and constitutional law. It surveys the due process and equal protection landscape through a mostly—descriptive lens to identify a cognizable fundamental right to select uses of GGE under the Constitution.


34. The FDA may also regulate GGE under provisions applicable to assisted reproductive technologies (“ART”), which relate to the handling of gametes and embryos. See 42 U.S.C. § 263a-1(a)–(c) (2012). For a general overview of ART regulations in the United States, see generally David Adamson, Regulation of Assisted Reproductive Technologies in the United States, 78 FERTILITY & STERILITY 932 (2002).

35. 741 F.3d 1314 (D.C. Cir. 2014).
36. Id. at 1317.
37. See discussion infra Part II. A putative fundamental right to perform select GGE interventions articulated in this Article should not be confused with the unrecognized rights of terminally ill patients to access unapproved drugs, see United States v. Rutherford, 442 U.S. 544, 546 (1979) (finding no constitutional right to try “a drug not recognized as ‘safe and effective’”), or access “a potentially toxic drug with no proven therapeutic benefit,” Abigail All. for Better Access to Developmental Drugs v. Von Eschenbach, 495 F.3d 695, 713 (D.C. Cir. 2007). Abigail, for example, rejected a presumptive right of a terminally ill patient desperately in need of a curative treatment to use a drug that could potentially
flows from jurisprudence in the areas of procreative, parental autonomy, and—to some extent—privacy rights, but it is not absolute.\footnote{38}

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...hasten death. \textit{Id.} This Article does not advocate that parents should assert a “right to try” GGE because there are no alternatives to conceiving a healthy child. To the contrary, this Article extensively links the FDA’s role in establishing the safety and efficacy of drugs and biological products to the GGE context. See discussion \textit{infra} Part I. This Article argues, however, that once safety and efficacy of select GGE interventions are established, which probably will occur at some point in the near future, the government likely cannot categorically ban access to the technology.

Unlike the distribution of unapproved drugs, research in human embryos is legal—at least when performed without the use of public funds. Drug manufacturers may not legally test unapproved drugs without FDA oversight, but little currently prevents geneticists, fertility specialists, and other researchers from continuing to test, refine, and develop GGE technologies for use in early-stage embryos. See, e.g., Hong Ma et al., \textit{Correction of a Pathogenic Gene Mutation in Human Embryos}, 548 \textit{Nature} 413, 413 (2017) (correcting pathogenic heritable mutations in human embryos via GGE). This marks a fundamental distinction between the right-to-try cases and GGE technologies. Scientists in the United States and abroad are conducting research in human and animal embryos to address current limitations of genome-editing technologies, which will lead to more precise genome-editing tools to make GGE safe and effective. At some point in the future, the only impediment to clinical use of GGE may be the current legislative ban on FDA review of Investigational New Drug Applications and Biologic Licensing Applications for GGE purposes. See \textit{infra} Section I.D. But such a ban may not withstand the pressures of rapid and continuous scientific advances that lead to precise, safe, and effective GGE.


Robertson believed that the use of genetic technology to make certain prebirth decisions is “an essential aspect of an individual’s procreative liberty, and that the harms thought to flow from prebirth selection decisions are insufficient to justify interference with them.” Robertson, \textit{Genetic Selection}, \textit{supra}, at 468. “Individuals, not government or third parties, are the best judge of whether [a particular package of reproductive burdens and benefits] is in their own best interest.” \textit{Id.} at 469. Robertson’s thinking on the fundamental status of reproductive choices has influenced subsequent scholarly works, including this Article.

Although Robertson’s scholarship has helped to pave the road for a potential, cognizable constitutional right to select offspring genetic modifications in some contexts,
Here, the Article builds upon existing scholarship and presents an interpretive model for this body of jurisprudence in the GGE context,\(^{39}\) which promotes extrapolation of applicable legal principles that can guide and promote coherent public policy.

The final contribution merges the foregoing analysis to expand the literature and propose a novel legal- and science-based normative framework to delineate primordial limits for a right to perform GGE based upon four categories: (1) therapeutic uses to remedy disease; (2) prophylactic purposes, which may or may not be therapeutic; (3) cosmetic or enhancement purposes; and (4) uses involving modification of traits that raise concerns of discrimination already prohibited by the law. This conceptual and structural approach outlines a legal blueprint for a path to GGE clinical interventions. It also aims to encourage scholarly and public discussions about whether, and the extent to which, editing the genetic composition of the human germline should be permitted, and in some instances protected—a subject arguably among the most significant and consequential of this generation.

This Article is divided into three main parts. Part I analyzes GGE through an administrative law lens. Section I.A provides a brief history of federal public-health and consumer-protection laws in the United

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39. See supra note 38.
States, leading to the establishment and expansion of the FDA’s jurisdiction over various aspects of public health.  

Section I.B then examines the emergence of FDA oversight of somatic cell gene therapy, which has established precedents applicable to GGE. By examining existing laws applicable to gene therapy, this section identifies potential regulatory gaps that could be viewed as rendering some types of GGE beyond the FDA’s regulatory reach, but contends that any such gaps are the product of the FDA’s forbearance in claiming jurisdiction of GGE.

Section I.C proposes a novel regulatory path for GGE that flows from the D.C. Circuit’s ruling in *Regenerative Sciences*, which held that specific stem cell mixtures can be regulated as drugs or biological products within the meaning of the FDCA and the PHSA. The approach identifies potential classifications for GGE products and reinforces FDA jurisdiction over GGE products and therapies.

Finally, Section I.D argues against the current de facto legislative ban on GGE clinical applications, in which human embryos undergo intentional genomic modification. This Article asserts that such a ban is unnecessary because it creates more societal costs than benefits and prevents the FDA from (1) carrying out its mission to protect the public health by ensuring the safety and efficacy of drugs, biological products, and medical devices and (2) exercising full jurisdicational power over an area that is a mere extension of what has traditionally been subject to regulation by the Agency.

Taken as a whole, Part I provides a legal foundation to support the view that the FDA is well equipped to address the challenges of regulating emerging technologies intended for GGE—particularly from safety and efficacy standpoints—that fall within the scope of its jurisdiction.

Part II of this Article contends that permanent legislative or administrative bans on GGE cannot withstand constitutional scrutiny and will likely succumb to litigation because they impinge on a cognizable fundamental right that protects select uses of GGE. This fundamental right flows from jurisprudence in the areas of procreative, parental, and—to some extent—privacy rights, but it is not absolute.
This part examines GGE in the context of an enduring, and often contentious, debate regarding the methodological framework under which the Constitution should be interpreted. The Article acknowledges the interpretive dichotomy that surrounds the invocation of the Due Process Clauses of the Fifth and Fourteenth Amendments to adjudicate cases and controversies under Article III of the Constitution. Whether the extant body of substantive due process jurisprudence is proper when viewed through the lenses of originalism and nonoriginalism, however, is beyond the scope of this Article. And no position on the issue is taken herein. Accordingly, Sections II.A–C undertake a—mostly—descriptive, rather than normative, analysis of the existing jurisprudence in this area of the law.

Section II.D briefly examines Roe v. Wade and its progeny to argue that although issues related to abortion and GGE may appear intertwined at first glance, Roe’s brand of substantive due process is likely to be of little significance in the GGE realm. Section II.E then highlights a crucial role for framing a question centered on the right to perform GGE and provides examples of the types of questions that may come for review before the courts. Overall, Part II concludes that current precedents in substantive due process and equal protection jurisprudence collectively pave a path for the recognition of a right to perform GGE in select contexts.

Part III shifts gears to articulate a normative framework consisting of four distinct categories of GGE: (1) therapeutic uses to remedy disease; (2) prophylactic purposes, which may or may not be therapeutic; (3) cosmetic or enhancement purposes; and (4) uses involving modification of traits that raise concerns of discrimination already prohibited by law. The four-category spectrum suggested here facilitates creation of initial boundaries for GGE and outlines a legal blueprint. Under this approach, Category 1 GGE purposes are permitted and constitute a fundamental right; their prohibition cannot withstand strict constitutional scrutiny. Conversely, Category 4 GGE

45. U.S. CONST. amend. V (“[N]or shall any person . . . be deprived of life, liberty, or property, without due process of law . . . .”); id. amend. XIV, § 1 (“[N]or shall any State deprive any person of life, liberty, or property, without due process of law . . . .”).
46. See infra text accompanying notes 273–77.
47. 410 U.S. 113 (1973).
48. See infra discussion Section II.D.
49. See infra discussion Section II.E.
50. See infra discussion Sections III.A–D.
uses are prohibited because they create a likelihood of discrimination against specific groups and are not constitutionally justifiable.

Lastly, Part III of this Article explains that, from a scientific standpoint, many GGE applications that fall within the sphere of Categories 2 and 3 involve uncharacterized and complex associations between multiple genetic targets. Thus, it is unlikely that the technology to address such types of GGE interventions will be ready for clinical use in the near future. Time currently favors the creation of a rational and robust legal approach to GGE. Accordingly, because Categories 2 and 3 concern GGE uses that are not technologically feasible at this time—and perhaps may not be even in the near future—premature laws and regulations concerning the sanction or prohibition of GGE prophylactic, cosmetic, and enhancement interventions should be avoided.

I. REGULATION OF GERMLINE GENOME EDITING

A. Food and Drug Administration Jurisdiction

The FDA is the federal agency within the U.S. Department of Health and Human Services “responsible for protecting the public health by ensuring the safety, efficacy, and security of human . . . drugs, biological products, and medical devices.” It is the “oldest comprehensive [federal] consumer protection agency” in the United States. The history of the Agency is replete with important lessons relevant to the discussion of GGE and other emerging technologies. The Agency’s past highlights the significance of balancing the federal government’s goal of ensuring consumer protection in the marketplace and the private sector’s opposition to regulatory reform in various contexts. It also brings into focus the pivotal role of public opinion in shifting the fulcrum when government or corporate malfeasance disturbs such balance.

51. See infra discussion Sections III.B–C.
52. What We Do, supra note 31.
54. See discussion infra Sections I.A.1–3.
55. See discussion infra Sections I.A.1–3. See generally, e.g., Carol Ballentine, Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident, FDA CONSUMER, June 1981, reprinted in SULFANILAMIDE DISASTER, https://www.fda.gov/media/110479/download [https://perma.cc/DZR4-UCJT] (noting that the 1937 Elixir of Sulfanilamide drug scandal increased the jurisdictional powers of the FDA); Michelle Meadows, A Century of
Above all, the FDA’s history showcases, in principle, the separation of powers in our democratic system. Over the past century, Congress has enacted laws that granted new and broad regulatory powers to the administrative agency. The executive agency has then promulgated rules under its statutory mandates and sought to enforce perceived violations of the laws. And the judiciary has either endorsed or checked the Agency’s power by interpreting the regulations in the context of cases or controversies under Article III of the Constitution.

Setting the proper historical context also provides an opportunity to learn from past mistakes and take proactive steps toward adequate regulation of emerging technologies. Accordingly, the next section examines why Congress has consolidated federal oversight within the FDA to regulate the food and drug industries and how the FDA has become one of the quintessential consumer-protection watchdog agencies. This backdrop of the FDA’s status as the consumer-protection federal agency tasked with ensuring safety and efficacy of drugs, biological products, and medical devices underscores the notion that the FDA is well suited to regulate GGE and GGE-related emerging technologies.

1. Administrative Antecedents

The FDA’s inception can be traced back to 1839 when Congress appropriated funds to the Patent Office for agricultural purposes, including the “collection of agricultural statistics.” The congressional appropriations subsequently led to the creation of a chemical enforcement system.

Ensuring Safe Foods and Cosmetics, FDA CONSUMER, Jan.–Feb. 2006, at 6 (chronicling the effects induced by public outrage in the 1906 meat-packing scandal on the jurisdictional powers of the FDA).

56. It bears pointing out that some scholars have noted—with light discomfort—that administrative agencies, including the FDA, are increasingly relying on the issuance of nonbinding guidance documents and other less formal administrative tools to implement their statutory authority, while shifting away from the promulgation of binding rules. See, e.g., Lars Noah, Governance by the Backdoor: Administrative Law(lessness?) at the FDA, 93 NEB. L. REV. 89, 90 (2014).


laboratory within the Agricultural Division of the Patent Office in 1848.\textsuperscript{59} Since that date, the federal government has continuously used chemical analysis to monitor the safety of products available to consumers.\textsuperscript{60}

Over the next decade, calls for an independent department to oversee agricultural matters led to legislation that established the U.S. Department of Agriculture ("USDA") in May of 1862.\textsuperscript{61} President Abraham Lincoln then appointed a chemist to head a new USDA Chemical Division,\textsuperscript{62} which comprised what was formerly known as the Chemical Laboratory of the Agricultural Division of the Patent Office.\textsuperscript{63} Under the leadership of Harvey W. Wiley, who was appointed chief chemist in 1883,\textsuperscript{64} the Division of Chemistry\textsuperscript{65} began to undertake seminal studies on food analysis, particularly pertaining to the detection of food adulteration.\textsuperscript{66} The research was published in a series of ten reports summarizing the best current methods of detecting and analyzing adulteration in foods.\textsuperscript{67}

Wiley’s reports aroused public attention and led to the introduction of a food inspection bill in 1887,\textsuperscript{68} as well as the first pure food bill in 1889.\textsuperscript{69} By the turn of the twentieth century, Wiley’s

\textsuperscript{59} Id.; \textit{When and Why Was FDA Formed?}, FDA, https://www.fda.gov/aboutfda/transparency/basics/ucm214403.htm [https://perma.cc/4H89-JBCA].

\textsuperscript{60} Chemical analysis was initially used to monitor the safety of agricultural products, but the scope expanded in subsequent decades to encompass other types of consumer products. \textit{Fight for Consumer Protection}, supra note 53.

\textsuperscript{61} Act of May 15, 1862, ch. 72, 12 Stat. 387. The Act charged the newly formed USDA with duties “to acquire and to diffuse . . . useful information on subjects connected with agriculture . . . and to procure, propagate, and distribute . . . new and valuable seeds and plants.” Id. § 1, 12 Stat. at 387.


\textsuperscript{63} Hutt, supra note 58, at 17–18.

\textsuperscript{64} \textit{See Dr. Harvey W. Wiley, of Indiana, Class of 1871 of the Indiana Medical College, 25 INDIANA MED. J. 446, 447 (1907) [hereinafter Dr. Harvey W. Wiley].}

\textsuperscript{65} The Chemical Division of the USDA became the USDA Division of Chemistry in 1890. Hutt, supra note 58, at 18.

\textsuperscript{66} \textit{See Dr. Harvey W. Wiley, supra note 64, at 446–47. Before undertaking his role as chief of the Division of Chemistry, Wiley was the State Chemist of Indiana. Id.}

\textsuperscript{67} The first report, for example, examined consumer dairy products. \textit{See USDA, DIV. OF CHEMISTRY, BULLETIN NO. 13, FOODS AND FOOD ADULTERANTS. PART FIRST: DAIRY PRODUCTS 3 (1887).} Subsequent reports were published over the span of the next fifteen years. W.D. Bigelow, \textit{Obituary: Harvey Washington Wiley, 72 SCIENCE 311, 311 (1930).}

\textsuperscript{68} Dr. Harvey W. Wiley, supra note 64, at 447.

\textsuperscript{69} Bigelow, supra note 67, at 311. For additional accounts of the history of the FDA in the late nineteenth and early twentieth centuries, see Lewis A. Grossman, \textit{Food, Drugs, and
advocacy\textsuperscript{70} for food and drug safety had contributed to the introduction of nearly one hundred bills that sought to address pervasive abuses in the consumer product marketplace.\textsuperscript{71} Each of those bills succumbed to the influence of powerful industry and manufacturing groups that strongly opposed regulatory reform.\textsuperscript{72}

But in 1906, the release of the novel \textit{The Jungle},\textsuperscript{73} which chronicled the exploitation of immigrant workers and a litany of repugnant and unsanitary practices characteristic of the meat-packing industry of the early twentieth century,\textsuperscript{74} stoked massive public fear and uproar.\textsuperscript{75} Within weeks of the novel’s publication, President Theodore Roosevelt appointed a Special Committee to investigate practices at the meat-packing houses of the Chicago stockyards.\textsuperscript{76}


\textsuperscript{70} See Mary K. Bruch & Elaine Larson, \textit{An Early Historical Perspective on the FDA’s Regulation of OTC Drugs}, 10 \textsc{Infection Control \& Hosp. Epidemiology} 527, 527–28 (1989). For his leadership and contributions to the promotion of food and drug safety during his nearly thirty-year career, Wiley became widely known as the “Father of the FDA.” See, \textit{e.g.}, \textsc{William H. Eaglstein, The FDA for Doctors} 89 (2014).

\textsuperscript{71} \textit{When and Why Was FDA Formed?}, supra note 59.

\textsuperscript{72} Bigelow, supra note 67, at 311; see also Dale A. Stirling, \textit{Profiles in Toxicology: Harvey W. Wiley}, 67 \textsc{Toxicological Sci.} 157, 157 (2002) (noting that attempts at passing food-safety legislation had failed until the enactment of the Pure Food and Drug Act of 1906).

\textsuperscript{73} \textsc{Upton Sinclair, The Jungle} (1906).

\textsuperscript{74} Sinclair’s primary impetus for writing the novel was to promote a socialist movement in the United States. Accordingly, he expressed discontent that the novel’s focus on the plight and injustice experienced by immigrant workers at the hands of the meat-packing industry, along with its political message, took a backseat to the public uproar engendered by his relatively brief depictions of unsanitary conditions at the Chicago stockyards. Indeed, after his novel had become a commercial success, Sinclair published an essay in \textit{Cosmopolitan Magazine}, in which he candidly stated,

\begin{quote}
I wished to frighten the country by a picture of what its industrial masters were doing to their victims; entirely by chance I had stumbled on another discovery—what they were doing to the meat supply of the civilized world. In other words, \textit{I aimed at the public’s heart, and by accident I hit it in the stomach.}
\end{quote}


the investigation, which lasted more than two weeks, documented a long list of food handling and preparation methods deemed dangerous to human health. The Special Committee’s report lent support to Roosevelt’s urgent call to enact laws sanctioning the power of the federal government to inspect, supervise the preparation methods of, and establish sanitation norms for meat and meat food products entering into interstate commerce.


Public clamor concerning the meat-packing exposé coupled with Wiley’s long-standing advocacy for the institutionalization of food and drug safety eventually paved the road for regulatory reform. On June 30, 1906, the Pure Food and Drug Act (“PFDA”) was enacted into law. It sought to prevent “the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors.” The landmark legislation—signed into law on the same day as the Federal Meat Inspection Act—left an indelible mark during the formative years of what would eventually become the FDA.

The PFDA had several notable provisions. First, the Act made it unlawful to manufacture and introduce into interstate commerce any article of food or drug that was deemed “adulterated” or “misbranded” within the meaning of the law, and it prescribed fines

77. Id.
78. Id.
80. Id. § 1, 34 Stat. at 768.
82. Pure Food and Drug Act of 1906, § 1, 34 Stat. at 768.
83. See id. § 2, 34 Stat. at 768.
84. Id. § 7, 34 Stat. at 769–70. The PFDA defined adulterated articles, for the first time, as (1) drugs that differed from recognized standards of strength, quality, or purity; (2) confectionery with ingredients that were deleterious or detrimental to health; or (3) food that contained injurious mixtures or substitutes, had constituent parts abstracted, featured addition of poisonous or deleterious ingredients, concealed damage or inferior quality, or consisted of a decomposed animal or vegetable substance. Id.
85. Id. § 8, 34 Stat. at 770–71. Misbranded articles were also defined, for the first time, as (1) drugs that bore a false name, featured false contents, failed to include a label that lacked the quantity or proportion of specific numerated substances; or (2) food that was an
or imprisonment as penalty for such violations. Second, the legislation assigned authority to the USDA to make rules and regulations to implement provisions of the Act. Third, the law granted enforcement powers to the Bureau of Chemistry, including the power to examine specimens of foods and drugs manufactured or sold in interstate commerce. Fourth, the Act outlined due process provisions applicable in the event that testing by the Bureau of Chemistry revealed adulteration or misbranding of food and drugs within the meaning of the PFDA. Lastly, the law introduced the antecedent of the modern definition of “drug” as “any substance or mixture . . . intended to be used for the cure, mitigation, or prevention of disease” and recognized the U.S. Pharmacopeia and National Formulary as authoritative drug entities.

