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THE ART OF REGULATING ART

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INTRODUCTION

Technology now makes it possible not only to test the genes in human embryos through pre-implantation genetic testing (PGT) but also to edit them. While PGT is not regulated in the United States, other countries impose limitations on its use. In contrast to PGT, germline gene editing ("GGE") is banned in the United States and subject to varying levels of regulation in other countries. The two technologies are similar in allowing for the selection of specific traits in the resulting offspring, although they differ in many other respects.

This article examines the two technologies and explores the differing approaches to the regulation of PGT and GGE. The regulatory issues sweep quite broadly. They involve not just the medical risks, which are relatively straightforward, but also broader social concerns about access to the technologies, equality and discrimination, implications for the disability community, eugenics, and exceptionalizing assisted reproductive technologies ("ART") as compared with non-ART reproduction.

We explore the potential regulatory approaches that might be used for PGT and GGE, noting the benefits and limits of each approach. While conceding some differences in the two technologies, we argue that PGT, GGE, and other forms of ART should be regulated together. We suggest potential regulatory models that might be used, including a revamping of the FDA or the creation of a new regulatory entity altogether. We conclude by recognizing the particularly challenging aspects of such regulation, which raise constitutional and normative issues, including the relationship between such regulation and contested political issues relating to equality, disability rights, distinctions between reproduction in and outside the bedroom, and the imposition of majoritarian values on deeply personal decisions.

I. THE SCIENCE

To set the stage for understanding the regulation of these technologies, we begin with an overview of PGT and genetic modification, placing them in the context of ongoing developments in reproductive technology.

PGT, the newer of the two technologies, involves genetic analysis of embryos created by in vitro fertilization ("IVF") so that a prospective parent can learn about the child's genetic composition. It developed as an

alternative to prenatal genetic testing and termination as a mechanism to avoid disease in future children.[1]

In contrast, genetic manipulation, which is almost fifty years old,[2] involves active efforts to change an individual's genetic makeup. Not surprisingly, the technology used to modify the human genome has evolved considerably in the last several decades. Initially, scientists tried to use viruses or retroviruses (viruses that use RNA rather than DNA) as vectors to carry and insert DNA fragments into patients (either directly or via extracted cells that would be reintroduced to the patient). For some time, researchers struggled to achieve success with the technology and to ensure that the DNA was inserted into the right part of the genome to avoid disruption to other genes.[3] Finally, in 2017, the FDA approved the "first directly administered gene therapy . . . that targets a disease caused by mutations in a specific gene" to treat a heritable form of vision loss.[4]

In the meantime, researchers explored other methods to alter genes, including special proteins called zinc finger nucleases ("ZFNs") and transcription activator-like effector nucleases ("TALENs") that cut targeted areas of the genome. While this method of gene editing is precise, it is also

1. Sonia M. Suter, *The Tyranny of Choice: Reproductive Selection in the Future*, 5 J.L. & BIOSCIENCES 262, 264 (2018) [hereinafter "Suter, *Tyranny of Choice*"] ("However, it is possible for PGT to be used by prospective parents to select characteristics of their children beyond those linked with serious immediate health concerns."); Susannah Baruch, J.D., *Preimplantation Genetic Diagnosis and Parental Preferences: Beyond Deadly Disease*, 8 HOUS. J. HEALTH L. & POL'Y 245, 245–46 (2008).

2. Dana Caroll, *Gene Editing: Past, Present, and Future*, 521 YALE J. BIOLOGICAL MED. 653 (2017) (describing the first targeted genomic changes in yeast and mice in the 1970s and 1980s). Until recently, this technology was called preimplantation genetic diagnosis (PGD) because it analyzed embryos for specific genetic diseases when a family history increased the risk of those conditions. Over time, fertility clinics also began to offer preimplantation genetic screening (PGS), a process that screens embryos for chromosomal anomalies. In 2017, "preimplantation genetic screening (PGS) and diagnosis (PGD) were re-termed preimplantation genetic testing (PGT)." Santiago Munné, *Status of Preimplantation Genetic Testing and Embryo Selection*, 37 RBMO 393, 393 (2018). When PGT is used to test embryos for monogenic (single gene) disorders, like Tay Sachs or sickle cell anemia, it is called PGT-M. And when it tests embryos for chromosomal anomalies, it is called PGT-A. The vast majority (90%) of PGT today is PGT-A, and it is offered not only to women of advanced maternal age or with a history of recurrent miscarriages, but also "to improve the selection of embryos with the most potential to implant and produce a viable pregnancy." *Id.*