The PFDA was the first of more than two hundred laws that constitute the backbone of our federal public-health and consumer-protection system. It represented an unprecedented expansion of federal oversight over food and drug law, and consolidated federal jurisdiction over food and drug products intended for interstate commerce into a single federal agency with broad regulatory powers. Thus, the PFDA essentially established the FDA’s modern regulatory functions, which laid the groundwork for building the basic elements of consumer protection that stand to this day.

Following the PFDA’s enactment, the Bureau of Chemistry undertook the task of enforcing the new law. Under Wiley’s leadership, the Bureau gained strength and stature as an administrative
body.\textsuperscript{95} Its appropriations more than sextupled, the staff expanded, and a new building was set aside for operations.\textsuperscript{96} Soon thereafter, however, Wiley encountered strong opposition from business and manufacturing interests that sought to curtail the Bureau’s new regulatory powers.\textsuperscript{97}

Litigation ensued and led to a string of judicial decisions that stymied the Bureau’s enforcement mechanisms and constricted the regulatory scope of the PFDA,\textsuperscript{98} often in perplexing ways that ran contrary to the advancement of public welfare.\textsuperscript{99} This apparent influence of business interests over the execution of the PFDA was deeply troubling to advocates of increased regulation.\textsuperscript{100} It also

\begin{itemize}
  \item \textsuperscript{95} Harvey Washington Wiley, M.D., FDA, https://www.fda.gov/AboutFDA/FOrgsHistory/Leaders/ucm093765.htm [https://perma.cc/C8TS-FBG4].
  \item \textsuperscript{96} Id.
  \item \textsuperscript{97} See, e.g., Wiley, supra note 94, at 261–73 (recounting select legal battles stemming from prosecution of PFDA violations).
  \item \textsuperscript{98} See, e.g., United States v. Lexington Mill & Elevator Co., 232 U.S. 399, 411 (1914) (holding that the government has the burden to establish that a poisonous or deleterious food additive may render a food article injurious to health before it can be condemned, and that the mere presence of such an additive is not sufficient to render the article of food illegal); United States v. Johnson, 221 U.S. 488, 497–98 (1911) (holding that the PFDA applied only to false or misleading statements about the ingredients or identity of a drug and did not prohibit false curative claims).
  \item Notably, the Supreme Court’s ruling in Johnson did not end the controversy. Congress sought to overcome Johnson’s narrowing of the scope and power of the Bureau of Chemistry by enacting the Sherley Amendment. Sherley Amendment to the Pure Food and Drugs Act, ch. 352, 37 Stat. 416 (1912), repealed by Federal Food, Drug, and Cosmetic Act, ch. 675, § 902(a), 52 Stat. 1040, 1059 (1938) (codified as amended at 21 U.S.C. § 387b (2012)). The revision was intended to prohibit false and fraudulent curative or therapeutic claims of health benefits that had been upheld in Johnson. Subsequent judicial interpretation, however, made enforcing the Sherley Amendment problematic because of the high threshold required to establish fraudulent intent. See Stephen Wilson, Food & Drug Regulation 81–82 (1942); see also C. W. Crawford, Technical Problems in Food and Drug Law Enforcement, 1 Law & Contemp. Probs. 36, 41 (1933) (describing how defense counsel for a ketchup company delegitimized effective methods of determining spoilage by framing them as “encroachments [by] mendaciously meddling bureaucracy” threatening “[t]raditional American freedom[s]”).
  \item \textsuperscript{99} See, e.g., Crawford, supra note 98, at 36 (“It has been rightly said that the policy of the Federal Food and Drugs Act regarding added poisonous substances in food is an inverted one since the law places the obligation on the Government to show that the contaminated food may be harmful to health, rather than on the manufacturer to show that it will not.”).
  \item \textsuperscript{100} For instance, Wiley expressed the following concern:

There is a distinct tendency to put regulations and rules for the enforcement of the law into the hands of the industries engaged in the food and drug activities. I consider this one of the most pernicious threats to pure food and drugs. . . . When we permit business in general to regulate the quality and character of our food and drug supplies, we are treading upon very dangerous ground. . . . It is never advisable to surrender entirely food and drug control to business interests. There is much to
highlighted the simple fact that the chief law responsible for launching the FDA into the modern era of health and consumer protection was far from perfect.101 In the end, despite the enforcement hurdles associated with the PFDA, the landmark legislation succeeded in establishing foundations and a preliminary framework for the system of food and drug law that has prevailed for more than a century.

3. Expanding the Core of Modern Food and Drug Law

A key turning point in the history of the FDA arrived in the late 1920s and early 1930s.102 Pressure began to mount to address a long list of inherent shortcomings within the PFDA that rendered it toothless against flagrant abuses and misdeeds in the marketplace.103 The FDA recommended a complete overhaul of the 1906 law104 and advocated for stronger legislation.105 But the proposed bill stalled in Congress and

be done yet before we can point to a food and drug control that is wholly interested in the welfare of the consumer.

WILEY, supra note 94, at 273.

101. Indeed, Wiley, the PFDA’s author and chief enforcer, lamented the gradual decrease of enthusiasm in the years after the bill was signed into law. He contemporaneously expressed that “[the PFDA] is regarded as established and in perfect operation. This is a great mistake. There are practices which are permitted under the present administration of the law that are in direct opposition to fundamental principles.” Id. at 272–73.

102. By 1927, the Bureau of Chemistry underwent reorganization to separate its regulatory and research branches. Milestones in U.S. Food and Drug Law History, FDA, https://www.fda.gov/aboutfda/history/forgshistory/evolvingpowers/ucm2007256.htm [https://perma.cc/QP8M-4KTL] [hereinafter Milestones]. The regulatory division of the Bureau became the Food, Drug, and Insecticide Administration, which was subsequently abbreviated to Food and Drug Administration in 1930. Id. Although the FDA was baptized with its current name in 1930, it was still part of the USDA. Then in 1940, it was transferred to the Federal Security Agency, which was twice renamed: the Department of Health Education and Welfare in 1953 and Department of Health and Human Services in 1979. History of FDA’s Internal Organization, FDA, https://www.fda.gov/AboutFDA/History/ForgsHistory/default.htm [https://perma.cc/2LNU-WUGZ]. The FDA currently resides within the DHHS. Id.

103. For a brief account of said shortcomings, including the lack of oversight over cosmetics, patent medicines, false advertising, food preservatives, etc., and vagueness vis-à-vis food adulteration, see CHARLES O. JACKSON, FOOD AND DRUG LEGISLATION IN THE NEW DEAL 3–8 (1970).

104. Milestones, supra note 102.

105. In the aftermath of the New Deal, the FDA engaged in a public relations campaign aimed at addressing the need for new, stronger federal laws to adequately enforce food and drug safety and protect consumers from dangerous products that were marketed legally. To reach a wide range of audiences in government, the press, and the general public, the Agency assembled a collection of graphic depictions and turned it into an exhibit that became known as the “Chamber of Horrors.” John P. Swann, How Chemists Pushed for Consumer Protection: The Food and Drugs Act of 1906, CHEMICAL HERITAGE, Summer 2006, at 6, reprinted in HOW CHEMISTS PUSHED FOR CONSUMER PROTECTION: THE FOOD
triggered a five-year legislative battle. Progress on enacting a new law stagnated until a public tragedy involving a so-called Elixir of Sulfanilamide drug became publicized in 1937.

The drug contained diethylene glycol, a toxic and untested organic solvent commonly used in a wide range of industrial products. As the drug hit the market, reports of mass poisonings, including the death of 107 people—mostly children—highlighted the pressing need to enact a tighter food and drug law to protect consumers. Thus, it took a wave of public outrage—much like the meat-packing scandals during the passage of the PFDA in 1906—to break congressional gridlock and pass the legislation through Congress.

On June 25, 1938, Congress enacted the FDCA. The legislation aimed to “prohibit the movement in interstate commerce of adulterated and misbranded food, drugs, devices, and cosmetics.” It repealed the PFDA of 1906 and replaced it with a sweeping statute that constitutes the core of today’s food and drug law. The FDCA addressed many of the weaknesses of the PFDA, expanded the FDA’s jurisdictional powers over new areas, and closed loopholes derived from judicial interpretations of the antecedent regulatory scheme.

For instance, under the FDCA, the FDA assumed authority to regulate therapeutic claims on drug labels, thereby repealing the Sherley Amendment requirement that one must prove intent to defraud or mislead in a misbranding case. The Act expanded the FDA’s jurisdiction to encompass regulation of cosmetics and medical devices. It broadened the scope and definition of terms including

AND DRUGS ACT OF 1906, https://www.fda.gov/media/110307/download [https://perma.cc/PT4D-H8SQ]. The exhibit consisted of a series of ghastly images depicting harmful effects caused by various unsafe products, which were lawfully marketed to consumers at the time. Id.

106. Milestones, supra note 102.
107. Id.; FDA History Office, supra note 62, at 151.
108. See Leo J. Schep et al., Diethylene Glycol Poisoning, 47 CLINICAL TOXICOLOGY 525, 525 (2009).
110. See supra notes 73–78 and accompanying text.
112. Id. (quoting the long title of the Act).
113. Id. § 502(a), (j)(1), 52 Stat. at 1050–51.
114. See supra note 98 and accompanying text.
food, drug, label, and misbranded article. The law further specified the FDA’s authority to conduct inspections of any “factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held.” The FDCA also charged the FDA with promulgating rules to set tolerance limits for unavoidable poisonous ingredients in foods. Drug labels were now required to indicate, in language likely to be read and understood by an ordinary individual, whether the drug contained any habit-forming substances or derivatives.

Importantly, the FDCA instituted a mandatory premarket approval scheme for new drugs. No drug manufacturer could introduce a new drug into interstate commerce without first filing an application that contained sufficient information to establish the drug’s safety before the FDA. Had this feature been in place prior to 1938, the Elixir of Sulfanilamide crisis might have been averted.

Armed with an arsenal of new jurisdictional powers, the FDA began to enforce provisions of the FDCA. Predictably, the Agency faced litigation challenges. However, as courts began to examine and interpret the FDCA, the Agency’s authority was upheld in pivotal cases that ultimately strengthened the FDA’s jurisdiction over public-health and consumer-protection matters.

116. Id. § 201(f), 52 Stat. at 1040. The definition of “food” explicitly included chewing gum. Id.
117. Id. § 201(g), 52 Stat. at 1041. The term “drug” under the FDCA of 1938 meant “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and . . . . articles (other than food) intended to affect the structure or any function of the body of man or other animals.” Id.
118. Id. § 201(k), 52 Stat. at 1041.
119. Id. § 201(n), 52 Stat. at 1041.
120. Id. § 704, 52 Stat. at 1057. The FDCA also authorized inspectors “to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics.” Id.
121. Id. § 406(a), 52 Stat. at 1049.
122. Id. § 502(c)–(d), 52 Stat. at 1050.
123. Id. § 505(a), 52 Stat. at 1052.
124. See, e.g., United States v. Sullivan, 332 U.S. 689, 697–98 (1948) (holding that the FDCA did not exceed its constitutional authority under the Commerce Clause when a retailer was charged with performing acts that resulted in a drug being misbranded while held for sale after shipment in interstate commerce); Alberty Food Prods. v. United States, 194 F.2d 463, 464 (9th Cir. 1952) (affirming a lower court’s ruling that the drugs in question were misbranded under the FDCA because the label lacked adequate directions for use). But see United States v. Cardiff, 344 U.S. 174, 176–77 (1952) (holding that refusal to grant permission to inspect a factory pursuant to the FDCA cannot constitute a crime because the Act is too vague to be enforced under criminal law).
Further expansion of that authority came with the enactment of the PHSA, another legislative milestone that consolidated and updated laws related to the administration of the Public Health Service. The PHSA addressed a broad spectrum of health concerns, including the establishment of the federal government’s quarantine powers to prevent the spread of communicable diseases, the government’s duty to promote and coordinate research and investigations into the causes and treatment of disease, and the regulation of biological products applicable to the prevention, treatment, or cure of diseases.

Another key legislative achievement for consumer protections came in 1962 with the enactment of the Kefauver-Harris Amendments. Prior to this landmark legislation, drug manufacturers merely had to establish safety before introducing a drug into interstate commerce. But the Kefauver-Harris Amendments “established a framework that required drug manufacturers to prove scientifically that a medication was not only safe, but effective.” The law significantly enhanced the FDA’s authority over drugs, although it also increased the cost of developing new drugs by imposing premarket review, effectiveness, and other requirements on the drug industry.

In the decades since their enactment, both the FDCA and PHSA—alongside other laws related to public health and consumer protection—have undergone numerous amendments that have amplified the scope of FDA jurisdiction over health care in the United States. Today, the FDA regulates more than $2.5 trillion worth of

126. See id. § 311, 58 Stat. at 693; id. § 361(a), 58 Stat. at 703.
127. Id. § 301, 58 Stat. at 691–92.
128. Id. § 351, 58 Stat. at 702–03.
food, medical products, and tobacco. It exercises jurisdiction over food safety, drug safety and efficacy, biological products ranging from blood to vaccines, cosmetics, medical devices, consumer products that emit radiation, veterinary products, and tobacco products. Products regulated by the FDA constitute roughly twenty cents of every dollar spent by American consumers. Simply put, the FDA has become one of the most powerful and effective agencies in the federal government. Despite its sheer size and power, the FDA has earned a favorable reputation among the public, with consumers reporting higher levels of trust in the FDA than the federal government as a whole.

In addition to protecting consumers, the FDA strives to (1) advance “the public health by helping to speed innovations that make medical products more effective, safer, and more affordable” and (2) educate the public by providing access to “accurate, science-based information” needed for consumers to make choices about the use of “medical products and foods to maintain and improve their health.” Moreover, the Agency plays a significant role in the federal government’s counterterrorism capabilities by ensuring the security of the food supply and developing strategies to respond to public-health threats.


136. Fact Sheet, supra note 134. The Agency also employs over 18,000 individuals, see FDA, 2020 JUSTIFICATION OF ESTIMATES FOR APPROPRIATIONS COMMITTEES 343 (2020), https://www.fda.gov/media/121408/download [https://perma.cc/SHV8-AUF5], and for fiscal year 2020 requested a federal budget of $6.1 billion, id. at 8.

137. Cf. Seok-Eun Kim, The Role of Trust in the Modern Administrative State: An Integrative Model, 37 ADMIN. & SOC’Y 611, 613 (2005) (“American political theories are often quite explicit in their inherent distaste for strong bureaucratic powers because of concern about ensuring accountability.”).

138. See, e.g., Sarah D. Kowitt et al., Awareness and Trust of the FDA and CDC: Results from a National Sample of US Adults and Adolescents, 12 PLOS ONE, no. e0177546, May 16, 2017, at 1, 4–6 (reporting results of a study that found 79% of adolescents and 63% of adults have high levels of trust in the FDA compared to 43% of adults with a “[g]reat deal or a fair amount of trust in the federal [government]”; see also PEW RESEARCH CTR., BEYOND DISTRUST: HOW AMERICANS VIEW THEIR GOVERNMENT 58 (2015) (reporting a 51% favorable rating of the FDA among the public compared to Congress’s 27% favorable rating).

139. What We Do, supra note 31.

140. Id.

141. Id.
As is evident from its historical antecedents, the FDA has become what it is today due largely to its pivotal function of protecting consumers from systemic abuses perpetrated by select industry and manufacturing groups. The FDCA, PHSA, and other laws related to public health and consumer protection have been the statutory means through which the Agency has fulfilled that broad policy goal. The FDA’s long-standing history of consumer protection is significant for purposes of this discussion because it has laid a legal foundation to support the view that the FDA is well equipped to address the challenges of regulating emerging technologies—particularly from safety and efficacy standpoints—that fall within the scope of its jurisdiction. Indeed, the FDA has already paved ample groundwork in the once-emerging fields of recombinant DNA technology and gene therapy, which have set precedents in many respects analogous to the issue of GGE.

B. *The Somatic Cell Gene-Therapy Model*

During the 1970s, the discovery of restriction enzymes capable of triggering sequence-specific cleavage of DNA molecules triggered a scientific revolution of colossal proportions.142 In a matter of a few years, research into new recombinant DNA techniques ushered in the era of modern biotechnology that has changed the world.143 In the midst of this molecular enlightenment, which suddenly brought genetic engineering within the realm of possibility, scientists began to posit whether genetic manipulation in humans could be used for genetic therapies to treat, cure, or ameliorate heritable diseases144 and other conditions.145 Less than twenty years later, results from the first approved nuclear gene transfer in a group of five patients with

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143. *Id.* at 621.
144. A heritable disease refers to a genetic disorder—namely, a type of genetic abnormality giving rise to a medical condition—that is passed down from one generation to the next via the germline. See *Specific Genetic Disorders*, NAT’L HUM. GENOME RES. INST., https://www.genome.gov/10001204/specific-genetic-disorders/ [https://perma.cc/39XZ-GUS7]. For a list of some common heritable diseases, see *id.* (including achondroplasia, some forms of hereditary breast cancer, hemophilia, Cystic Fibrosis, familial Parkinson’s disease, phenylketonuria, Marfan syndrome, and Tay-Sachs).
metastatic melanoma—an advanced cancer—established proof of concept for this novel approach to human gene therapy.\(^{146}\)

This modern-medicine breakthrough raised questions regarding how human gene therapy would be regulated. Soon, manufacturers of products intended for use in emerging gene therapies sought regulatory status clarifications from the federal government.\(^{147}\) The FDA answered that call in a statement published in 1993.\(^{148}\) Pursuant to its jurisdictional authority under the FDCA\(^ {149}\) and the PHSA,\(^ {150}\) the FDA asserted jurisdiction to regulate human somatic cell\(^ {151}\) and gene-therapy products.\(^ {152}\)

In the late 1990s, gene therapy experienced severe setbacks after the unfortunate death of Jesse Gelsinger, an eighteen-year-old patient suffering from partial ornithine transcarbamylase (“OTC”) deficiency,\(^ {153}\) who died from a gene-therapy treatment in a clinical trial in 1999.\(^ {154}\) However, following improvements in nonviral and viral gene-transfer vectors over the last two decades, gene therapy is now viewed as a viable tool to address a wide range of diseases.\(^ {155}\) Two gene-therapy treatments—Glybera\(^ R\) and Strimvelis—have already gained approval in Europe,\(^ {156}\) and Kymriah recently became the first FDA-approved gene-therapy product in the United States.\(^ {157}\)


\(^{148}\) See id.


\(^{151}\) “Somatic cells are all of the body’s cells except the reproductive cells.” Enríquez, *supra* note 2, at 633 n.178.


\(^{153}\) OTC is “a rare metabolic disease that can cause a dangerous build-up of ammonia in the body.” Sally Lehrman, *Virus Treatment Questioned After Gene Therapy Death*, 401 NATURE 517, 517 (1999).

\(^{154}\) See id.


\(^{156}\) See Keeler et al., *supra* note 155, at 242.

\(^{157}\) See *infra* note 169 and accompanying text.
1. Gene Therapy—A Synopsis

The FDA originally defined human gene therapy as “a technique that modifies a person’s genes to treat or cure disease” via manipulation of gene expression or the alteration of biological properties of living cells. The cells may be modified in vivo or ex vivo for subsequent administration to humans. Genetic modifications performed under the latter approach also constitute a form of somatic cell therapy, which refers to the administration of autologous, allogeneic, or xenogeneic “living non-germline cells . . . for therapeutic, diagnostic, or preventive purposes.” “Cellular products intended for use as somatic cell therapy are biological products subject to regulation pursuant to the PHS[A] . . . and also fall within the definition of drugs in the [FDCA].”

Among current gene-therapy products within the purview of the FDA authority are plasmid DNA molecules, viral and bacterial vectors, human gene-editing technology, and patient-derived cellular gene-therapy products. These products are deemed to be biological products subject to regulation by the FDA’s Center for Biologics Evaluation and Research (“CBER”). In 2017, Kymriah became the first FDA-approved gene-therapy product in the United States for the

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159. *In vivo* refers to a process, experimentation, or occurrence that takes place directly inside the body of a living organism. Thus, an *in vivo* cell modification refers to a change that occurs in a cell that is directly inside the body of a living organism.

160. *Ex vivo* refers to a process, experimentation, or occurrence that takes place outside of the body of a living organism. Thus, an *ex vivo* cell modification refers to a change that occurs in a cell that is outside of the body of a living organism.

161. GUIDANCE FOR SOMATIC CELL THERAPY, supra note 158, at 3.

162. Autologous refers to cells or tissues derived from the same individual.

163. Allogeneic refers to cells or tissues derived from a different individual of the same species and, thus, said cells or tissues may or may not be immunologically compatible.

164. Xenogeneic refers to cells or tissues derived from individuals of different species.

165. GUIDANCE FOR SOMATIC CELL THERAPY, supra note 158, at 3 (emphasis added).


168. *Id.*
treatment of “certain pediatric and young adult patients with a form of acute lymphoblastic leukemia.”

Notwithstanding the FDA’s long-established jurisdiction over gene therapies aimed at somatic cell modification, to date the Agency has remained silent regarding its authority to regulate products intended to modify the human germline. The FDA recently expressed views that technologies for human genome editing can be regulated under the gene-therapy framework. In July 2018, the Agency published proposed draft regulations asserting jurisdiction over gene-therapy products involving genome editing. However, such authority


170. On January 18, 2017, then-FDA Commissioner Robert Califf published a statement asserting that the FDA intends to regulate genome-editing products using a product-specific, risk- and science-based approach. See Robert M. Califf & Ritu Nalubola, FDA’s Science-Based Approach to Genome Edited Products, FDA VOICE (Jan. 18, 2017), https://perma.cc/X936-U9JJ, reprinted in Robert M. Califf & Ritu Nalubola, FDA’s Science-Based Approach to Genome Edited Products, CHECK ORPHAN (Jan. 19, 2017), http://www.checkorphan.org/news/fda2019s-science-based-approach-to-genome-edited-products [https://perma.cc/C7H3-QDG7]. On the issue of human medical products that feature gene-editing components of therapeutic nature, the FDA indicated that regulation would proceed under the existing gene-therapy framework. See id. At the same time, the FDA clarified that the statement regarding gene-editing products applies only to nonheritable somatic cell therapy and not to germline gene therapy. Id. The statement appeared on FDA Voice, the FDA’s official blog. Id.

Interestingly, the statement on the FDA’s intended approach toward the regulation of genome-edited products was taken down from the FDA website on or around October 3, 2018, and replaced with a collection of perspectives from FDA experts. See FDA Voices: Perspectives from FDA Experts, FDA, [https://www.fda.gov/newssevents/newsroom/fdavoices/default.htm]. It is not clear whether removal of the policy statement signals that the FDA intended to proceed with a different approach under the direction of Scott Gottlieb, the new FDA Commissioner appointed by the Trump Administration who, unexpectedly, resigned from his post in March 2019, see Sheila Kaplan & Jan Hoffman, F.D.A. Commissioner Scott Gottlieb, Who Fought Teenage Vaping, Resigns, N.Y. TIMES (Mar. 5, 2019), https://www.nytimes.com/2019/03/05/health/scott-gottlieb-resigns-fda.html [https://perma.cc/74CR-FLXL], or merely that the FDA’s blog was reorganized.

explicitly applies to somatic cell-based gene therapies and excludes GGE interventions.\textsuperscript{172}

2. Regulatory Gaps and Limitations of the Gene-Therapy Model

The FDA’s clear intent to regulate technologies for human genome editing under the gene-therapy framework coupled with its silence vis-à-vis gene therapies involving GGE brings uncertainty to a new field of law. Although both somatic and germline treatments could be used for gene therapy and other therapeutic applications, the current gene-therapy model simply does not fit GGE intervention.

Two important points reveal large gaps in the gene-therapy regulatory scheme and deserve special attention. First, the Agency has explicitly excluded modification of germline cells from its definition of gene therapy over the last three decades.\textsuperscript{173} This is significant because it is unclear whether the FDA intends to regulate GGE differently—presumably because it is fully cognizant of the limitations inherent in the current gene-therapy framework that render it inapplicable toward GGE modifications—or whether the Agency believes it lacks the authority to regulate such technologies at all, which is unlikely. The methods used to achieve GGE therapies are likely to overlap extensively with those used in present gene-therapy approaches that are in preapproval stages or have already been approved. Thus, assuming that a particular type of gene therapy warrants approval because it is safe and effective, the dispositive distinction between somatic and GGE interventions appears to turn on the intended results of the therapy—namely, whether the modification remains confined to the individual patient or has the potential to be inherited by the individual’s progeny.\textsuperscript{174}


\textsuperscript{173} See sources cited supra notes 152, 158, 171–72 and accompanying text.

\textsuperscript{174} A focus on discriminating between particular types of gene therapy based on the intended results derived from them raises many legal issues beyond the scope of administrative law. One concerns constitutional issues related to a fundamental right to edit one’s own germ cells, which is explored in Parts II and III of this Article.
Second, the FDA’s explicit narrowing of the scope of gene therapy to treat or cure disease could create a deep regulatory void. The Agency’s circumscription to therapeutic applications means that nontherapeutic GGE interventions would, in theory, fall beyond the Agency’s regulatory reach. Failure to broaden the scope of GGE past the therapeutic realm might enable an alternate system of deregulation in which the potential modification of traits for cosmetic or enhancement purposes is not sufficiently scrutinized.

C. Establishing Jurisdictional Authority over Germline Genome Editing

As noted above, the establishment of FDA jurisdiction over GGE under the current gene-therapy framework is problematic. Therefore, this Article proposes that the FDA should instead assert authority over the regulation of all types of GGE products—regardless of whether they are intended for therapeutic uses—as drugs and biological products within the meaning of the FDCA and PHSA. In so doing, the Article outlines a new regulatory path for GGE that flows from the D.C. Circuit’s ruling in Regenerative Sciences, which held that the FDA can regulate specific stem cell mixtures as drugs or biological products within the meaning of the FDCA and PHSA.

1. United States v. Regenerative Sciences, LLC

In Regenerative Sciences, a Colorado clinic operated by two physicians marketed Regenexx-C, a procedure involving a cultured stem cell mixture, as part of a medical therapy for treatment of arthritis and other orthopedic conditions. The treatment involved extraction of mesenchymal stem cells (“MSCs”) from a patient’s bone marrow, followed by a culturing process of approximately two weeks that

175. See What is Gene Therapy?, supra note 158.
176. In practice, however, it is difficult to imagine the FDA declaring it lacks authority to regulate some human genetic interventions simply because they involve aesthetic or enhancement purposes rather than therapeutic purposes.
178. Id. at 251. MSCs are a type of multipotent stem cells capable of differentiating into various cell lineages, including fat, muscle, bone, cartilage, and other cells. See Umberto Galderisi, Antonio Giordano & Marco G. Paggi, The Bad and the Good of Mesenchymal Stem Cells in Cancer: Boosters of Tumor Growth and Vehicles for Targeted Delivery of Anticancer Agents, WORLD J. STEM CELLS, Feb. 26, 2010, at 5, 6. MSCs are of clinical interest because they can be easily isolated from bone marrow and expanded in vitro. Id.
179. Regenerative Sci., 878 F. Supp. 2d at 251–52; see also Are the Regenexx Procedures Performed in the U.S. Approved by the FDA?, REGENEXX, https://www.regenexx.com/
allowed the stem cells to differentiate and proliferate, and the addition of an antibiotic to prevent bacterial contamination of the cells. The mixture was subsequently injected back into the patient’s body at a target site.

The Regenexx-C procedure became the subject of FDA scrutiny when stem cell therapies were increasingly identified as being part of an unregulated, Wild West-like cottage industry. Despite the promise of stem cell medicine and its potential to eradicate many diseases, the uncertain risks and efficacy of stem cell therapies, which by default rendered them premature for clinical use, cautioned against their broad and unregulated use. Dangerous side effects had already been reported for some of these unregulated stem cell therapies, which were not subject to traditional clinical-trial protocols. Private clinics began to thrive in an environment of little to no regulation by marketing therapies directly to consumers, often via the internet (Figures 2–4).

Providers of stem cell therapies generally portrayed stem cell medicine as safe and frequently made unsubstantiated and false claims about the efficacy of costly stem cell procedures for a broad range of aesthetic and medical conditions, including aging, skin care, diabetes, orthopedic injuries, Parkinson’s Disease, spinal cord injuries, osteoarthritis, stroke, autism, hair loss, erectile dysfunction, pain, and many others. Even today, many private clinics that constitute the


181. Id. at 251–52.
182. See generally Chris E.P. Goldring et al., Assessing the Safety of Stem Cell Therapeutics, 8 CELL STEM CELL 618 (2011) (describing safety issues and knowledge gaps in novel stem cell treatments); Hans Lassmann, Stem Cell and Progenitor Cell Transplantation in Multiple Sclerosis: The Discrepancy Between Neurobiological Attraction and Clinical Feasibility, 233 J. NEUROLOGICAL SCI. 83 (2005) (commenting that despite progress in stem cell research, the feasibility and safety of stem cell therapies remain unresolved).
185. See, e.g., Israel Berger et al., Global Distribution of Businesses Marketing Stem Cell-Based Interventions, 19 CELL STEM CELL 158, 158, 160 (2016) (analyzing the content of hundreds of websites marketing stem cell–based interventions and finding that many made vague therapeutic claims unsupported by data generated in randomized, controlled, and independent clinical trials); Lau et al., supra note 184, at 593 (“We therefore find that the treatments offered on stem cell websites are generally unsupported by clinical evidence.”).
backbone of the stem cell therapy industry remain largely underregulated, have spread globally (Figure 4), and are no longer confined to developing countries where weak laws or lax enforcement has enabled the clinics to operate with relative impunity.\textsuperscript{186}
Figure 2. Stem Cell Clinics Offering Direct-to-Consumer Marketing of Stem Cell–Based Interventions in the United States

The figure shows the number of clinics per U.S. state. California (forty-nine clinics), Florida (thirty-five clinics), and New York (fifteen clinics) have the highest number of stem cell clinics in the country. No clinics were recorded in Delaware, Kansas, Kentucky, Maine, Nebraska, New Hampshire, New Mexico, North Dakota, Rhode Island, South Dakota, and Vermont (colored in gray). No data is available for Alaska or Hawaii (also colored in gray).

In a span of just a few years, U.S. stem cell businesses engaged in direct-to-consumer marketing have expanded to offer procedures at nearly six hundred clinics as of 2016, a trend that is consistent in other

187. The choropleth map was generated using the data set reported in Berger et al., supra note 185, at tbl.S1.
188. Leigh Turner & Paul Knoepfler, Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry, 19 CELL STEM CELL 154, 154 (2016); cf. Berger et al., supra note 185, at 158 (“[Berger and colleagues] identified 187 unique websites in the US offering interventions at 215 clinics, while Turner and Knoepfler found 351 distinct businesses offering interventions at 570 physical locations. Due to differences in search strategy stringency, inclusion and exclusion criteria, and search engines used, it is not possible to
developed countries. In a globalized world, clinics now compete for a share of the so-called stem cell tourism pie.

**Figure 3. Stem Cell Clinics Offering Direct-to-Consumer Marketing of Stem Cell–Based Interventions in Canada**

The figure shows the number of clinics per Canadian province or territory. Ontario (twenty-four clinics), British Columbia (eight

make direct comparisons between these analyses, but the implication is that growth of the industry in the US has been rapid and pronounced.


191. The choropleth map was generated using the data set reported in Turner, *supra* note 189, at 646–47.
clinics), and Alberta (six clinics) have the highest number of stem cell clinics providing access to stem cell–based interventions in the country. No clinics were identified in other Canadian provinces—Manitoba, New Brunswick, Newfoundland and Labrador, and Prince Edward Island—or territories—Northwest Territories, Nunavut, and Yukon (colored in gray with linear hatching).

Against a backdrop of public-health concerns surrounding overoptimistic and unsubstantiated stem cell interventions, which thwart adequate patient informed consent and examination of clinical outcomes, the federal government took action. The FDA filed a request to permanently enjoin the Colorado clinic from administering the Regenexx-C cell mixture as part of a medical procedure.\footnote{192. United States v. Regenerative Scis., LLC, 878 F. Supp. 2d 248, 262–63 (D.D.C. 2012), aff’d, 741 F.3d 1314 (D.C. Cir. 2014).} The FDA argued that the mixture was a drug and biological product subject to FDA jurisdiction.\footnote{193. \textit{Id.} at 254.} The defendants countered the FDA’s position by arguing that the Agency lacked jurisdiction to regulate its mixture because it was not a drug or biological product, but rather a medical procedure that was part of the practice of medicine,\footnote{194. A body of literature has examined in recent years the extent to which the FDA regulates the practice of medicine, which has been traditionally recognized as a matter of state jurisdiction. \textit{See, e.g.}, Lars Noah, \textit{Ambivalent Commitments to Federalism in Controlling the Practice of Medicine}, 53 \textit{Kan. L. Rev.} 149, 150–51 (2004); Zettler, \textit{supra} note 69, at 849–50.} which is an area governed by states and not the federal government.\footnote{195. \textit{Regenerative Scis.}, 878 F. Supp. 2d at 254–55.} The district court
ruled in favor of the FDA, and the D.C. Circuit affirmed that ruling. In reaching its decision, the D.C. Circuit considered the definitions of “drug” and “biological product.” Under the FDCA, a drug is an “article[] intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” or “intended to affect the structure or any function of the body.” A biological product under section 351 of the PHSA as it is currently codified is any “virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings.” The appellate panel held that these two statutory definitions clearly applied to the stem cell mixture under review. Moreover, the panel rejected the practice-of-medicine claims because the FDA had focused on the mixture itself—and its safety in human use—as opposed to the medical procedure in

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196. Id. at 263. Some scholars have criticized the FDA’s actions against the Regenexx-C stem cell mixture on various grounds. See, e.g., RICHARD A. EPSTEIN, MANHATTAN INST., THE FDA’S MISGUIDED REGULATION OF STEM-CELL PROCEDURES: HOW ADMINISTRATIVE OVERREACH BLOCKS MEDICAL INNOVATION 4–7 (2013) (arguing the stem cell procedure in Regenerative Sciences is not interstate commerce or a drug under the FDCA); Mary Ann Chirba & Stephanie M. Garfield, FDA Oversight of Autologous Stem Cell Therapies: Legitimate Regulation of Drugs and Devices or Groundless Interference with the Practice of Medicine?, 7 J. HEALTH & BIOMEDICAL L. 233, 238 (2011) (arguing that the FDA’s position “impedes medical advances”). Epstein, for example, has argued that the FDA lacks authority to regulate the stem cell procedure because the statutory definition of interstate commerce under the FDCA is not as expansive as Congress’s constitutional authority to regulate interstate commerce under the Supreme Court’s decision in Wickard v. Filburn, 317 U.S. 111 (1942). See EPSTEIN, supra, at 5–6. He acknowledged that under modern law the FDA has authority to regulate a business engaging in the type of interstate commerce at issue in Regenerative Sciences but argued that the FDCA, which was enacted before Wickard, does not grant the federal government power to apply constitutional authority where only statutory authority exists. See id. at 5. Regardless of whether such an argument has merit, the Regenerative Sciences decisions indicate that the stem cell clinic’s marketing, clientele, and other interstate activities warrant the exercise of FDA jurisdiction under the Commerce Clause power. See infra notes 212–18 and accompanying text (pointing out that the above criticisms overlook the focus of the FDA on protecting consumer safety by regulating private clinics that market therapies with unsubstantiated claims).

198. Id. at 1319.
201. Regenerative Scis., 741 F.3d at 1319.
which the mixture was utilized.\textsuperscript{202} In essence, the mixture was considered a drug or biological product regardless of whether or not it was used in conjunction with a medical procedure.\textsuperscript{203}

The panel also agreed with the FDA’s position that the mixture was a cellular product intended for somatic cell therapy.\textsuperscript{204} Cellular products fall within the definition of drugs and biological products subject to FDA regulation\textsuperscript{205} unless they are minimally manipulated.\textsuperscript{206} “Minimal manipulation” means “processing that does not alter the relevant biological characteristics.”\textsuperscript{207} The court determined that the mixture at issue in \textit{Regenerative Sciences} had been more than minimally manipulated because, for example, (1) the culturing process can “determine the growth and biological characteristics” of the cell population, and (2) the addition of certain substances to the culture affect stem cell differentiation.\textsuperscript{208} Indeed,

\begin{itemize}
\item \textsuperscript{202} See \textit{Regenerative Scis.}, 741 F.3d at 1319.
\item \textsuperscript{203} \textit{Id. at} 1321–22; see also 21 C.F.R. § 1271.3(d)(4) (2018).
\item \textsuperscript{205} \textit{Regenerative Scis.}, 741 F.3d at 1321. It should be noted, however, that minimal manipulation is not the only criterion under which cellular products fall within the definition of drugs or biological products.
\item \textsuperscript{206} 21 C.F.R. § 1271.3(f)(2) (2018).
\item \textsuperscript{207} \textit{Regenerative Scis.}, 741 F.3d at 1322.
\end{itemize}
**Figure 4. Stem Cell Clinics Offering Direct-to-Consumer Marketing of Stem Cell–Based Interventions Globally**

The figure shows the number of clinics per country. The United States (187 clinics), India (35 clinics), Mexico (28 clinics), China (23 clinics), Australia (19 clinics), England (16 clinics), Thailand (14 clinics), Malaysia (12 clinics), and Germany (11 clinics) have more than 10 stem cell clinics in each country. The Cayman

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209. The choropleth map was generated using the data set reported in Berger et al., *supra* note 185, at tbl.S1.
Islands—the only place where the Regenexx-C procedure is now available and the Bahamas have the highest number of stem cell clinics providing access to stem cell–based interventions per capita in the world. No data was reported for clinics in countries colored in gray.

the culturing process and its effects on the safety of MSCs intended for clinical use are often overlooked by critics of the case. 212

211. Berger et al., supra note 185, at 158.
212. See supra note 196 and accompanying text. Consider the claims that FDA interference in Regenerative Sciences was unjustified because (1) use of autologous donor stem cells eliminates the risk of transmitting infectious or genetic diseases and (2) stem cell processing under locally controlled circumstances is no riskier than other standard laboratory procedures outside FDA jurisdiction. See Epstein, supra note 196, at 17. Such claims overlook the vast empirical scientific evidence associated with documented changes in stem cell characteristics following prolonged in vitro expansion of MSCs and other types of stem cells. See studies cited infra notes 214, 216.

Similarly, the view that “extracting and re-injecting a patient’s own cells is not that different from other reparative or surgical procedures,” such as coronary artery bypass graft surgery—in which the saphenous vein from a patient’s leg is removed and transferred to the site of an occluded artery—or spinal surgery—in which a piece of bone from a patient’s pelvis or rib is used to fuse vertebrae—is not quite accurate. Chirba & Garfield, supra note 196, at 235. This view confounds the level of invasiveness associated with the transfer of a patient’s differentiated autologous tissue to another site of the patient’s body with the transfer of autologous multipotent stem cells to another site following in vitro expansion. The former involves tissue that cannot differentiate into other subtypes, whereas the latter involves stem cells that can proliferate and differentiate on their own into multiple tissue types. Such a declaration is akin to analogizing the transfer of an inert piece of wood into a small garden enclosure to straighten out a crooked plant with the transfer of a tomato plant that can grow and proliferate in the small garden enclosure over time.

To be clear, issues surrounding the decentralization of medical research, the impact of overregulation on innovation, and the role of administrative agencies in the advancement of emerging technologies that can benefit humankind are interesting, multifaceted, and worthy of discussion. Those topics, however, are beyond the central scope of Regenerative Sciences. Simply put, the stem cell procedure at issue in that case, which involved the expansion of stem cells in vitro over a period of approximately two weeks, should absolutely be regulated by the FDA because of the serious potential safety issues associated with in vitro stem cell expansion. See studies cited infra notes 214, 216.

It should be noted that in the aftermath of Regenerative Sciences, Regenexx clinics began to market Regenexx-SD, or “same-day,” stem cell procedures in the United States. See Regenexx Procedures, supra note 179. During the SD procedures, a “patient’s cells are harvested in the morning, isolated and processed, then re-injected into the patient’s injured area—all within a period of a few hours.” Id. Thus, unlike Regenexx-C, the Regenexx-SD procedures fall within the Same Surgical Procedure Exception for human cells, tissues, and cellular and tissue-based products (“HCT/Ps”) outlined under 21 C.F.R. § 1271.15(b), which permits the removal and implantation of autologous HCT/Ps so long as they are performed within the same surgical procedure. 21 C.F.R. § 1271.15(b) (2018); see also Ctr. for
Under a jurisprudence of scientific empiricism, the type of therapy at issue in *Regenerative Sciences* should fall within the FDA’s regulatory jurisdiction because prolonged in vitro expansion and culture of stem cells has been shown to induce genomic instability, spontaneous malignant transformation (cancer), chromosomal abnormalities, loss of multipotency, and aberrant patterns of gene expression. The progressive accumulation of DNA damage in stem cells increases with time of culture and can ultimately lead to loss of stemness and differentiation potential.