3. One of the early successes in gene therapy resulted in the treatment of several babies with severe combined immune deficiency in France. Tragically, however, some developed leukemia just a few years later because the inserted DNA activated a cancer gene. *See* MAXWELL J. MEHLMAN, MARK A. ROTHSTEIN, AND SONIA M. SUTER, GENETICS: ETHICS, LAW AND POLICY 241–301 (5th ed. 2020) [hereinafter G&L 5th] (describing the initial research on gene therapy). Another tragedy occurred when a gene therapy experiment took the life of Jesse Gelsinger in 1999. The 18-year-old had suffered from a genetic condition that affected his ability to metabolize ammonia. *See id.*; Sheryl G. Stolberg, *The BioTech Death of Jesse Gelsinger*, N.Y. TIMES, SUN. MAG., Nov. 28, 1999, at 137.

4. FDA News Release, *FDA Approves Novel Gene Therapy to Treat Patients with a Rare Form of Inherited Vision Loss,* FDA (Dec. 18, 2017), https://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss [https://perma.cc/P8UJ-4NZA].

costly, time-consuming, and technologically challenging to engineer the proteins that target the genes.[5] The discovery of CRISPR (clustered regularly interspersed palindromic repeats)/Cas9 in 2012 overcame these limitations by using RNA, rather than proteins, to guide the Cas9 nuclease to the targeted part of the genome to be edited.[6]

CRISPR-Cas9 has revolutionized genome editing in both humans and nonhuman animals.[7] Not only is it faster, more efficient, and cheaper than prior gene editing techniques, it also has the potential for a wide range of applications.[8] The technique allows researchers to create permanent edits to the genome[9] by targeted insertions or deletions of nucleotides on any section of the DNA molecule to modify a specific gene.[10] As a result, it allows physicians and scientists to change and "fix" an organism's DNA by altering genetic material at specific locations in the genome.

Notwithstanding its increasing utility, CRISPR-Cas9 is still somewhat risky and may result in off-target mutations. Unintended mutations can either disrupt gene expression entirely or cause the gene to function improperly,[11] as occurred with earlier gene therapy experiments.[12] With off-target

5. See NAT'L ACADS. SCIS. ENG'G MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, & GOVERNANCE 64 (2017) [hereinafter Nat'l Acads., *Human Genome Editing*]. ZFNs have been used in promising clinical trials to treat a genetic condition called Hunter syndrome. Heidi Ledford, *First Test of In-Body Gene Editing Shows Promise*, NATURE (Sept. 5, 2018), https://www.nature.com/articles/d41586-018-06195-6 [https://perma.cc/EVP2-YYXR].

6. Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 65.

7. "CRISPR-Cas9 was adapted from a naturally occurring genome editing system in bacteria. The bacteria capture snippets of DNA from invading viruses and use them to create DNA segments known as CRISPR arrays. . . . The bacteria then use Cas9 or a similar enzyme to cut the DNA apart, which disables the virus." *What Are Genome Editing and CRISPR-Cas9?*, NAT'L INST. OF HEALTH, https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting[https://perma.cc/SQ2B-2NKZ] (last visited Nov. 17, 2020).

8. Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 65 (noting its applications in "biotechnology, agriculture, insect control, and gene therapy").

9. DNA, of course, is the basic molecule that is "the hereditary material in all living cells," and consists of double helix strands. *DNA*, GENOME NEWS NETWORK, http://www.genomenewsnetwork.org/resources/whats_a_genome/Chp1_4_1.shtml [https://perma.cc/5US3-ZW2Z] (last visited Nov. 13, 2020). DNA is composed of smaller units—nucleotides—that are "strung together in a row." *Id.* Genes are composed of varying lengths of DNA that code for one protein; a protein is the building block of muscles and tissues, and it also produces enzymes, which carry out chemical processes in the body. The twenty-three pairs of chromosomes that each human has are composed of tens of thousands of genes. Finally, the genome is an organism's complete DNA. *See Mapping the Genome*, THE IFOD: THE INTERESTING FACT OF THE DAY BLOG (Aug. 30, 2017), https://www.theifod.com/mapping-the-genome/ [https://perma.cc/FJ2V-43Y5].

10. Hannah R. Kempton & Lei S. Qi, *When Genome Editing Goes Off-Target*, 364 SCI. 234 (2019).

11. Kendall Lovell, Note, *Crispr/Cas9 Technologies: A Call for A New Form of Tort,* 19 SAN DIEGO INT'L L.J. 407, 412 (2018).

12. This is where gene therapy went wrong, with some of the trials to treat a heritable form of immune deficiency resulting in leukemia in some of the children. *See supra* note 3; Sonia M. Suter, *The "Repugnance" Lens of* Gonzales v. Carhart *and Other Theories of Reproductive Rights: Evaluating Advanced Reproductive Technologies*, 76 GEO. WASH. L. REV 1514, 1538 (2008) [hereinafter "Suter,

mutations, the edits could occur within the wrong part of the gene (or regulatory components of the gene) or outside of the gene, potentially in other genes. Because such off-target mutations have unintended consequences (for both research and clinical applications), scientists are developing different techniques to evaluate when the technology goes "off-target" and makes a modification other than in the targeted gene.[13] There are other risks as well.[14]

Nonetheless, CRISPR-Cas9 has multiple uses in addition to its role in basic research in disease prevention. It is useful for the prevention or treatment of disease by treating somatic cells (such as skin, liver, lung, heart cells, and blood), which affect only the individual involved and are not involved in reproduction.[15] And, it has the potential to prevent disease by editing reproductive, or germ, cells[16] (sperm and eggs in humans), which impact not just the resulting baby, but also may affect that baby's future offspring.[17] Whether used in somatic or germ cells, the technology thus may prove helpful in treating various illnesses, such as sickle cell disease, cystic fibrosis, blood disorders, heart disease, HIV/AIDS, and even several forms of cancer.[18] Indeed, clinical trials in the United States are underway, with

Repugnance Lens"]; Donald B. Kohn et al., *Occurrence of Leukaemia Following Gene Therapy Leukaemia Following Gene Therapy of X-Linked SCID*, 3 NAT. REV. CANCER 877 (2003).

13. Kempton & Qi, *supra* note 10; Beeke Wienert et al., *Unbiased Detection of CRISPR Off-Targets In Vivo Using DISCOVER-Seq*, 364 SCI. 286 (2019).

14. Additional harms include "the inappropriate activation of cancer-causing genes, and the rearrangement of chromosomes. Additionally, there are the risks of on-target changes with unintended consequences, the creation of mosaics of altered and unaltered cells, and the introduction of changes that generate an immune response. In addition to these potential medical harms, there are also potential social harms." Françoise Baylis, *Counterpoint: The Potential Harms of Human Gene Editing Using CRISPR-Cas9*, 64 CLINICAL CHEMISTRY 489 (2018). For further discussion of off-target" effects, *see* Adam P. Cribbs & Sumeth M.W. Perera, *Science and Bioethics of CRISPR-Cas9 Gene Editing: An Analysis Towards Separating Facts and Fiction*, 90 YALE J. BIOLOGICAL MED. 625 (2017); *see also* Katherine Drabiak, *Untangling the Promises of Human Genome Editing*, 46 J. L. & MED. & ETHICS 991 (2018) (noting the technology's risks and raising questions about its efficiency).

15. Mildred Z. Solomon, *Gene Editing Humans: It's Not Just About Safety*, SCI. AM. (Aug. 20, 2019), https://blogs.scientificamerican.com/observations/gene-editing-humans-its-not-just-about-safety/ [https://perma.cc/VLN9-ATP6].

16. Germ cells then constitute the germline.

17. Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 111–12*;* Solomon, *supra* note 15.