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213 See [*Enríquez*, supra note 2, at 611–14 (defining a jurisprudence of scientific empiricism as “a normative structural legal framework . . . that is broadly adaptable to addressing questions of science in law”).


216 See, e.g., Hugo Alves et al., *A Link Between the Accumulation of DNA Damage and Loss of Multi-Potency of Human Mesenchymal Stromal Cells*, 14 *J. CELLULAR & MOLECULAR MED.* 2729, 2729 (2010).
Although scientists continue to research the causes underlying the above phenomena related to in vitro intracellular and extracellular influences on stem cells, private clinics have continued to profit from unapproved therapies that are costly and may have little to no therapeutic effect.217 The FDA recently filed requests for permanent injunctions against two stem cells clinics—US Stem Cell Clinic LLC of Sunrise, Florida, and California Stem Cell Treatment Center, Inc.—to enjoin them “from marketing stem cell products without FDA approval and for significant deviations from current good manufacturing practice requirements.”218

2. Potential Classifications of GGE Products

Although Regenerative Sciences applies to somatic stem cell therapies and is silent on the status of germ cells, the stem cell procedures examined in that case are relevant to GGE in many ways, particularly because the safety and efficacy of GGE interventions have yet to be proven. Accordingly, Regenerative Sciences establishes a firm regulatory path for the oversight of GGE by the FDA. The following classifications may apply to the regulation of GGE technologies.

a. Drug

Products intended for genome editing meet the FDCA’s definition of drug. Under the FDCA, a drug is an article “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” or “intended to affect the structure or any function of the body.”219 GGE techniques will most likely require extraction or collection of germ-cell samples from patients, followed by a culturing process and the addition of a CRISPR-based or other product that enables genome editing directly to gametes, zygotes, or human embryos.220 For purposes of in vitro fertilization, the modified germ cells will be used during fertilization and subsequent implantation into a patient’s uterus with

217. See Berger et al., supra note 185, at 158–59; Turner & Knoepfler, supra note 188, at 154–55.
220. See, e.g., Xiangjin Kang et al., Introducing Precise Genetic Modifications into Human 3PN Embryos by CRISPR/Cas-Mediated Genome Editing, 33 J. ASSISTED REPROD. & GENETICS 581, 581 (2016); Liang et al., supra note 9, at 364; Hong Ma et al., supra note 37, at 413; Tang et al., supra note 13, at 525.
the intent of causing a pregnancy. The product aimed at genome editing may or may not be used for therapeutic purposes, but it will certainly affect the structure and function of the target cells as it will trigger cuts on DNA and introduce changes that are intended to affect the wildtype characteristics of the target genetic locus. Moreover, the Supreme Court has shown deference to the FDA and held that the statutory definition of drug under the FDCA is a term of art that is broader than the strict medical definition of the word. For purposes of the FDCA, the interpretation of the term hinges on the article’s intended use, rather than its technical properties. Accordingly, the product for genome editing would squarely fit the definition of a drug under the FDCA.

b. Biological Product

Depending on its intended use and method of delivery, a product intended for genome editing may also fit the definition of a biological product under section 351 of the PHSA for purposes of GGE. The statute specifies that biological products may encompass viruses or sera with therapeutic applications. Technological advances have recently enabled GGE via delivery of large fragments of DNA into zygotes.

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221. Implantation of genetically modified embryos to induce a pregnancy has been achieved in cynomolgus monkeys, see Niu et al., supra note 12, at 836, and, more recently, in humans, see David Cyranoski & Heidi Ledford, International Outcry over Genome-Edited Baby Claim, 563 NATURE 607, 607–08 (2018).

222. Whether a genome-editing product ends up being used in therapeutic or nontherapeutic applications is significant—from a legal perspective—because the statute specifies that a drug is an “article[] intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease,” 21 U.S.C. § 321(g)(1)(B) (Supp. 2017), and thereby excludes nontherapeutic GGE purposes as outlined supra Sections I.B.1–2.

223. The term “wildtype” refers to the most common phenotype—observable characteristics or traits—for an organism in a natural breeding population. See Wildtype, BIOLOGY ONLINE DICTIONARY, biology-online.org/dictionary/wildtype [https://perma.cc/R9SL-SPFK].

224. The “target genetic locus” in this context means the particular chromosomal position—the DNA site within the genome—to which a genome-editing enzyme is recruited to cut DNA.


226. See id.

227. See 21 U.S.C. § 321(g)(1)(c) (Supp. 2017) (defining drugs as “articles (other than food) intended to affect the structure or any function of the body of man or other animals,” which, when read broadly, includes genome editing).


229. See id.
using adeno-associated virus\(^{230}\) ("AAV") vectors\(^{231}\) thereby extending FDA jurisdiction to this type of GGE intervention. Biological products within the meaning of the PHSA also include vaccines intended for therapeutic purposes\(^{232}\) Thus, GGE products for prophylactic uses would also fit the statutory definition of a biological product subject to FDA jurisdiction.

Interestingly, proteins for therapeutic use are included in the statutory definition of a biological product, which would encompass all modern protein-based tools for genome editing—including zinc finger-, TALE-, and CRISPR-based systems—so long as they are not "chemically synthesized."\(^{233}\) In theory, this exception creates a loophole in the statute, whereby a researcher using a purified, recombinant protein to trigger genome editing for GGE purposes is subject to regulation under the PHSA, but another researcher using a chemically synthesized version of the same protein is not.\(^{234}\) Lastly, unless Congress amends the definition of biological products under the PHSA, it should be noted that the statutory text, in its current incarnation, precludes regulation of any GGE products intended for nontherapeutic uses as biological products subject to FDA oversight.\(^{235}\)

c. Medical Device

Under section 201(h) of the FDCA as it is currently codified, a medical “device” is

an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory . . . intended for use

\(^{230}\) AAV is a nonpathogenic virus that infects humans—as well as nonhuman primates—and carries a relatively small, linear, single-stranded DNA genome. Shyam Daya & Kenneth I. Berns, *Gene Therapy Using Adeno-Associated Virus Vectors*, 21 CLINICAL MICROBIOLOGY REVIEWS 583, 583 (2008). AAV’s small size and nonpathogenic properties have enabled the development of AAV-based vector biotechnologies for use in gene-therapy clinical trials to treat a diverse range of human diseases. See id. at 586, 588–90.


\(^{232}\) See § 262(i)(1).

\(^{233}\) See id. ("The term "biological product' means a . . . protein (except any chemically synthesized polypeptide) . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings.").

\(^{234}\) From a biochemical perspective, the purified and chemically synthesized versions of the same protein would be indistinguishable. Both proteins would comprise the same amino acid sequence regardless of the origin source.

\(^{235}\) See § 262(i)(1) (requiring explicitly that biological products be “applicable to the prevention, treatment, or cure of a disease or condition of human beings”).
in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man . . . or intended to affect the structure or any function of the body . . . and which does not achieve its primary intended purposes through chemical action . . . and which is not dependent upon being metabolized for the achievement of its primary intended purpose.236

GGE products intended for therapeutic use are likely to be classified as contrivances or in vitro reagents that affect the structure or function of their targets. However, as it applies to GGE, in which the primary purpose is to modify a target nucleotide sequence, the chemical action clause of the statutory text would render GGE products beyond the meaning of a medical device under the FDCA, primarily because effectors that catalyze DNA double-stranded breaks for genome editing achieve their primary goal through enzymatic—i.e., chemical—action.237 Accordingly, GGE products are not likely to constitute medical devices under the statute.

237. Interestingly, a distinction could theoretically be made between GGE that relies on programmable base-editing enzymes—as opposed to genome-editing enzymes—and somatic epigenome editing to control patterns of gene expression. Although both methods rely on the use of a deactivated genome-editing enzyme, such as dCas9, the former utilizes a base-editing enzyme that mediates a chemical reaction to achieve its primary purpose, see, e.g., Nicole M. Gaudelli et al., Programmable Base Editing of A•T to G•C in Genomic DNA Without DNA Cleavage, 551 NATURE 464, 464 (2017) (using adenine base editors to mediate A•T to G•C conversion); 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, 2631–32 (2018) (discussing the use of base editors to solve “genetic diseases at the embryo stage”), whereas the latter merely relies on physical interactions between the deactivated genome-editing enzyme and its target molecule to activate or inhibit gene expression, see, e.g., Luke A. Gilbert et al., Genome-Scale CRISPR-Mediated Control of Gene Repression and Activation, 159 CELL 647, 647–48 (2014). In other words, each method achieves its primary intended purpose either via chemical action—in the base-editing GGE case—or physical action—in the epigenome-editing case. Only the somatic epigenome-editing product would thus constitute a medical device under the law.

The aforementioned analysis would depend largely on how the FDA interprets the term “chemical action.” The Agency recently published a guidance that describes the FDA’s position that chemical action should be interpreted consistently with the term “pharmacological action” as that term is generally understood in the medical field. See FDA, CLASSIFICATION OF PRODUCTS AS DRUGS AND DEVICES & ADDITIONAL PRODUCT CLASSIFICATION ISSUES: GUIDANCE FOR INDUSTRY AND FDA STAFF 7 (2017), https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM258957.pdf [https://perma.cc/AA6F-7T7R]. The guidance is not legally binding but offers the Agency’s current thinking on the topic. Because the term “pharmacological action” in the medical field includes the mere binding of molecules through electrostatic, hydrophobic, and other types of interactions without the need for catalytic activity, see id. at 7 n.4, the somatic
d. Combination Product

A combination product is a product comprised of two or more different types of regulated components.\textsuperscript{238} Thus, a GGE product may be a combination product if it is both a drug and a biological product within the meaning of section 503(g) of the FDCA.\textsuperscript{239} Combination products are assigned to an FDA center with primary jurisdiction for its premarket review and regulation based on a determination of the product’s “primary mode of action.”\textsuperscript{240} Therefore, the Center for Drug Evaluation and Research would have primary jurisdiction over a drug-biological GGE product, while CBER would have primary jurisdiction of a biological-drug GGE product.

3. Minimal Manipulation

Germ cells undergoing modification during GGE interventions will likely be deemed more than minimally manipulated under both the FDA rules and the \textit{Regenerative Sciences} standard. As noted above, any processing that alters the relevant characteristics of cells or tissues cannot constitute minimal manipulation.\textsuperscript{241} Alteration of specific biological characteristics of germ cells is at the core of GGE, and, thus, the addition of products that enable genome editing is intended to affect not merely how the germ cell differentiates but also the cell’s own genetic identity. Because GGE interventions involve microinjection, viral-based delivery of packaged molecules to activate genome editing, and other types of micromanipulations, the modified germ cells would not qualify as section 361 products subject to minimal FDA oversight.\textsuperscript{242} In essence, the germ cells are more than minimally manipulated and involve “combination of the cells or tissues with another article,”\textsuperscript{243} namely an effector that catalyzes genome editing.

The aforementioned analysis of the potential classifications for GGE regulation, coupled with the current lack of scientific evidence to establish the safety and efficacy of genome editing—in both somatic epigenome-editing product would no longer constitute a medical device under the guidance interpretation of the FDCA.

\textsuperscript{238} See 21 C.F.R. § 3.2(e) (2018).
\textsuperscript{240} See id. § 353(g)(1).
\textsuperscript{241} See 21 C.F.R. § 1271.3(f) (2018).
\textsuperscript{242} See id. § 1271.10(a)(1)–(4).
\textsuperscript{243} Id.
and germ cells—provides the FDA strong footing to assert its jurisdiction over GGE.244

D. Congressional Proscription of Clinical Applications of Germline Genome Editing

The FDA stands on a strong legal foundation to assert jurisdiction over GGE and should do so promptly to restrict the rise of a premature industry aimed at engineering genetically modified humans. The safety and efficacy of GGE technologies must be adequately addressed from a scientific perspective before clinical GGE interventions can proceed. At the same time, robust public debate must focus on the potential social and ethical benefits and risks of GGE interventions.

Once jurisdictional hurdles are cleared, any manufacturer of products intended for use in clinical applications of GGE would be required to submit an Investigational New Drug Application (“IND”)245 and a Biologic Licensing Application (“BLA”),246 which must be approved prior to marketing GGE interventions. However, the FDA is currently prohibited from reviewing any INDs under a provision in the Consolidated Appropriations Act (“CAA”) of 2016,247 which Congress has since renewed.248 The provision states that

None of the funds made available by this Act may be used to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product . . . in research in which a human embryo is intentionally created or modified to include a heritable genetic modification. Any such submission shall be deemed to have not been received by the Secretary, and the exemption may not go into effect.249

To be clear, there currently is no law explicitly banning human GGE. Although no federal funds may be used to perform research on

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244. In addition to regulation under the gene-therapy framework and the Regenerative Sciences standard, the FDA may also regulate GGE under provisions applicable to assisted reproductive technologies, which relate to the handling of gametes and embryos. See 42 U.S.C. § 263a-1(a)–(c) (2012).
human embryos since passage of the Dickey-Wicker Amendment, such research is legal in the United States, so long as it is privately funded. The rider provision of the CAA merely restricts the FDA’s ability to acknowledge receipt of—an application for clinical use of GGE technology in an embryo. However, that limitation is significant because all drugs and biological products, including gene therapies, must be approved by the FDA before they can be marketed and used in clinical settings. Such approval cannot occur if the Agency cannot review INDs and BLAs for GGE purposes.

In essence, because Congress would likely find it difficult to enact a law that directly bans GGE—particularly given increasingly favorable public attitudes toward the use of technologies for genome editing—it has used its power of the purse to achieve a similar policy result.

With the rider provision of the CAA, Congress introduced a de facto ban on any clinical applications of GGE and prohibited the FDA from assessing and evaluating the safety and efficacy of any GGE clinical intervention. Such a legislative ban is unnecessary and counterintuitive as it prevents the FDA from carrying out its mission to protect the public health by ensuring the safety and efficacy of drugs, biological products, and medical devices.

By restricting the FDA’s oversight over GGE INDs, Congress is also interfering with the Agency’s “responsib[ility] to advance the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products . . . and improve their health.” Indeed, the FDA’s role within the regulatory system is not limited to its consumer-protection responsibilities. The Agency also plays an important role in incentivizing the creation of robust scientific information about products. By foreclosing FDA review of GGE technologies,

250. See supra note 32 and accompanying text.
251. See, e.g., Spivak et al., supra note 32, at 38, app. tbls.1–4 (compiling data over the last few decades on bills related to then-controversial technologies with reproductive applications to demonstrate that, despite widespread concerns and contentious debate among members of Congress, the vast majority of proposed prohibitions never became law).
252. See studies cited infra notes 390–93.
253. See Spivak et al., supra note 32, at 37.
254. See What We Do, supra note 31.
255. Id.
256. See generally, e.g., Rebecca S. Eisenberg, The Role of the FDA in Innovation Policy, 13 MICH. TELECOMM. TECH. L. REV. 345 (2007) (reexamining “the role of FDA regulation in motivating investment in biopharmaceutical innovation”).
Congress is hindering efforts to develop robust scientific data on GGE applications.

Furthermore, Congress has not presented evidence to demonstrate that the FDA would be unable to fulfill its regulatory duties concerning GGE technologies. Simply put, the current ban is unnecessary because, given the FDA’s long record of enforcing regulations aimed at consumer protection, no evidence suggests that the FDA would approve any GGE intervention without first subjecting it to the long and rigorous process required to establish its safety and efficacy. To the contrary, the FDA has discretion to apply clinical holds to delay or suspend an ongoing clinical investigation due to unreasonable risks to research subjects or discovery of information that undermines confidence in such study. Indeed, the FDA recently availed itself of this authority by instituting a clinical hold\textsuperscript{257} on a CRISPR-based therapy.\textsuperscript{258}

Lastly, the ban increases the likelihood that GGE technologies will be pushed to develop in other jurisdictions,\textsuperscript{259} where regulations may be inadequate from social and ethical standpoints.\textsuperscript{260} Accordingly,

\textsuperscript{257} A “clinical hold” refers to an order to delay or suspend a clinical investigation. The conditions for issuing a clinical hold may include unreasonable risk to research subjects or discovery of information that undermines confidence in the investigators or the study protocol. See 21 C.F.R. § 312.42 (2018).


\textsuperscript{259} See, e.g., John Zhang et al., First Live Birth Using Human Oocytes Reconstituted by Spindle Nuclear Transfer for Mitochondrial DNA Mutation Causing Leigh Syndrome, 106 FERTILITY & STERILITY (ISSUE 3 SUPP.) e375, e375–76 (2016) (reporting the birth of a baby conceived via mitochondrial replacement therapy in Mexico aided by an American physician from New York who could not perform the procedure in the United States); Zhang et al., supra note 25, at 365 (same); see also Rob Stein, Clinic Claims Success in Making Babies with 3 Parents’ DNA, NPR (June 6, 2018, 5:11 AM), https://www.npr.org/sections/health-shots/2018/06/06/615900972/inside-the-ukrainian-clinic-making-3-parent-babies—for-women-who-are-infertile [https://perma.cc/L9T9-56YF] (noting that a Ukrainian clinic is currently marketing in the United States a $15,000 procedure involving the use of DNA from three different people to help infertile women—who are willing to travel to Ukraine—to conceive a biological child).

\textsuperscript{260} See Katrin Weigmann, The Ethics of Global Clinical Trials, 16 EMBO REP. 566, 567 (2015) (noting that stringent FDA regulations are one major reason why clinical trials move to low- and middle-income countries). Notably, emerging reproductive technologies can present difficult challenges related to patient informed consent, confidentiality, access to information, and long-term follow-up. See generally, e.g., Jonathan M. Breslin et al., Top 10
Health Care Ethics Challenges Facing the Public: Views of Toronto Bioethicists, 6 BMC MED. ETHICS, no. 5, June 26, 2005, at 1 (discussing various ethical challenges posed by innovation in the medical profession). Consider, for instance, the case of the Chinese twin girls born in November 2018 whose genomes were edited at the CCR5 locus. To obtain informed consent from parents enrolling in the clinical trial, He Jiankui described the research as an “AIDS vaccine development project” that would bestow upon “gene editing [sic] babies . . . the genotype of the Northern European to naturally immunize against the HIV-1 virus.” He Jiankui, Informed Consent Version: Female 3.0, at 1 (unpublished consent form), http://web.archive.org/web/20181126212007/http:/www.sust-genome.org.cn/source/pdf/Informed-consent-women-English.pdf [https://perma.cc/RR9Y-54DX]. The consent form was a twenty-three-page document filled with technical jargon, see generally id., which underscores the question of whether patients were able to provide adequate informed consent to the research that would be performed on embryos intended for subsequent implantation and pregnancy.

One striking aspect of the consent form is the disclaimer of risks associated with off-target effects, which were identified as “[t]he primary risk of gene editing” without actually disclosing the deleterious consequences of genomic mutations that could arise from potential targeting of unintended DNA sites. See id. at 4. Assuming arguendo that patients thoroughly understood the implications of off-target genome editing, the waiver of liability clause disclaiming responsibility for off-target effects is dubious from ethical and legal perspectives. The consent form’s acknowledgment that the risks associated with the clinical trial are “beyond the risk consequences of the existing medical science and technology,” see id., arguably establishes prima facie evidence that safety and efficacy concerns are substantial enough to warrant halting the trial. In the United States, for example, proceeding with such a trial at the early stages of technological development before safety and efficacy issues have been addressed from a scientific perspective likely constitutes a reckless or grossly negligent act, which would automatically void the waiver of liability. See 45 C.F.R. § 46.116(a)(6) (2018) (“No informed consent may include any exculpatory language through which the subject . . . is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.”); Step 3: Clinical Research, FDA, https://www.fda.gov/patients/drug-development-process/step-3-clinical-research [https://perma.cc/49MM-Y4XX] (describing the safety and efficacy information which must be reviewed by the FDA before clinical trials can legally begin). It also bears noting that although the consent form loosely mentions the risk of off-target effects, it does not inform patients of potential unintended on-target effects that could arise from editing the CCR5 locus on embryos, including susceptibility to other diseases that might be relevant in the patients’ geographic location or unknown cognitive outcomes. See infra notes 440–42.

Lastly, He Jiankui admitted “he obtained consent from the couples himself, rather than having a trained, uninvolved professional do it.” Sharon Begley, Amid Uproar, Chinese Scientist Defends Creating Gene-Edited Babies, STAT (Nov. 28, 2018), https://www.statnews.com/2018/11/28/chinese-scientist-defends-creating-gene-edited-babies/ [https://perma.cc/SFF7-96YP]. And despite He Jiankui’s claim that he explained the meaning of the consent form “to each family line by line and paragraph by paragraph,” see id., it is hard to imagine that all patients enrolled in the clinical trial provided informed consent. Similar to the problems associated with obtaining informed consent in the case of the Chinese twin girls outlined above—which stemmed from clear institutional failures and gaps in the Chinese regulatory system—other issues that fall within social and ethical ambit may be inadequately addressed in jurisdictions that lack robust regulatory systems with clear and established rules to ensure patient protections.
the legislative ban imposes higher scientific, research, and social costs that are not outweighed by their potential benefits.

II. THE CONSTITUTION AND A FUNDAMENTAL RIGHT TO GERMLINE GENOME EDITING

The current de facto legislative ban on GGE clinical applications may be lawful for now, but it is merely a temporary fix that cannot adequately address many legal challenges that are looming on the horizon. Although human GGE technologies are not quite “ready for primetime,” fundamental research to address current technological limitations of genome editing, including the identification and reduction of off-target effects, prevention of mosaicism, and improvements in target efficiency, specificity, delivery, and other areas constitute active and prolific fields of scientific inquiry. Collectively, the results from today’s research will pave the road to overcome current obstacles in genome editing.

At some point in the near future, the technology will become primed for clinical applications, which in turn will likely lead to

261. Enríquez, supra note 2, at 666.
262. See, e.g., Pinar Akcakaya et al., In Vivo CRISPR Editing with No Detectable Genome-Wide Off-Target Mutations, 561 NATURE 416, 416, 419 (2018).
263. See, e.g., Yetki Aslan et al., High-Efficiency Non-Mosaic CRISPR-Mediated Knock-In and Indel Mutation in F0 Xenopus, 144 DEVELOPMENT 2852, 2852, 2855 (2017).
264. See, e.g., Jean-Baptiste Renaud et al., Improved Genome Editing Efficiency and Flexibility Using Modified Oligonucleotides with TALEN and CRISPR-Cas9 Nucleases, 14 CELL REP. 2263, 2263–64 (2016).
265. See, e.g., Ian M. Slaymaker et al., Rationally Engineered Cas9 Nucleases with Improved Specificity, 351 SCIENCE 84, 84 (2016); Josh Tycko, Vic E. Myer & Patrick D. Hsu, Methods for Optimizing CRISPR-Cas9 Genome Editing Specificity, 63 MOLECULAR CELL 355, 355 (2016).
266. See, e.g., Wenhua Zhou et al., Enhanced Cytosolic Delivery and Release of CRISPR/Cas9 by Black Phosphorus Nanosheets for Genome Editing, 57 ANGEWANDTE CHEMIE 10, 268, 10,271 (2018).
267. See, e.g., Alejandro Chavez et al., Precise Cas9 Targeting Enables Genomic Mutation Prevention, 115 PROC. NAT’L ACADEM. SCI. 3669, 3669–73 (2018); Van Trung Chu et al., Increasing the Efficiency of Homology-Directed Repair for CRISPR-Cas9-Induced Precise Gene Editing in Mammalian Cells, 33 NATURE BIOTECHNOLOGY 543, 543 (2015); Paul Enríquez, CRISPR-Mediated Epigenome Editing, 89 YALE J. BIOLOGY & MED. 471, 483 (2016); Benjamin P. Kleinstiver et al., High-Fidelity CRISPR-Cas9 Nucleases with No Detectable Genome-Wide Off-Target Effects, 529 NATURE 490, 490 (2016) (reducing off-target effects).
claims brought by parents wishing to use GGE technologies. The next section of this Article contends that permanent legislative or administrative bans on select uses of GGE cannot withstand constitutional scrutiny and, thus, will likely succumb to litigation because they impinge on a cognizable fundamental right.

In Washington v. Glucksberg, 521 U.S. 702 (1997), the Supreme Court articulated a two-prong test to determine whether a fundamental right exists under substantive due process. See id. at 720–21. First, the asserted right must be “objectively, ‘deeply rooted in this Nation’s history and tradition.’” Id. (quoting Moore v. City of East Cleveland, 431 U.S. 494, 503 (1977) (plurality opinion)). Second, the party must articulate a “careful description” of the asserted fundamental liberty interest.” Id. If the right is deemed fundamental, strict scrutiny applies, “which forbids the government to infringe certain ‘fundamental’ liberty interests at all, no matter what process is provided, unless the infringement is narrowly tailored to serve a compelling state interest.” Reno v. Flores, 507 U.S. 292, 302 (1993). If the right in question is not fundamental, “[t]he general rule is that legislation is presumed to be valid and will be sustained if the classification drawn by the statute is rationally related to a legitimate state interest.”

A narrow interpretation of Glucksberg could, at first glance, appear to foreclose the emergence of a right to perform select GGE interventions because modern GGE is a nascent biotechnology and no deeply rooted history exists that chronicles GGE uses. Under a broader interpretation of Glucksberg, however, the right might be articulated as, inter alia, the right to bear healthy offspring, make offspring health determinations, guarantee the success of biological procreation, or be free from government interference in procreative decisions related to GGE—all of which derive from already-existing fundamental rights.

Although Glucksberg outlined the modern test to determine fundamental rights, subsequent case law has abandoned its rigid interpretation. Notably, the Supreme Court has indicated that “[h]istory and tradition are the starting point but not in all cases the ending point of the substantive due process inquiry.” Lawrence v. Texas, 539 U.S. 558, 572 (2003) (quoting County of Sacramento v. Lewis, 523 U.S. 833, 857 (1998) (Kennedy, J., concurring)); see also Obergefell v. Hodges, 135 S. Ct. 2584, 2602 (2015) (asserting that the definition of rights “in a most circumscribed manner, with central reference to specific historical practices, . . . may have been appropriate for the asserted right” of physician-assisted suicide at issue in Glucksberg but is not the approach the Court has “used in discussing other fundamental rights, including marriage and intimacy”). “[R]ights come not from ancient sources alone. They rise, too, from a better informed understanding of how constitutional imperatives define a liberty that remains urgent in our own era.” Obergefell, 135 S. Ct. at 2602.

In essence, Lawrence and Obergefell jointly abrogate Glucksberg’s rigid approach to determining fundamental rights. And just as “Loving did not ask about a ‘right to interracial marriage,’” the right to perform select uses of GGE articulated in this Article may encompass a right “in its comprehensive sense,” see id., that fits within the rights of procreation, parental autonomy, and—to some extent—privacy, see infra Sections II.A–D.
protects select uses of GGE. This fundamental right flows from jurisprudence in the areas of procreative, family autonomy, and—to some extent—privacy rights, but it is not absolute.

An analytical checkpoint is indispensable at this juncture. Although the next section examines an issue that has never before been the subject of judicial review, it does so in the context of an enduring, and often contentious, debate regarding the methodological framework under which the Constitution should be interpreted. At the outset, it is imperative to note that the invocation of the Due Process Clauses of the Fifth and Fourteenth Amendments\(^{270}\) to adjudicate cases and controversies under Article III of the Constitution has “at times been a treacherous field for [the Supreme] Court.”\(^{271}\) The doctrine has spawned a litany of controversial decisions,\(^{272}\) many of which are discussed below.

At its core, the doctrine of substantive due process concerns the inquiry “of whether the government’s deprivation of a person’s life, liberty or property is justified by a sufficient purpose.”\(^{273}\) The term “liberty” in the clause has been interpreted broadly to encompass protection of certain fundamental rights unenumerated in the Constitution.\(^{274}\) Supporters of the doctrine state that it has been used to safeguard some of the “most precious liberties” found in modern constitutional law.\(^{275}\) Yet critics of that interpretive method have gone as far as labeling it “the most anticonstitutional branch of constitutional law.”\(^{276}\)

This Article acknowledges the interpretive dichotomy of this area of constitutional law. Whether the extant body of substantive due process jurisprudence is proper when viewed through the lenses of originalism and nonoriginalism, however, is beyond the scope of this Article. And no position on the issue is taken herein. With this context as a backdrop, this part undertakes a—mostly—descriptive, rather

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270. U.S. CONST. amend. V (“[N]or shall any person . . . be deprived of life, liberty, or property, without due process of law . . . ”); id. amend. XIV, § 1 (“[N]or shall any State deprive any person of life, liberty, or property, without due process of law . . . ”).
272. See infra Sections II.A–D.
275. Chemerinsky, supra note 273, at 1501.
than normative, analysis of the existing jurisprudence in this area of the law. The part concludes that the current substantive due process precedents, collectively, pave a path for the recognition of a right to perform GGE in select contexts.277

A. Jurisprudence on the Family-Unit Sphere and Parental Autonomy

1. Substantive Due Process and the Family Rights Doctrine

The origins of a constitutional doctrine of autonomy involving parental choice and the family-unit sphere trace back to the 1920s.278 In Meyer v. Nebraska,279 the Supreme Court recognized the core of what is now a parent’s fundamental right to make child-rearing decisions.

Meyer involved a challenge to a Nebraska statute that prohibited teaching in any language except English at public or private schools.280 Under that law, foreign languages could be taught only beyond the eighth grade.281 A parochial-school teacher was tried and convicted for unlawfully teaching a ten-year-old child to read in the German language,282 and the Nebraska Supreme Court affirmed his conviction.283

277. One caveat is that, given the contention in this area of the law, such a path is potentially susceptible to the composition of the Court at a particular point in time, as some Justices have expressed a willingness to discard the doctrine in the past. See, e.g., United States v. Windsor, 570 U.S. 744, 794 (2013) (Scalia, J., dissenting) (“The majority never utters the dread words ‘substantive due process,’ perhaps sensing the disrepute into which that doctrine has fallen . . . .”); Griswold v. Connecticut, 381 U.S. 479, 530 (1965) (Stewart, J., dissenting) (“I can find no such general right of privacy in the Bill of Rights, in any other part of the Constitution, or in any case ever before decided by this Court.”).

278. See infra notes 279–306 and accompanying text outlining rights in the family context. It bears noting some have argued that the enactment of the Fourteenth Amendment during the Reconstruction era is itself evidence of the existence of the sort of liberty articulated by the Court in the 1920s. See Peggy Cooper Davis, Neglected Stories and the Lawfulness of Roe v. Wade, 28 HARV. C.R.-C.L. L. REV. 299, 309–10 (1993). This is because the framers of the Reconstruction Amendments had

vivid impressions of what it meant to be denied rights of family, for the denial of those rights was a hallmark of slavery in the United States . . . that inverted concepts of human dignity, citizenship and natural law. . . . [T]he Fourteenth Amendment [was] the instrument with which to re-enshrine family liberty as an inalienable aspect of national citizenship and natural law.

Id. at 309 (citations omitted).
279. 262 U.S. 390 (1923).
280. Id. at 397.
281. Id.
282. Id. at 396.
Understanding the wider historical context is essential to appreciate why Meyer arrived at the Supreme Court. After the United States entered World War I by declaring war against Germany in 1917, a wave of anti-German sentiment swept the nation. Animus toward German culture among government and private actors led to the breakdown of civil liberties. Government officials publicly averred that the freedom of speech in the federal and state constitutions does not guarantee the right to speak in any language other than English.

By 1923, thirty-four states—including Nebraska—had enacted legislation mandating English-only instruction at public and private elementary schools. Meanwhile, the pseudoscientific eugenics movement had gained vast popularity, and the assimilation of immigrants in America had become a major concern.

286. For instance, Americans were encouraged to spy on and report individuals who displayed disloyalty, spoke critically of the war, taught German language at schools, or supported pacifism. Schaffer, supra note 284, at 19–20.
287. See id. at 20 (recounting the Iowa governor’s proclamation that prohibited conversations in non-English languages in public places, along with statements to declare English as the only official language of the United States and Iowa).
288. Ovando, supra note 285, at 5.
289. For an examination of the eugenics movement, its pseudoscientific roots, and its rise to legitimacy in the United States in the late 1800s and early 1900s, see Enríquez, supra note 2, at 679–80, 687–91.
290. See Paul Popenoe & Roswell Hill Johnson, Applied Eugenics 298–301 (1918). Popenoe and Johnson, for example, asserted, “It is essential if America is to be strong eugenically that it slow down the flood of immigrants who are not easily assimilable.” Id. at 306. The rhetoric related to immigration in the early twentieth century bears some resemblance to that of today’s anti-immigration debate. Compare id. at 303–04 (attributing a rise in crime, pauperism, violence, and alcoholism to the wave of immigration of “inferior” people from southern and eastern European countries), with Ann Coulter, ¡Adiós, América!: The Left’s Plan to Turn Our Country into a Third World Hellhole 18 (2015) (arguing that the “mass immigration of the poorest of the poor to
Operating in front of this historical backdrop, the Supreme Court examined the constitutionality of the Nebraska statute, which the Nebraska Supreme Court had ruled reasonable and duly enacted within the state’s police powers.\footnote{Meyer v. Nebraska, 262 U.S. 390, 397–98 (1923).} The state court had held that allowing foreigners to rear and educate their children in a foreign language was not only contrary to the country’s best interests but also inimical to American safety.\footnote{Id. at 399.}

In a landmark ruling, the Supreme Court reversed the state court’s judgment and held that the Due Process Clause of the Fourteenth Amendment, “without doubt,” protected the liberty “to marry, establish a home and bring up children . . . and generally to enjoy those privileges long recognized at common law as essential to the orderly pursuit of happiness by free men.”\footnote{Id. at 399–400.} In so doing, it interpreted the term “liberty” broadly and endorsed the concept that “the individual has certain fundamental rights which must be respected.”\footnote{Id. at 401.} Thus, an instructor has a constitutional right to teach a foreign language to a child whose parents “engage him so to instruct their [child].”\footnote{Id. at 400.} The liberty guaranteed by the Fourteenth Amendment “may not be interfered with, under the guise of protecting the public interest, by legislative action which is arbitrary or without reasonable relation to some purpose within the competency of the state to effect.”\footnote{Id. at 399–400.}

America is bad for the whole country” and is responsible for an increase in welfare consumption and crimes such as credit card fraud, human trafficking, child prostitution, and robberies perpetrated by immigrants who are not expected to assimilate into American culture), and Amber Phillips, ‘They’re Rapists.’ President Trump’s Campaign Launch Speech Two Years Later, Annotated, WASH. POST (June 16, 2017), https://www.washingtonpost.com/news/the-fix/wp/2017/06/16/theyre-rapists-presidents-trump-campaign-launch-speech-two-years-later-annotated/?noredirect=on&utm_term=.04fb55351cd [https://perma.cc/SQ5T-Q7D5] (memorializing President Donald Trump’s remarks during his campaign for the 2016 presidential election in which he stated, “When Mexico sends its people, they’re not sending their best. . . . They’re sending people that have lots of problems, and they’re bringing those problems with [sic] us. They’re bringing drugs. They’re bringing crime. They’re rapists. And some, I assume, are good people.”).
Two years later, in Pierce v. Society of Sisters, the Court extended the newly minted Meyer principle of fundamental familial rights to another family context. Pierce concerned amendments to the Oregon Compulsory Education Act of 1922, which compelled parents to send their children to public schools. Enforcement of the Act posed a threat to the existence of the primary private-school model. In a unanimous decision, the Court struck down Oregon’s statute as unconstitutional because it “unreasonably interfered with the liberty of parents and guardians to direct the upbringing and education of children under their control.”

Under the Meyer doctrine, the Constitution’s “fundamental theory of liberty . . . excludes any general power of the state to standardize its children by forcing them to accept instruction from public teachers only.” More significantly, Meyer memorialized the constitutionally established principle that “[t]he child is not the mere creature of the state; those who nurture him and direct his destiny have the right, coupled with the high duty, to recognize and prepare him for additional obligations.” The doctrinal consequences of the substantive due process applied in Meyer and Pierce have had long-lasting effects on American jurisprudence. The liberty involving family
and parental autonomy remains relevant a century later\(^\text{306}\) and has laid a foundation for the application of substantive due process—albeit controversially—in the context of other personal liberties.

2. Restrictions—or Lack Thereof—on Liberty Under the Parental Autonomy Doctrine

Despite the broad liberties vis-à-vis the family-unit sphere and parental autonomy predicated in *Meyer* and *Pierce*, the judiciary has recognized that the right to make parental decisions about the rearing of one’s children is not absolute and may be limited by governmental action in certain contexts.

The Court endorsed such restrictions on parental autonomy in *Prince v. Massachusetts*,\(^\text{307}\) in which the Commonwealth demonstrated a cognizable interest in protecting the welfare of children.\(^\text{308}\) *Prince* dealt with a challenge to a Massachusetts child-labor law that forbade individuals from furnishing or selling articles to any minor with the knowledge that the minor intended to sell the article in contravention of the law.\(^\text{309}\) The government convicted Sarah Prince, a Jehovah’s Witness and guardian of her nine-year-old niece, of violating child-labor laws when she allowed her niece to distribute religious literature in exchange for voluntary contributions while Prince was preaching on a public street.\(^\text{310}\)

The *Prince* Court acknowledged the parental autonomy enshrined in the substantive due process rulings of *Meyer* and *Pierce*.\(^\text{311}\) However, it also noted “the family itself is not beyond regulation in the public interest, as against a claim of religious liberty. And neither rights of religion nor rights of parenthood are beyond limitation.”\(^\text{312}\) The Court further articulated activities that could overcome the constitutional bar of parental autonomy, such as compelling parents to send children to school, regulating child labor, and mandating compulsory vaccination so as not to expose the community or the child to preventable disease or death.\(^\text{313}\) Thus, *Prince* signaled an inclination to restrict the scope of *Meyer* and *Pierce* in certain contexts.

\(^{306}\) See discussion supra Section II.A; discussion infra Sections II.B–C.

\(^{307}\) 321 U.S. 158 (1944).

\(^{308}\) Id. at 165.

\(^{309}\) Id. at 161.

\(^{310}\) Id. at 161–62.

\(^{311}\) Id. at 166.

\(^{312}\) Id. (citations omitted).

\(^{313}\) See id. at 166–67.
But *Prince* appears to be an outlier case that is incongruous to subsequent seminal cases examining the bundle of parental and family autonomy rights.\footnote{See infra notes 317–28 and accompanying text.} Indeed, Justice Murphy’s persuasive dissent in *Prince* appears to have laid the foundation for broadening the scope of parental rights decades later.\footnote{Cf. *Prince*, 321 U.S. at 175 (Murphy, J., dissenting) (“[P]arents or guardians [cannot] be subjected to criminal liability because of vague possibilities that their religious teachings might cause injury to the child. The evils must be grave, immediate, substantial. Yet there is not the slightest indication in this record, or in sources subject to judicial notice, that children engaged in distributing literature pursuant to their religious beliefs have been or are likely to be subject to any [health or moral harms].” (citation omitted)); see also Wisconsin v. Yoder, 406 U.S. 205, 234–36 (1972) (holding that Amish parents have a right to exempt their teenage children from mandatory-school-attendance laws on constitutional grounds related to the right to control child-rearing decisions and the free exercise of religion).} Restrictions on parental autonomy rights would apply only to instances where “grave, immediate, [or] substantial” harm to the child were under consideration.\footnote{*Prince*, 321 U.S. at 175 (Murphy, J., dissenting).}

In *Wisconsin v. Yoder*,\footnote{406 U.S. 205 (1972).} the Court ruled that Amish parents have a constitutional right under the First and Fourteenth Amendments to refuse to comply with state laws that mandate children attend school beyond the eighth grade.\footnote{Id. at 234.} Although states may lawfully regulate the duration of children’s education, the governmental interest of ensuring an educated citizenry “is not totally free from a balancing process when it impinges on fundamental rights and interests, such as those specifically protected by the Free Exercise Clause of the First Amendment, and the traditional interest of parents with respect to the religious upbringing of their children.”\footnote{Id. at 214.}

The argument that enforcement of Wisconsin’s law compelling education beyond the eighth grade would “gravely endanger if not destroy the free exercise of [Amish] religious beliefs” persuaded the Court.\footnote{Id. at 219.} Curiously, the *Yoder* Court emphasized that the decision to terminate primary instruction at an early age does not perpetrate “any harm to the physical or mental health of the child or to the public safety, peace, order, or welfare.”\footnote{Id. at 230.} Yet, this emphasis creates tension with *Prince*, in which distribution of religious literature and preaching
on a public street led to the conclusion that children would be exposed to potential emotional, psychological, or physical harm and injury.\textsuperscript{322}

Another case that highlights the Supreme Court’s expansion of broad deference to parental autonomy rights is \textit{Parham v. J.R.}\textsuperscript{323} The \textit{Parham} Court held that the power to make choices related to child rearing does not automatically transfer from parents to a governmental agency simply because it involves certain risks or is not agreeable to a child.\textsuperscript{324} Thus, when it comes to commitment of a child in a mental institution, parents “retain a substantial, if not the dominant, role in the decision, absent a finding of neglect or abuse.”\textsuperscript{325} The rationale underlying such wide discretion stems from the historical presumption that parents often act in the best interest of their children.\textsuperscript{326}

The foregoing cases establish great parental latitude over the control of a child’s upbringing. The interest of parents in directing a child’s upbringing “is perhaps the oldest of the fundamental liberty interests recognized” by the Supreme Court.\textsuperscript{327} Rights concerning the family-unit sphere and parental autonomy can be limited by a state’s interest in protecting children against parental decisions that “jeopardize the health or safety of the child, or have a potential for significant social burdens.”\textsuperscript{328} However, the substantive due process liberty rights in this area are fairly broad in scope, such that parents may institutionalize their offspring or even curtail educational opportunities at an early age without government intervention.

\subsection*{B. The Fundamental Right to Procreate}

The fundamental right of individuals to procreate was first articulated in \textit{Skinner v. Oklahoma}.\textsuperscript{329} The case involved the Oklahoma
Habitual Criminal Sterilization Act,\footnote{330. Act of May 8, 1935, ch. 26, 1935 Okla. Sess. Laws 94, \textit{invalidated by} Skinner v. Oklahoma, 316 U.S. 535 (1942).} which allowed the compulsory sterilization of individuals convicted of crimes amounting to felonies involving moral turpitude.\footnote{331. \textit{Skinner}, 316 U.S. at 536.} Compulsory sterilizations had been legitimized in American society for decades prior to \textit{Skinner} as a convenient method to propel eugenical laws and policies.\footnote{332. Between 1907 and 1979, more than 65,000 compulsory sterilizations took place in thirty-two states across America. Enríquez, supra note 2, at 689–90.} Indeed, in 1927, the Supreme Court in \textit{Buck v. Bell}\footnote{333. 274 U.S. 200 (1927).} had upheld the constitutionality of sexual sterilization practices targeting the mentally disabled.\footnote{334. \textit{See} id. at 207–08.} From a procedural standpoint, \textit{Skinner} extended an opportunity for the Court to answer whether (1) the State exceeded the lawful exercise of its police powers in view of scant scientific evidence to buttress a theory of heritability of criminal behavior,\footnote{335. Justice Jackson filed a brief concurrence in \textit{Skinner} in which he stated that the eugenic purpose of the Oklahoma statute raised “other constitutional questions of gravity” because the state of scientific knowledge at the time was uncertain as to the heritability of select behavioral traits. \textit{See} Skinner, 316 U.S. at 546 (Jackson, J., concurring). I have, in prior work, explored the fascinating question surrounding the judiciary’s reluctance, if not flagrant antipathy at times, to overcome the false dichotomy frequently associated with mutually exclusive roles for science and law. Enríquez, supra note 2, at 679–91. For instance, I have argued against the conventional view that \textit{Buck’s} holding is illegitimate because it rests on pseudoscience. An examination of the state of scientific knowledge at the time \textit{Buck} was decided reveals that no legitimate scientific debate existed regarding the heritability of human cognitive abilities or mental deficiencies. \textit{Buck} relied on no scientific evidence. Instead, it relied on deceptive propaganda that had been de facto incorporated into popular culture over a period of decades. \textit{See} id. at 685–91.} (2) due process was lacking due to inadequate review of a prisoner’s purported genetic predisposition to father undesirable offspring, and (3) the sterilization provisions of the Act constituted cruel and unusual punishment under the Fourteenth Amendment.\footnote{336. \textit{Skinner}, 316 U.S. at 537–38.} The Court overlooked all those issues and instead chose to focus on whether the Act violated the Equal Protection Clause of the Fourteenth Amendment.\footnote{337. \textit{Id.} at 538.} The \textit{Skinner} Court held that Oklahoma’s sterilization law violated principles of equal protection under the Fourteenth Amendment because it discriminated on the basis of seemingly arbitrary distinctions between felonies of the same type.\footnote{338. \textit{Id.} at 541.} Thus, individuals convicted of
grand larceny or embezzlement—both felonies—were subject to unequal treatment under the law; the larcenist could be subject to sterilization, while the embezzler could not.  

More importantly, *Skinner* explicitly articulated the fundamental status of human procreation by framing the issue presented as one concerning a basic right “to the perpetuation of a race—the right to have offspring.” According to the Court, individuals have fundamental civil rights to marry and procreate, which are crucial to the survival of our species. The power to sterilize, if exercised, may have subtle, far-reaching and devastating effects. . . There is no redemption for the individual whom the law touches. Any experiment which the State conducts is to his irreparable injury. He is forever deprived of a basic liberty.”

Because of the delicate nature of the right to procreate, the Court emphasized that strict scrutiny is the only judicial standard of review that could apply to state action encroaching on the ability of humans to reproduce. The irreversibility of sterilization procedures, as well as the social and biological implications of reproduction, provided an analytical foundation to promote the majority’s view that the sort of sterilization provisions under Oklahoma’s Habitual Criminal Sterilization Act should be held to the highest scrutiny possible.

Although *Skinner* applied only to punitive sterilizations and failed to overturn *Buck*, it nevertheless stands as a landmark decision that conceptualized the guarantee of procreative rights under the Constitution.

### C. Jurisprudence on Reproductive and Procreative Autonomy and Privacy

The fundamental rights elucidated in *Meyer, Pierce, Skinner*, and other cases related to parental choice, procreation, and the family-unit sphere had a lasting impact on early twentieth-century American jurisprudence. Collectively, these cases caused a tectonic shift in the
interpretation of equal protection and due process law. As time passed, it became clear that such precedents could, and would, ultimately support a revolution that marked the dawn of the right of privacy and other reproductive rights.\footnote{346}{See Griswold v. Connecticut, 381 U.S. 479, 502–03 (1965) (White, J., concurring) (citing Meyer, Pierce, Prince, Skinner, and other cases concerning liberty guarantees under the Fourteenth Amendment).}

\textit{Griswold v. Connecticut} was the landmark case that unveiled a right to privacy under the Constitution.\footnote{347}{381 U.S. 479 (1965).} The case involved a challenge to a Connecticut statute that prohibited (1) the use of “any drug, medicinal article or instrument for the purpose of preventing conception” and (2) individuals to assist, abet, counsel, cause, or command others to violate the law.\footnote{348}{Id. at 479.}

\textit{Griswold}’s arrival at the Court was anything but stochastic. The Connecticut anticontraception statute under review had been enacted nearly a century earlier in 1879.\footnote{349}{Id. at 480.} It came at the heels of what became known as the Comstock Laws, a set of federal and state statutes enacted in the 1870s designed to punish obscene behavior, providers of abortion, and the use of contraception.\footnote{350}{D\textsc{avid} J. G\textsc{arrow}, \textsc{Liberty and Sexuality: The Right to Privacy and the Making of Roe v. Wade} 1 (1994).} The Comstock Act was not the first piece of legislation that aimed to regulate the distribution of obscene material in the United States.\footnote{351}{The Comstock Act of 1873 criminalized the act of knowingly sending “obscene, lewd, or lascivious” materials through the mail. \textsc{Paul R. Abramson} \& \textsc{Steven D. Pinkerton, With Pleasure: Thoughts on the Nature of Human Sexuality} 177 (rev. ed. 2002). The Act’s name was derived from Anthony Comstock, founder of the New York Society for the Suppression of Vice and special agent of the U.S. Postal Service, who had, for years, engaged in a series of anti-obscenity campaigns aimed at ridding society of all masturbation, pornography, contraceptives, and nonreproductive sexual activity. \textit{Id.} at 176–77.}

\textit{Griswold}’s arrival at the Court was anything but stochastic. The Connecticut anticontraception statute under review had been enacted nearly a century earlier in 1879.\footnote{352}{Nicola \textsc{Beisel}, \textsc{Imperiled Innocents: Anthony Comstock and Family Reproduction in Victorian America} 36–38 (1997).} It came at the heels of what became known as the Comstock Laws, a set of federal and state statutes enacted in the 1870s designed to punish obscene behavior, providers of abortion, and the use of contraception.\footnote{353}{See Abramson \& Pinkerton, supra note 351, at 178. Laws banning pornography had been enacted at the state level as early as 1821 and at the federal level as early as 1842 with the passage of the U.S. Customs Act. \textit{Id.}; \textsc{Judith Giesberg}, \textsc{Sex and the Civil War: Soldiers, Pornography, and the Making of American Morality} 12 (2017).}

\textit{Griswold}’s arrival at the Court was anything but stochastic. The Connecticut anticontraception statute under review had been enacted nearly a century earlier in 1879.\footnote{354}{See \textsc{Mary Ware Dennett}, \textsc{Birth Control Laws: Shall We Keep Them Change Them or Abolish Them} app. at 268–70 (1926). \textsc{See generally} J.C. Ruppenthal,
By the mid-1930s, with no progress made to repeal the Connecticut law, some physicians began to quietly open birth control clinics throughout the state.355 At first, the clinics thrived due to low enforcement of the anticontraception law.356 Poor women gained access to birth control advice previously available only to those who could afford private physicians.357 With time, however, enforcement of the law led to the prosecution and conviction of physicians who distributed contraceptives at the birth control clinics.358

On November 1961, Estelle Griswold, the Executive Director of the Planned Parenthood League of Connecticut, and Lee Buxton, a licensed physician and professor at the Yale Medical School, were arrested after they opened a birth control clinic in New Haven.359 Connecticut prosecuted and convicted them for providing information and medical advice to married people with the intent that the information would prevent conception.360 Griswold and Buxton appealed their convictions, and the Supreme Court granted certiorari to consider the constitutionality of the anticontraception statute.361

The Griswold majority found that the “Framers did not intend that the first eight amendments be construed to exhaust the basic and fundamental rights which the Constitution guaranteed to the people.”362 Accordingly, the majority identified a “zone of privacy” created by the fundamental constitutional guarantees of the Bill of Rights.363 The privacy right articulated by the Court concerned the right to be free from governmental intrusion, which arose from the “penumbras” and “emanations” of other constitutional guarantees.364 In the contraceptive context at bar, the majority opined that the idea of government intrusion into “the sacred precincts of marital bedrooms” was “repulsive to the notions of privacy surrounding the marriage relationship.”365

Criminal Statutes on Birth Control, 10 J. AM. INST. CRIM. L. & CRIMINOLOGY 48 (1919) (providing a survey of said laws).

355. GARROW, supra note 350, at 1.

356. Id.

357. Id.


360. Id.

361. Id.

362. Id. at 490.

363. Id. at 484–85.

364. Id. at 483–84.

365. Id. at 485–86.
The right to marital privacy with respect to intimate conduct born out of *Griswold* subsequently led to the conceptualization of a right to reproductive and procreative autonomy enshrined in *Eisenstadt v. Baird*.\footnote{405 U.S. 438 (1972).} In *Eisenstadt*, the Court extended *Griswold*'s holding outside the marital context to rule that unmarried couples also have a right to use contraception.\footnote{Id. at 453.} Significantly, the Court famously noted that “[i]f the right of privacy means anything, it is the right of the individual, married or single, to be free from unwarranted governmental intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child.”\footnote{Id. (emphasis added).} The Court further expanded this privacy-based right against government intrusion into matters of procreation in *Carey v. Population Services International*.\footnote{431 U.S. 678 (1977).} In *Carey*, the Court ruled that the right to privacy extends to decisions affecting procreation not only for adults but for minors as well.\footnote{Id. at 693.} Thus, these cases establish a robust fundamental right for individuals to make decisions about how and when to procreate.

**D. The (In)Applicability of Roe**

In 1973, the Supreme Court held in *Roe v. Wade*\footnote{410 U.S. 113 (1973).} that the liberty protected under substantive due process includes a right to privacy that supports a woman’s constitutional right to terminate her pregnancy.\footnote{Id. at 164–67.} That constitutional right, however, has been restricted in recent decades with the introduction of the “undue burden” standard articulated in *Planned Parenthood of Southeastern Pennsylvania v. Casey*.\footnote{505 U.S. 833 (1992) (per curiam) (holding certain restrictions on the right to an abortion are constitutional unless they impose an “undue burden”).} Undue burden refers to governmental action that “has the purpose or effect of placing a substantial obstacle in the path of a woman seeking an abortion of a nonviable fetus.”\footnote{Id. at 877.} Although *Roe* and *Casey* held that women have a fundamental right to an abortion, the cases have to some extent confounded the privacy-based substantive due process jurisprudence.\footnote{For instance, *Roe* held that strict scrutiny applied, but *Casey*'s joint opinion failed to articulate a level of scrutiny and instead concocted the new undue burden standard. See}
Issues related to abortion and GGE may appear intertwined at first glance. Both involve questions of reproductive liberties. However, Roe’s brand of substantive due process may be less significant in the GGE realm, particularly when it comes to therapeutic GGE interventions. As will be discussed in Part III, clinical interventions to cure or ameliorate disease in an embryo—with the intent to save a child from premature death—are at the opposite end of what abortion achieves. In the former case, a parent wishes to conceive a child without a harmful genetic mutation, whereas in the latter, the parent does not wish to bring the embryo to term. Similarly, therapeutic GGE brings into focus the prospect of eliminating the need to create dozens of embryos during in vitro fertilization (“IVF”), which ultimately get discarded or frozen and stored indefinitely.376

The one area related to abortion that is presumably more relevant to GGE than the type of substantive due process applied in Roe and its progeny is related to cases involving government restrictions on public funding for abortion.377 Thus, restrictions on the use of government funds to perform GGE interventions are likely constitutional.

E. Framing the Issue

A final pivotal consideration in the discussion of whether a fundamental right to GGE might exist under the Constitution is the

376 See Julie Steffann et al., Could Failure in Preimplantation Genetic Diagnosis Justify Editing the Human Embryo Genome?, 22 CELL STEM CELL 481, 481–82 (2018) (analyzing results from the Preimplantation Genetic Diagnosis (“PGD”) Centre of Béclère-Necker hospitals in Paris over a five-year period to reveal that PGD aimed at helping couples bear healthy children had a 73% failure rate). The study performed by Steffann and colleagues found that out of 3047 embryos obtained from 358 couples, only 2038 embryos were successfully diagnosed. Id. at 481–82 & app. Of the embryos diagnosed, 53% (1079) were unaffected by genetic disease while 47% (959) tested positive for genetic disease and were discarded. Id. The unaffected embryos were transferred or cryopreserved and ultimately resulted in only 95 deliveries, in which 118 babies were born. Id.

377 See generally, e.g., Harris v. McRae, 448 U.S. 297 (1980) (holding that states participating in Medicaid are not obligated to fund medically necessary abortions when the state cannot be reimbursed under federal law); Beal v. Doe, 432 U.S. 438 (1977) (holding that a state’s refusal to extend Medicaid coverage to nontherapeutic abortions contravened federal law); Poelker v. Doe, 432 U.S. 519 (1977) (per curiam) (holding that a city was not constitutionally required to provide publicly financed hospital services for elective abortions even if the city provides such services for childbirth).
ultimate framing of the issue. Consider, for example, the arrival of Bowers v. Hardwick\textsuperscript{378} at the Court. In that case, the issue presented was “whether the Federal Constitution confers a fundamental right upon homosexuals to engage in sodomy,” which had been illegal “for a very long time.”\textsuperscript{379} Nearly two decades later, the Court reviewed virtually the same question in Lawrence v. Texas,\textsuperscript{380} except that it was framed as whether “two persons of the same sex [can] engage in certain intimate sexual conduct.”\textsuperscript{381} Unsurprisingly, the Bowers Court did not find a liberty right to engage in homosexual sodomy under the Constitution,\textsuperscript{382} whereas the Lawrence Court ruled that consenting adults of the same sex have a constitutionally protected liberty right to engage in intimate sexual conduct.\textsuperscript{383}

Similarly, in Washington v. Glucksberg,\textsuperscript{384} the Court reviewed whether a “prohibition against “caus[ing]” or “aid[ing]” a suicide offends the . . . Constitution.”\textsuperscript{385} This framing stands in contrast to alternative phrasing in concurring opinions in that case, which articulated other possible versions such as the “merciful termination of suffering,”\textsuperscript{386} “the narrower question whether a mentally competent person who is experiencing great suffering has a constitutionally cognizable interest in controlling the circumstances of his or her imminent death,”\textsuperscript{387} and “the avoidance of severe physical pain (connected with death).”\textsuperscript{388}

Carefully framing an issue for judicial review has many parallels to the design of questions intended for polling and surveys to reveal public attitudes about controversial topics. “Polling, of course, is not quite a science and certainly is not an exact one. . . . [I]t is highly vulnerable to the use of specific terminology and ambiguity in framing the questions asked.”\textsuperscript{389}

\begin{footnotesize}
\begin{itemize}
\item \textsuperscript{378} 478 U.S. 186 (1986), overruled by Lawrence v. Texas, 539 U.S. 558 (2003).
\item \textsuperscript{379} Id. at 190 (emphasis added). The case was decided during the time of the AIDS epidemic, and, thus, framing the issue as a right of homosexuals to engage in sexual conduct likely played an outcome-determining role.
\item \textsuperscript{380} 539 U.S. 558 (2003).
\item \textsuperscript{381} Id. at 562.
\item \textsuperscript{382} Bowers, 478 U.S. at 189.
\item \textsuperscript{383} Lawrence, 539 U.S. at 578–79.
\item \textsuperscript{384} 521 U.S. 702 (1997).
\item \textsuperscript{385} Id. at 705–06.
\item \textsuperscript{386} Id. at 754–55 (Souter, J., concurring).
\item \textsuperscript{387} Id. at 736 (O’Connor, J., concurring).
\item \textsuperscript{388} Id. at 791 (Breyer, J., concurring).
\item \textsuperscript{389} Enríquez, supra note 2, at 675.
\end{itemize}
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Consider, for instance, recent polls on public attitudes on the use of technologies for genome editing. A greater percentage of respondents in multiple surveys supported the use of gene-editing tools to “cure life-threatening” or “debilitating” diseases. In contrast, one poll reported that a majority of respondents believed that “changing the genes of unborn babies . . . to reduce their risk of developing certain serious diseases” should be illegal. “Public sentiment has considerable influence over allocation of resources, political policy, and participation rates in studies, all of which affect the course of research.” And just as public sentiment can be influenced by the manner in which a particular issue is presented, so too can judicial sentiment be affected. Undoubtedly, judicial review is anything but impervious to the proverbial anatomy of the question presented before a court.

The foregoing case law and discussion highlight a crucial role for framing a question centered on the right to perform GGE. Different


391. See, e.g., McCaughey et al., supra note 390, at 569 (noting that 59.0% and 59.4% of survey respondents approved the use of gene editing in children and adults to cure life-threatening or debilitating diseases, respectively); accord Scheufele, supra note 390, at 553 (finding the use of human genome editing for therapeutic purposes is acceptable to 64% of respondents for somatic therapies and 65% of respondents for germline therapies); Uchiyama et al., supra note 390, at 745 (“[R]esults clearly indicated that the Japanese people generally accepted the use of genome editing for disease-related genes.”).

392. See STAT & HARVARD T.H. CHAN SCH. OF PUB. HEALTH, supra note 390, at 2 (emphasis added) (reporting that 26% of respondents believed “changing the genes of unborn babies” should be legal in a therapeutic context, while 65% believed it should be illegal to do so). It should be noted that phrasing the question as one involving changing unborn babies to reduce the risk of disease, rather than using a technology to cure disease, may underlie the contrast in the respondents’ attitudes toward gene editing among the various polls.

393. McCaughey et al., supra note 390, at 571.
outcomes likely would be associated with questions framed as whether parents have a constitutional right to, among other things, (1) perform GGE to bear a healthy child, (2) genetically modify offspring, (3) engineer “designer babies,” (4) prevent life-threatening disease or death by correcting deleterious genetic mutations in their child, (5) use reproductive technology to cure genetic disease, (6) customize traits in their offspring, or (7) bear biological children by treating their germ cells with medicinal advances.

III. A LEGAL- AND SCIENCE-BASED POLICY FRAMEWORK FOR THE FUTURE OF GERMLINE GENOME EDITING

Part II laid out a doctrinal foundation of jurisprudence in areas of parental, family, procreative, and reproductive autonomy guaranteed by the Due Process and Equal Protection Clauses of the Constitution. But jurisprudence in this realm must be framed in the context of GGE in order to derive applicable legal principles that ultimately can guide and promote coherent public policy. This part argues that these constitutional underpinnings of jurisprudence in the family-unit sphere serve as the basis for a cognizable fundamental right to perform specific types of GGE. Of course, like many of the rights identified via substantive due process—such as the rights to control a child’s upbringing, marry, have an abortion, and others—394—the right to perform GGE would not be absolute.395

Congressional or judicial fiat may delineate, at some point in the near future, the extent and limitations of a right to perform GGE in select contexts. However, no framework currently exists to draw clear lines that distinguish between permissible and impermissible uses of GGE technologies. The normative framework proposed below identifies four distinct categories of GGE: (1) therapeutic uses to remedy disease; (2) prophylactic purposes, which may or may not be of therapeutic nature; (3) cosmetic or enhancement purposes; and (4)

394. Indeed, other fundamental rights enumerated by the Supreme Court are not absolute and could be subject to governmental restrictions. See, e.g., Obergefell v. Hodges, 135 S. Ct. 2584, 2599 (2015) (implicitly restricting the fundamental right to marry only to “couples” or individuals in a “two-person union” (emphasis added)); Planned Parenthood of Se. Pa. v. Casey, 505 U.S. 833, 876 (1992) (per curiam) (holding certain restrictions on the right to an abortion are constitutional unless they impose an “undue burden”); Wisconsin v. Yoder, 406 U.S. 205, 234 (1972) (articulating limits to parental autonomy when a child’s safety or health are at risk). Accordingly, a fundamental right to perform GGE in certain contexts most likely would still be subject to some level of governmental interference that meets the burden of strict scrutiny. See discussion infra Sections III.A–D.

395. See discussion supra Sections II.A–D.
uses involving modification of traits that raise concerns of discrimination that is already prohibited by the law.

The four-category spectrum proposed here facilitates the creation of initial boundaries for GGE and outlines a putative regulatory and legal blueprint. Furthermore, the approach avoids the squabbles that frequently rise from the conventional tendency to group GGE applications into therapeutic uses on one hand, and enhancements on the other. That outdated model is inefficient and susceptible to analytical derailments stemming from awkward attempts to fit therapeutic, eugenical, and so-called “designer baby” enhancements into a single doctrinal model.

The normative framework proposed here, however, deconstructs the nuances inherent in various applications of GGE. Hence, under Category 1, GGE purposes are permitted, can withstand strict constitutional scrutiny, and constitute a fundamental right. Conversely, Category 4 GGE uses at the opposite end of the spectrum are prohibited because they create a likelihood of discrimination against specific groups and are not constitutionally justifiable. Lastly, many GGE applications that fall within the sphere of Categories 2 and 3 involve polygenic, as opposed to monogenic, conditions. As a result, it is unlikely that the technology to address these GGE interventions will be ready for clinical use in the near future. Because of this fact, premature laws and regulations concerning the sanction or prohibition of GGE prophylactic, cosmetic, and enhancement interventions should be avoided at this point in time.

A. Category I—Therapeutic Uses

The first category of GGE applications concerns therapeutic uses to remedy disease. For parents carrying genetic mutations that increase the likelihood of conceiving a child susceptible to a serious genetic disease, it is quite likely that the awareness of their genetic composition fundamentally affects their decision whether to become parents. The Supreme Court has noted that “[i]f the right of privacy means anything, it is the right of the individual, married or single, to be

396. The term “polygenic” refers to traits that are determined by the contribution of more than one gene.
397. The term “monogenic” refers to traits that are determined by the effects of a single gene.
398. In particular, this section refers primarily to a myriad of monogenic diseases, which likely will be the main focus of early genome-editing therapies. See Enríquez, supra note 2, at 636.
free from unwarranted governmental intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child.\footnote{399}{See Eisenstadt v. Baird, 405 U.S. 438, 453 (1972) (emphasis added).}

The prospect of bringing a child into this world to suffer a debilitating, life-long illness would certainly play a fundamental role in an individual’s decision to pursue parenthood within the meaning of our existing substantive due process jurisprudence. After all, what good is the existence of a “right to have offspring” or procreate\footnote{400}{Skinner v. Oklahoma, 316 U.S. 535, 536 (1942).} if that offspring is destined to suffer disease and premature death? Governmental authority aimed at denying parents the ability to perform GGE for therapeutic purposes when their child faces the probability of suffering from an imminent, life-threatening, genetic disease\footnote{401}{The probability of developing a genetic disease depends on many factors, including patterns of inheritance. See, e.g., If a Genetic Disorder Runs in My Family, What Are the Chances that My Children Will Have the Condition?, GENETICS HOME REFERENCE, https://ghr.nlm.nih.gov/primer/inheritance/riskassessment [https://perma.cc/V2S2-5CFT]. In general, children are most at risk of inheriting a serious genetic condition when both parents are homozygous for particular mutations that can lead to certain diseases.} would have overt, “far-reaching[,] and devastating effects” on the health and survival of said child that arguably go beyond the prohibition of the power to sterilize articulated in \textit{Skinner}.\footnote{402}{Cf. \textit{Skinner}, 316 U.S. at 541 (holding that “[t]he power to sterilize, if exercised, may have subtle, far-reaching and devastating effects” on individuals affected by the law).}
Congenital disease may force upon a child, as well as all members of her family unit, “a distressful life and future. Psychological harm may be imminent. Mental and physical health may be taxed by child care.”\footnote{403}{Roe v. Wade, 410 U.S. 113, 153 (1973).}
Denial of a fundamental right to perform GGE under this scenario arguably runs contrary to the guarantees found in the Constitution, which protect the right to procreation as crucial to the survival of the species.\footnote{404}{Id.}

A discussion of the right to procreate calls for deeper analytical exploration of the basis underlying the incorporation of a putative right to rescue one’s offspring from imminent illness or death as part of the human procreational prerogative. The core of this argument is that the basic fundamental right to “perpetuat[e] a [human] race” and “have offspring”\footnote{405}{\textit{Skinner}, 316 U.S. at 536.} articulated in \textit{Skinner} pertains specifically to a right rooted in the success of \textit{biological} procreation. This inference must be
drawn from *Skinner*’s holding because merely having offspring does not, in and of itself, guarantee the perpetuation of the human race. In order to perpetuate one’s genetic composition in the human gene pool, one’s offspring must be viable, fertile, and capable of developing to an age at which the individual can procreate and have offspring herself. The right to procreate under the constitutional structure of *Skinner*’s holding is, thus, essentially meaningless if one’s children are destined to an early death at the hands of genetic disease.

That conceptual exposition is also supported by dicta in *Skinner* noting that the power to sterilize “can cause races or types which are inimical to the dominant group to wither and disappear.” 406 Again, a reference to favorable or adequate biological procreation appears nowhere explicitly in the opinion. But the majority’s concern that specific “races or types”—namely, traits that can be traced to specific genotypes—can “wither and disappear” speaks clearly to the proposition that, without a fundamental right to biological procreation that limits governmental intrusion into procreative matters, some individuals belonging to nondominant groups might find themselves defenseless against invidious government action and will ultimately be unable to pass down their genes to subsequent generations. Procreation in that sense calls for more than just producing offspring; it calls for producing offspring healthy enough to fulfill the biological role of perpetuating one’s genotype within the constitutional structure erected by *Skinner*.

Although the Supreme Court has counseled caution and restraint in the application of substantive due process, “it does not counsel abandonment.” 409 Parents who must choose between having a child destined to be ill or forgoing the benefits of biological parenthood entirely would be, in essence, abandoned by the Constitution.

406. *Id.* at 541 (emphasis added).
407. *Id.*
408. One important consideration relates to the definition of the term “healthy.” For instance, does a child with rheumatoid arthritis who is severely crippled and ill but grows up to marry and have children qualify as healthy within the meaning of *Skinner*? Does an individual with Cystic Fibrosis (“CF”) who grows up to become a parent and dies at a young age from CF-related complications—but nevertheless was able to bear children who also carry CF-associated mutations—qualify as healthy within the meaning of *Skinner*? These questions are more difficult to resolve under a fundamental right to procreate but may be more soluble under the principles embedded in the right to parental autonomy. In any event, at a minimum, *Skinner* arguably endorses a substantive reading of biological procreation in the context of a right to have offspring healthy enough to develop and grow to an age when they will be able to reproduce and pass down their genetic makeup to a new generation.
Accordingly, it is difficult to imagine a more compelling scenario for the application of modern substantive due process. Furthermore, the decision to enter into a marriage relationship has been recognized as the core of family in our society. But what shall we then make of the decision to enter the ultimate relationship that perpetuates the human race—namely, the parent-child relationship—which, unlike marriage, is ever-lasting, not susceptible to divorce, and often becomes more significant and life altering than the decision to marry? Assuming GGE technologies become safe and effective for clinical use, if the rights of procreation, parental autonomy, and privacy mean "anything at all," they must imply some right to enter the parent-child relationship unencumbered by the burdens of disease stemming from random or inherited genetic mutations many individuals bear no responsibility for carrying.

For individuals who carry alleles associated with genetic diseases, the right to be free from state intervention in the decision to bear children without deleterious genetic mutations via GGE intervention likely triggers strict scrutiny. Thus, the government may find it difficult to establish a compelling state interest that would justify wholly prohibiting GGE interventions. After all, bearing healthy children

411. Although the legal status of the parent-child relationship is unaffected by divorce between two parents, it should be noted that the law recognizes circumstances under which the parent-child bond can be severed. See, e.g., Adoptive Couple v. Baby Girl, 570 U.S. 637, 641–42 (2013) (terminating paternal rights of a biological father who never had custody of his child); Michael H. v. Gerald D., 491 U.S. 110, 131–32 (1989) (restricting parental rights of unmarried fathers); Diamond v. Diamond, 283 P.3d 260, 261 (N.M. 2012) (addressing the issue of child emancipation); In re Moore, 306 N.C. 394, 405–06, 293 S.E.2d 127, 134 (1982) (terminating parental rights in response to child abuse or neglect). However, termination of parental rights, emancipation of minors, and other related principles are legal constructs. From a purely biological perspective, which encompasses the ambit of the fundamental right to “perpetuat[e] a [human] race . . . [and] have offspring” articulated in Skinner, see Skinner, 316 U.S. at 537, the parent-child genetic link is permanent.
412. Safety and efficacy are relative terms—“no technology is ever completely safe, or completely efficacious.” OFFICE OF TECH. ASSESSMENT, ASSESSING THE EFFICACY AND SAFETY OF MEDICAL TECHNOLOGIES 17 (1978), https://ota.fas.org/reports/7805.pdf [https://perma.cc/M6VU-ZJ4A]. “Efficacy is defined in terms of a benefit; safety, in terms of a risk. . . . Neither efficacy nor safety is absolute. Both are discussed in terms of probability and magnitude of benefit or harm.” Id. at 18 (emphasis omitted). Thus, for example, the FDA’s determination that a drug is safe does not indicate a complete absence of risk or potential harm. Safety means that the therapeutic “benefits of the drug outweigh the risks.” 21 U.S.C. § 355-1(a)(1) (Supp. 2017).
413. Zablocki, 434 U.S. at 386 (emphasis added).
414. Indeed, it is not difficult to imagine the opposite scenario in which the government might begin to mandate GGE intervention for prospective parents carrying deleterious genetic mutations, so as to promote a myriad of governmental interests related to the
significantly contributes to the pursuit of happiness in the family context.\textsuperscript{415} Moreover, the wide latitude afforded to parents in making decisions related to the upbringing of their offspring—including medical decisions that do not endanger the health or safety of the child\textsuperscript{416}—support a cognizable right to GGE interventions with therapeutic intent. In fact, the availability of GGE that is proven safe and effective brings into focus the prospect of allowing parents to make medical decisions that will promote and safeguard the health of the child by ensuring offspring will not carry genetic mutations for serious diseases.\textsuperscript{417}

Under a strict scrutiny analysis, the government might find it difficult to establish the existence of narrowly tailored measures to further the interest of denying GGE for therapeutic purposes. Indeed, for homozygous individuals carrying deleterious genetic mutations that all but guarantee that offspring will be susceptible to genetic diseases,\textsuperscript{418} there are likely few, if any, suitable alternative means\textsuperscript{419}—including protection of children and the reduction of social costs associated with health care and management of diseases. See Jacobson v. Massachusetts, 197 U.S. 11, 11–12 (1905) (upholding the authority of states to enforce compulsory vaccination statutes).

\textsuperscript{415} See Meyer v. Nebraska, 262 U.S. 390, 399 (1923).

\textsuperscript{416} See Parham v. J.R., 442 U.S. 584, 603 (1979) (“Most children, even in adolescence, simply are not able to make sound judgments concerning many decisions, including their need for medical care or treatment.”).

\textsuperscript{417} The prospect of using GGE for benign, therapeutic purposes actually overcomes one of the possible limitations outlined in Section II.A.2 relating to the protection of children from harm and exploitation articulated in Prince. See Prince v. Massachusetts, 321 U.S. 158, 166 (1944).

\textsuperscript{418} Several patterns of inheritance exist by which an individual may inherit a genetic condition, including, inter alia, autosomal dominant, autosomal recessive, codominant, and mitochondrial inheritance. For a brief explanation of each pattern, see, for example, What Are the Different Ways in Which a Genetic Condition Can Be Inherited?, GENETICS HOME REFERENCE, https://ghr.nlm.nih.gov/primer/inheritance/inheritancepatterns [https://perma.cc/Z3YJ-7Q6F]. The probability of inheriting a particular genetic disease varies depending on the pattern of inheritance and whether the parents are homozygous or heterozygous for a particular allele associated with genetic disease. Cases in which both parents are homozygous for a particular genetic disease are very rare, but they can occur. And potential arguments that GGE should be banned because only a small minority of couples would be affected by such prohibitions are likely to crumble before legal challenges brought by individuals asserting the principle that the Constitution protects the rights of individuals rather than the collective rights of groups. See District of Columbia v. Heller, 554 U.S. 570, 579 (2008) (explaining that “the right of the people” refers to individual and not “collective” rights).

\textsuperscript{419} The parents could elect to receive sperm, egg, or embryo donations from other individuals or decide to have an abortion as possible alternatives. Neither of these options, however, offers a path toward biological parenthood and, thus, cannot truly be considered alternatives within the general purview of the right to have biological offspring articulated in Skinner. See Skinner v. Oklahoma, 316 U.S. 535, 541 (1942). Furthermore, the argument
preimplantation genetic diagnosis ("PGD")—to conceive an otherwise healthy child without GGE intervention. Thus, the right to be free from government intrusion in the decision to pursue GGE for therapeutic purposes is an extension of the rights to procreate and exercise parental autonomy under current substantive due process jurisprudence. Once GGE's safety and efficacy are scientifically established, it may be difficult for the government to impose bans on access to the technology for therapeutic uses.

Lastly, there is some validity to the point that banning a technology that may assist deleterious mutation-carrying parents would not violate the right to procreate because they may still choose to conceive and assume the risks of bringing a child who may be susceptible to genetic disease. That some parents may choose not to reproduce because of an awareness of the burdens inherent in their genetic composition is a personal choice, which the government does not interfere with when it denies access to a particular reproductive technology. For instance, *Califano v. Jobst* articulated the principle that a "general rule is not rendered invalid simply because some persons" might be deterred from engaging in certain conduct. However, *Jobst* can be clearly distinguished from the GGE context, as

that the risk of transmitting genetic disease can be avoided via PGD coupled with abortion overlooks PGD's financial, medical, and emotional burdens; its low chance of success; and the large number of embryos that are discarded in the process, which some potential parents may object to from ethical or faith-based perspectives. See Steffann et al., supra note 37, at 481 ("In weighing the risks and benefits of [GGE], one needs to consider the potential of genome editing to cure genetic diseases at an early stage of life, and the concept that we have a moral duty to cure affected human embryos instead of discarding them.").

420. Preimplantation genetic diagnosis refers to an ART technique that facilitates genetic profiling of human embryos—obtained through IVF—for the purpose of testing for genetic abnormalities. Peter Braude et al., *Preimplantation Genetic Diagnosis*, 3 NATURE REVIEWS: GENETICS 941, 941 (2002). The screening takes place prior to implantation in a woman's uterus and, therefore, can be distinguished from in utero prenatal diagnosis or screening of an embryo or fetus. See id. PGD is often used as an alternative to abortion for parents with substantial risk of transmitting genetic disorders to their progeny by preventing a pregnancy from occurring in the first place. *Id.* at 942.


423. *Id.* at 54.
it concerned a limitation on the right to marry but only in the context of the distribution of government benefits under a specific program that would have been lost when the plaintiff remarried and would no longer be dependent on government assistance.424

As stated earlier, for some parents who carry deleterious genetic mutations, there is no alternative path to have a healthy child. That strikes at the core of the fundamental right to procreate. It also stands in contrast to Jobst, which was related to the loss of a government benefit and, thus, did not strike at the core of the fundamental right to marry. In the GGE context, parents contemplate a decision that goes beyond giving up a government benefit. Instead, parents must decide whether they are willing and able to bring a human being into the world who is likely destined to suffer from disease—a decision that carries substantial emotional, social, and financial costs.

As discussed above, the use of GGE intervention—for which scientific evidence exists to establish the safety and efficacy of the desired genetic modification—in the therapeutic context may constitute a fundamental right and could withstand strict constitutional scrutiny. However, the analysis in the foregoing section may be inapplicable to a right to perform GGE for nontherapeutic uses.

B. Category 2—Prophylactic Purposes

The second category of GGE applications refers to the use of GGE interventions for prophylactic purposes. This category shares many similarities to Category 1, but can be clearly distinguished by noting that prophylactic interventions may or may not be therapeutic in nature.

The use of GGE in this category is likely to be important, but may not be sufficient to withstand the pressures of strict scrutiny that Category 1 uses could. For example, parents may wish to confer immunity to the HIV virus425 upon an embryo, or protect it against potential risks of cardiovascular disease, diabetes, and some cancers. The parental autonomy highlighted under these scenarios would be weighed against potential state interests derived from access to the technology, fairness, and equality. Parents may have a constitutionally protected right to perform GGE intervention on an embryo to spare it from a life of suffering or premature death, but will they also have a

424. Id. at 48–50.
425. Roughly one percent of the world’s Caucasian population carries a genetic mutation in the CCR5 gene that confers immunity against the HIV virus. Enríquez, supra note 2, at 633–34; see also infra Figure 5. Clinical trials are currently underway to explore possible cures for HIV using genome-editing technologies. Enríquez, supra note 2, at 634.
constitutional right to modify the genes of their offspring based on the possibility that a given disease will affect them in the future? HIV immunity, for example, would not be relevant to a genetically modified individual unless, at some point, the person is exposed to the virus. In other words, parents may have a constitutional right to bear healthy children, but may or may not have a constitutional right to bear children who are immune to HIV.

The prophylactic category of GGE interventions also shines a light on the policy challenges presented by medical advances and technologies, which often affect the status of a particular disease in society. Case in point, NASEM recommended restricting GGE interventions to a “serious disease or condition” and to “prevent extension” to other uses.426 But adherence to that recommendation largely depends on a definition of what constitutes a “serious disease or condition” at a particular point in time, and whether extension to other potential uses at some point in the future might be palatable, or even desirable, from social, ethical, and policy perspectives.

Consider the case of HIV infection. During the 1980s and 1990s, when the AIDS epidemic caused a public-health crisis, HIV infection was considered a death sentence and certainly constituted a serious disease or condition that could even be transmitted to an individual’s offspring.427 However, scientific advances in antiretroviral drug therapies in the last two decades have dramatically altered medical outcomes associated with HIV diagnoses in the developed world, and many in the medical profession now consider HIV a chronic infection, on par with other chronic diseases such as diabetes.428

426. NASEM REPORT, supra note 21, at 7–8 (emphasis added).
427. See Kevin M. De Cock, Harold W. Jaffe & James W. Curran, Reflections on 30 Years of AIDS, 17 EMERGING INFECTIOUS DISEASES 1044, 1044 (2011) (describing AIDS as an “inevitably fatal disease” when it was first documented in the early 1980s, while noting that the disease would go on to cause approximately 30 million deaths).
In fact, individuals already have access to antiretroviral therapy for prophylactic purposes today. On the other hand, HIV continues to represent a serious threat to public health in poverty-stricken regions of the

429. Gilead Sciences, Inc. markets “TRUVADA for PrEP® (preeposure prophylaxis) [as] a prescription medicine that can help reduce the risk of getting HIV-1 through sex, when taken every day and used together with safer sex practices.” TRUVADA, https://www.truvada.com/ [https://perma.cc/2ZX9-87RN].
Figure 5. Structural Representation of the HIV-1 gp120 Viral Glycoprotein in Complex with a Human Chemokine Receptor CCR5 Prior to Fusion of Viral and Target-Cell Membranes

The figure illustrates the formation of the CCR5–gp120 complex, which has been proposed as the most crucial

430. The structural model was built using the atomic coordinates deposited in the Protein Data Bank, accession code 6MEO. 6MEO, PROTEIN DATA BANK, https://www.rcsb.org/structure/6MEO [https://perma.cc/B8EV-3NYX]. The cell membrane in the figure was adapted from a figure provided by the WikiJournal of Medicine, Blausen Med., Passive Transport by Diffusion Across a Cell Membrane, WikiJOURNAL MED., https://en.wikiversity.org/wiki/WikiJournal_of_Medicine/Medical_gallery_of_Blausen_Medical_2014#/media/File:Blausen_0213_CellularDiffusion.png [https://perma.cc/RC2X-FDJR], which is licensed under the Creative Commons Attribution-ShareAlike 4.0 International license, Attribution-ShareAlike 4.0 International License, CREATIVE COMMONS, https://creativecommons.org/licenses/by-sa/4.0/legalcode [https://perma.cc/65BG-NRTQ].
The figure also illustrates subsequent HIV-1 viral entry into CD4+ cells—a type of white blood cell bearing surface CD4 glycoproteins that are important for the function of the immune system. When the HIV-1 virion encounters CD4 glycoproteins on the cell surface (not shown), CD4 binds to a region of the gp120 viral protein (orange). The interaction induces conformational changes in a fragment of gp120 called the hypervariable region 3 (V3) loop (bright orange), which assumes a hook-like shape that docks inside the CCR5 (cyan and blue) coreceptor as shown in the figure. This crucial molecular “docking” of the gp120 viral protein to the human CCR5 coreceptor allows the mature HIV-1 envelope spike—comprised of the gp120 protein (orange) and gp41 fusion peptides (not shown)—to undergo further conformational changes that bring the virion closer to the cell membrane, so that the viral and human cell membranes can fuse together. Upon membrane fusion, the virus gains entry into the cell, where it can then replicate.

One important point for purposes of the discussion in this Article is that a small population of humans carries a mutant version of the CCR5 receptor involving deletion of thirty-two base pairs in the CCR5 gene (CCR5Δ32). The CCR5 receptor encoded by this mutant gene generates a truncated and nonfunctional version of the protein that disrupts the manner in which the entire receptor folds and functions in cell membranes. The figure shows the residues (colored in red) that are deleted in the mutant protein. The CCR5 receptor consists of seven integral membrane α-helices (four in cyan and three in dark blue) that are indispensable to maintain the structural integrity of the protein, including the shape of the receptor’s “pocket.” Deletion of the red residues disrupts proper formation of all the dark blue α-helices (5–7), which results in a “pocketless” CCR5 that no longer works. This CCR5Δ32 mutation has been shown to mediate resistance to the HIV-1 virus in humans in part because

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434. See supra note 425.
the gp120 protein cannot bind to the nonfunctional receptor. It is that particular CCR5-altering mutation that He Jiankui attempted to generate in the embryos that lead to the birth of the twin girls in China. But questions loom large as to whether the GGE performed in the embryos led to precise targeting of the CCR5 locus without off-target effects.

world, which highlights the spatial and temporal challenges of defining a “serious disease or condition” that should be addressed via GGE interventions.

The semantic problem of limiting GGE to serious diseases also lies beneath the analytical impetus for the recent Chinese GGE experiments. He Jiankui claimed that he edited the CCR5 gene in human embryos, which led to the birth of twins in China, in order to “show compassion” and help “people in need.” But, as pointed out earlier, there is a legitimate question about the compelling nature of He Jiankui’s experiments given the availability of alternate means to achieve the goal of helping an HIV-positive male conceive children without transmitting the HIV virus, such as the use of antiretroviral drug therapies or low-cost “semen washing” procedures commonly used to reduce HIV transmission in HIV-discordant couples.

Importantly, He Jiankui claimed that he is “against genome editing for enhancement” and that “he would conduct the experiment on his own unborn daughter if she were at risk with HIV infection.” But his experiments underscore the murkiness inherent in drawing clear distinctions between some prophylactic and enhancement GGE interventions.


436. NASEM REPORT, supra note 21, at 7.


439. See Shih & Johnson, supra note 437.
Conferring natural immunity to the HIV virus by deleting a fragment of the CCR5 receptor may, at first glance, appear to fit squarely within the confines of prophylactic intervention under Category 2 experiments because the manipulation is meant to prevent HIV infection upon a future exposure event. However, the CCR5 receptor has recently been implicated in diverse functional roles not related to HIV protection, including cognitive function, enhanced recovery following stroke, and increased susceptibility to the West Nile virus. Accordingly, He Jiankui’s experiments may very well have unintended consequences for the twin girls born from his experiment. Because the biological and physiological functions of the CCR5 receptor are not yet fully elucidated, the CCR5 gene is not a prudent target at this point in time, and He Jiankui could theoretically bear responsibility for latent harms brought on by his genetic manipulation—at least in jurisdictions willing to recognize such causes of action. The same principle applies to other potential targets of prophylactic GGE intervention in polygenic diseases for which genetic mechanisms and molecular pathways are not completely understood, such as obesity, cancer, and diabetes, among others.

The takeaway point is that prophylactic intervention ought to apply only to instances where the desired results match the intended purpose. Safety and efficacy must be clearly established, through empirical scientific evidence, for any molecular targets of GGE. And until researchers understand the molecular basis underlying many

440. Miou Zhou et al., *CCR5 Is a Suppressor for Cortical Plasticity and Hippocampal Learning and Memory*, 5 ELIFE, no. e20985, Dec. 20, 2016, at 1, 2 (reporting a previously unknown role for CCR5 in cognitive function).


444. This is not to say that researchers must know *everything* there is to know about a gene, or DNA target, before certain GGE interventions are allowed to proceed. Such a standard would be impracticable and could stunt scientific progress that seeks to address the evils of human disease and suffering. As with any medical intervention, the decision to perform GGE would involve many factors, including an assessment of the benefits and risks to the child and family.
human diseases and conditions—which will take a substantial amount of time—a robust link cannot exist between intended purpose and actual result in any GGE intervention. Therefore, under a jurisprudence of scientific empiricism, the constitutionally sanctioned assumption that parents can make decisions in the best interests of the child is inapplicable to Category 2 GGE interventions.\textsuperscript{445}

In sum, many GGE applications that fall within the sphere of Category 2 are likely to involve polygenic, as opposed to monogenic, conditions. As a result, the technology is unlikely to be ready for clinical use anytime soon. Thus, premature laws and regulations concerning the sanction or prohibition of GGE prophylactic interventions should be avoided.

\textbf{C. Category 3—Cosmetic or Enhancement Purposes}

The third category of GGE applications relates to interventions for cosmetic or enhancement purposes. Interventions under this category might involve genetic modifications associated with traits such as height, musculature, hair color, intellectual ability, and athletic ability, among others.

The issue here is similar to that in Category 2: Parents may have a constitutional right to bear healthy children, but do they have a constitutional right to bear children with brown hair and green eyes? The scope and authority of state intervention under Category 3 GGE uses may be stronger than those in Category 2. But this is not to say that all cosmetic or enhancement GGE applications should be prohibited. After all, parents can lawfully submit their children to cosmetic procedures—e.g., rhinoplasty, polydactyly reconstructive surgery, among others—without violating the Constitution.\textsuperscript{446}

\textsuperscript{445} See Parham v. J.R., 442 U.S. 584, 604 (1979) (noting that “the traditional presumption that the parents act in the best interests of their child should apply” absent evidence of neglect or abuse).

\textsuperscript{446} One notable distinction here is that parents who subject their children to some types of cosmetic surgeries will—depending on the child’s age at the time of the procedure—receive input from the child as to whether to go forward with said surgery, even when the parents are the ultimate decisionmakers. In contrast, parents who perform GGE on their embryos are purportedly the sole and final arbiters. This distinction, in a way, strengthens the legal basis for therapeutic GGE under \textit{Parham} and \textit{Yoder} when compared to cosmetic or enhancement GGE interventions. Parental autonomy in matters of child rearing, which includes the decision to subject a child to cosmetic reconstructive surgery, is fairly broad even if “not agreeable to the child.” See \textit{id.} at 603. An individual likely could grow up wishing her parents did not choose green eyes or a broad nose for her, but she is unlikely to grow up and decide that she would prefer her parents did nothing to correct a deleterious mutation that would lead to life-threatening disease. Implied consent is almost embedded
Assuming that GGE procedures for cosmetic or enhancement purposes could be performed safely and effectively at the molecular level, the issue then becomes whether or not such procedures should be treated differently merely because they are done at an embryonic stage.

Consider traits associated with obesity, smaller breast size, or baldness. Today, individuals may elect to undergo surgical procedures—such as gastric bypass surgery, abdominoplasty (tummy tuck), breast augmentation, or hair transplantation—to alter their physical appearance and improve self-image. If an individual carries certain alleles that predispose her to developing any of those traits—which are at least partly heritable—and wishes to perform GGE to reduce the likelihood of passing those alleles to her offspring, should the law be concerned with such types of GGE interventions? Assuming that safety and efficacy are not part of the equation, reasonable people may disagree about the answer to that question depending on a multitude of factors, including financial, egalitarian, ethical, and moral considerations.

In any event, as laid out in Section III.B, time currently favors the creation of a rational and robust legal approach to GGE concerning Categories 2 and 3. Because not all prophylactic, cosmetic, and enhancement concerns for GGE uses are scientifically based and their development is not technologically feasible at this time—and perhaps may not be even in the near future—premature laws and in a decision to perform therapeutic GGE intervention. Thus, the doctrine of parental autonomy and the presumption that parents generally “act in their child’s best interest” collectively strengthen the rationale for therapeutic GGE in cases where scientific evidence exists to establish the safety and efficacy of the desired genetic modification. See id. at 602–03.

447. See, e.g., Nicola Pirastu et al., GWAS for Male-Pattern Baldness Identifies 71 Susceptibility Loci Explaining 38% of the Risk, 8 NATURE COMM., no. 1584, Nov. 17, 2017, at 1, 7 (reporting data that suggests baldness is among the most heritable complex traits); Tracey D. Wade, Gu Zhu & Nicholas G. Martin, Body Mass Index and Breast Size in Women: Same or Different Genes?, 13 TWIN RES. & HUM. GENETICS 450, 450 (2010) (finding breast size is moderately heritable).

448. See, e.g., Enríquez, supra note 2, at 679–85 (providing a detailed outline of the current state of empirical scientific knowledge vis-à-vis the molecular and genetic basis of human intelligence and cognition to highlight the inherent complexity of polygenic traits and contrast it to widespread public misperceptions about genetic associations in trait formation and development); see also Hana Lango Allen et al., Hundreds of Variants Clustered in Genomic Loci and Biological Pathways Affect Human Height, 467 NATURE 832, 832 (2010) (reporting the existence of at least 180 genetic variants that influence height in humans).
regulations concerning the authorization or prohibition of Category 3 GGE interventions should also be avoided.

D. Category 4—Discrimination Already Prohibited by the Law

The last category of GGE applications concerns the potential modification of traits that raise concerns of discrimination already prohibited by the law. Like many of the traits that fall under Categories 2 and 3 of the proposed framework, Category 4 traits are unlikely to be within the realm of clinical possibility in the near future. Nevertheless, a special history of discrimination—against race, gender, sexual orientation, specific disabilities, etc.—counsels against sanctioning modifications of the genetic composition of germ cells related to these traits, regardless of whether or not it ever becomes possible to alter them. Because these traits create a likelihood of discrimination against specific groups, there is little to no constitutional justification to pursue GGE interventions in this realm.

Clear lines should be drawn to make Category 4 GGE uses unpalatable to perform in the clinical setting. And the Supreme Court’s equal protection and due process jurisprudence can serve as a robust guide that justifies prohibition of GGE interventions intended to modify traits that raise concerns of discrimination.

449. See supra Sections III.B–C.
450. Current legislation and jurisprudence interpreting the Americans with Disabilities Act of 1990 might be used to inform what qualifies as a disability that ought to be shielded from GGE interventions. See 42 U.S.C. §§ 12101–12102 (2012).
451. Although some of these traits cannot currently be engineered, they are routinely selected for or against using modern reproductive technologies without violating any laws. For instance, couples have been free to select the gender of embryos through IVF and PGD for decades. The same is true for parents who are deaf or have achondroplasia and other forms of dwarfism. Sexual orientation, on the other hand, is not a trait that can be screened for because a definitive genetic basis for it—if one even exists—has not been established. Regarding race, humans have selected and continue to select for this trait in offspring indirectly by choosing a mate who fits particular preferences.
Selection of all these traits using IVF and PGD is drastically different from modification of the same traits via GGE technologies. The former merely selects an already existing embryo that naturally features all the desired traits, whereas the latter would involve genetic engineering to modify nucleotides in an embryo’s genome with the intent that such manipulation would give rise to desired phenotypic characteristics. Genetic engineering of such complex polygenic traits is unlikely to be possible at this point in time, not merely because the technology is not yet capable of producing the intended result but simply because we do not know enough about the genetic basis underlying most of these traits.
452. The Supreme Court has at times invoked due process and equal protection principles to strike down precedents and laws that targeted some minorities and disadvantaged groups. See, e.g., Bowers v. Hardwick, 478 U.S. 186, 196 (1986) (upholding
As examined in this Article, therapeutic (Category 1) GGE interventions (yellow) are likely protected under the
Constitution and, thus, would be the most accessible to parents if GGE safety and efficacy are established. Governmental interference aimed at restricting access to these types of GGE interventions would need to pass the strict scrutiny test. At the top of the spectrum are potential GGE interventions that raise concerns of discrimination that is already prohibited by the law (Category 4) (red), which are almost certainly not protected as a fundamental right. Governmental action aimed at restricting Category 4 GGE interventions would merely need to pass a rational basis test. Thus, Category 4 GGE interventions could easily be restricted by the government. The figure shows select examples of each category and highlights the murkiness inherent in drawing clear distinctions between some prophylactic (Category 2) and cosmetic/enhancement (Category 3) GGE interventions, as in the case of obesity.

Consider the issue of race, which is inextricably linked to eugenics.\textsuperscript{453} Due to the sensitive history of racial discrimination and systemic racial inequalities in the United States—as well as abroad—it would be unwise to allow parents to edit genetic sequences associated with changing an embryo’s race—even if it were ever technologically feasible to do so. This principle would apply to cases in which parents of a majority group wish to bear offspring of a racial minority group and vice-versa.\textsuperscript{454} Government restrictions on these types of GGE interventions would almost certainly pass rational basis review because a legitimate government interest likely exists in avoiding the institutionalization of race-conscious reproductive policies that could lead to discrimination against select discrete and insular groups. Simply put, it is hard conceive any constitutional justification to endorse the use of GGE interventions to edit an embryo’s race.

Under the same reasoning, the Constitution would likewise not permit parents to use GGE methods to “edit out” a preexisting disability in a zygote or embryo, particularly because alternative means


\textsuperscript{454} Suppose that, in order to save their offspring from what some may consider social “disabilities” rooted in racial inequality and injustice, \textit{see generally} Kimani Paul-Emile, \textit{Blackness as Disability?}, 106 GEO. L.J. 293 (2018) (arguing it may be appropriate to think of being black as disabling in the United States), some minority parents choose to bear offspring with features that resemble a racial majority group. Government endorsement of such GGE purposes could lead to pervasive abuses and discriminatory practices that go far beyond the limits of a putative fundamental right to perform GGE articulated earlier in this Article.
currently exist—e.g., abortion and PGD—to achieve the ultimate result of not having disabled offspring. Although some might argue that removing a disability from an embryo’s genome has a therapeutic purpose, the history of discrimination against particular disabilities embedded in our culture cautions against that proposition. The analysis would change, however, if both parents bear genes that all but guarantee their offspring will be born with a disability. Under that scenario the parents lack alternative means to achieve their goal of bearing a child without a disability and, thus, could challenge GGE prohibitions under a strict scrutiny standard.

By the same token, parents should not be allowed to “edit in” disabilities into their embryos. Although members of specific groups with disabilities may sometimes wish to procreate and bear a child who shares their disability—e.g., blindness, deafness, etc.—society ought not endorse bestowing a disability upon human embryos. And the law ought not be used for such purposes either. Under this scenario, the disabled parents would also have alternative means to select, screen, or discard embryos bearing desirable traits.

In sum, our equal protection and due process jurisprudence supports drawing a line that prohibits individuals to either edit in or edit out traits associated with discrimination already prohibited by the law.\textsuperscript{455} Government restrictions on the use of GGE for Category 4 purposes—assuming they will ever become technologically feasible to perform—should be examined under a rational basis standard of review, which only require the government to articulate a legitimate purpose. The proposed framework under Category 4 aims to take eugenics out of the GGE equation. In so doing, it reduces the likelihood that eugenics and “designer babies” will pollute decisionmaking in the GGE context, which would ultimately promote fruitful dialogue and debate about the benefits and risks of availing humanity of the use of technologies for genome editing.\textsuperscript{456}

\textbf{CONCLUSION}

The advent of genome editing has made it possible for scientists to genetically modify the human germline in ways that were previously unimaginable. Each passing day, researchers continue to develop and

\textsuperscript{455} Cf. Ossareh, supra note 38, at 766 (“[T]here may be strong ethical motivations to limit certain types of modifications. However, in most cases, there is no principled legal reason to ban or restrict access to genetic modification . . . .”). In contrast, this Article demonstrates that existing jurisprudence can guide the conception of limits on a putative right to GGE interventions.

\textsuperscript{456} See Enríquez, supra note 2, at 613, 694.
refine the tools that are steadily inching humankind closer and closer to unlocking the powers of GGE, which will undoubtedly define the course human history. Today’s technological improvements aimed at establishing the safety and efficacy of genome editing will usher in tomorrow’s era of translational genome editing.

Despite the accrual of steady scientific advances, however, significant questions loom on the horizon concerning how interventions aimed at GGE should be treated under the law. News about the birth of the first gene-edited babies in China in November 2018 underscored the urgency with which the world needs to address the issue of germline interventions. The experiments performed to edit human embryos intended for implantation in a woman’s uterus were “irresponsible and failed to conform with international norms.” David Baltimore, the committee chair for the Second International Summit on Human Genome Editing, decried the “failure of self-regulation in the scientific community.” Admittedly, scientists have failed to preempt premature use of the technology despite international efforts to build principles of governance for human genome editing. Unfortunately, the shortcomings of self-regulation are not limited to a particular field of science and technology.

Within a cloud of uncertainty surrounding GGE, this Article marks a step toward bringing clarity to an emerging area of the law. In so doing, it examines the legality of GGE from administrative and constitutional law perspectives. The Article argues that the FDA is well positioned to regulate germline clinical interventions and proposed a new regulatory paradigm stemming from the D.C. Circuit’s ruling in United States v. Regenerative Sciences, LLC, which held that specific stem cell mixtures can be regulated as drugs or biological products within the meaning of the FDCA and the PHSA. Accordingly,


458. See Shih & Johnson, supra note 437.

legislative bans on GGE technologies are unnecessary and create more social costs than benefits.

The current temporary ban on clinical applications of GGE is likely unconstitutional because it infringes on a cognizable fundamental right to perform select uses of GGE under equal protection and substantive due process principles related to procreation, parental autonomy, and—to some extent—privacy rights. Such a fundamental right, however, is not without limits and the Article proposed a normative framework that considers various potential uses of GGE that are likely to materialize once safety and efficacy of the technology are established.

The time to create a legal blueprint for the future of GGE has come. This Article seeks to ignite a scholarly dialogue among lawyers and scientists and, more importantly, contribute to increasing public education and engagement of issues raised by scientific advances in GGE.460 Robust and substantive discussions among lawyers, scientists, policymakers, and the public are more important than ever in this watershed era of GGE.

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460. See Enríquez, supra note 2, at 694; Paul Enríquez, Correspondence, GM-Food Regulations: Engage the Public, 548 NATURE 31, 31 (2017).