18. Grant Hayes Frazier, *Defusing A Ticking Time Bomb: The Complicated Considerations Underlying Compulsory Human Genetic Editing*, 10 HASTINGS SCI. & TECH. L.J. 39, 40–41 (2019). For example, CRISPR-Cas9 technology somatic clinical trials are permitted, and the number of such trials is proliferating. *See, e.g.*, Tina Hesman Saey, *CRISPR Enters its First Human Clinical Trials*, SCIENCENEWS (Aug. 14, 2019), https://www.sciencenews.org/article/crispr-gene-editor-first-human-clinical-trials [https://perma.cc/RTD5-SNLP] (discussing trial for individuals with an inherited blindness, which subjects are initially injected with small amounts of the CRISPR editor to see how their retina responds and to test for safety). Such technology may also be useful for food production and biofuels. *See, e.g.*, Stephen S. Hall, C*risprCan Speed Up Nature–And Change How We Grow Food*, WIRED (July 17, 2018), https://www.wired.com/story/crispr-tomato-mutant-future-of-food/ [https://perma.cc/KVG4-UK3B] (noting that gene-edited potatoes have already been planted).

CRISPR-Cas9 being used, for example, in somatic cells for cancer treatments.[19] Moreover, the use of CRISPR-Cas9 for GGE is moving forward. Indeed, scientists reported in 2017 that they used CRISPR-Cas9 in embryos to excise a mutated DNA sequence that causes cardiomyopathy, a disease that leads to heart failure.[20] This was not a clinical experiment, however. Although the edited embryos were not implanted, this experiment shows the technology's possibilities.

Based on the success of such research, GGE is likely to be available, regardless of legal regulation or prohibitions in the United States, whether through a black market or through fertility tourism.[21] It is, however, premature to predict whether it will be widespread or of any practical utility, much less capable of conferring genetic enhancements.[22]

GGE and PGT are just two of the many developments in reproductive technologies. We predict that the next few decades will bring ever-increasingly sophisticated forms of genetic technologies that affect the germline.[23]

19. *E.g.*, Kat Eschner, *CRISPR is Now Being Used on Humans in the U.S.*, POPULAR SCI. (Apr. 17, 2019); *On Human Genome Editing II: Statement by the Organizing Committee of the Second International Summit on Human Genome Editing*, https://www.popsci.com/crispr-cancer-immunotherapy-pennsylvania/ [https://perma.cc/C4X9-GFD7]; NAT'L ACADS. SCIS. ENG'G MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, & GOVERNANCE 92–93 (Table 4-1) (Nov. 29, 2018) [hereinafter "Nat'l Acads., *Summit*"]; Lila Thulin, *Four U.S. CRISPR Trials Editing Human DNA to Research New Treatments*, SMITHSONIAN (Sept. 3, 2019), https://www.smithsonianmag.com/science-nature/four-us-crispr-trials-editing-human-dna-for-new-medical-treatments-180973029/ [https://perma.cc/98RG-5YAU]. These clinical trials in cancer research suggest gene editing seems safe. Shaoni Bhattacharya, *Genome Editing Seems Safe Suggests First Study in US Patients*, BIONEWS (Nov. 11, 2019), https://www.bionews.org.uk/page_146147 [https://perma.cc/H4FW-RJ6K].

20. Pam Belluck, *In Breakthrough, Scientists Edit a Dangerous Mutation from Genes in Human Embryos*, N.Y. TIMES (Aug. 2, 2017), https://www.nytimes.com/2017/08/02/science/gene-editing-human-embryos.html [https://perma.cc/J3FY-RJTF].

21. The Second International Summit on Human Genome Editing, held in 2018, recognized the risks in permitting germline editing, but also noted that "[p]rogress over the last three years and the discussions at the current summit, however, suggest that it is time to define a rigorous, responsible translational pathway toward such trials." Nat'l Acads, *Summit*, *supra* note 19. To be sure, scientists have repeatedly called for a moratorium, while others advise planning for responsible use. *See, e.g.*, Heidi Ledford, *CRISPR Babies: When Will the World Be Ready*?, NATURE (June 19, 2019), https://www.nature.com/articles/d41586-019-01906-z [https://perma.cc/X93Q-2VK3]; Eric S. Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, NATURE (Mar. 13, 2019), https://www.nature.com/articles/d41586-019-00726-5 [https://perma.cc/A6A5-SK5L]; Landon J. Getz & Graham Dellaire, *Moratorium on Human Genome Editing: Time to Get it Right,* HASTINGS CTR. (Mar. 29, 2019), https://www.thehastingscenter.org/moratorium-on-human-genome-editing-time-to-get-it-right/ [https://perma.cc/JDV2-CUVN]; *but see* Eli Y. Adashi & I. Glenn Cohen, *Heritable Genome Editing: Is a Moratorium Needed?*, 332 JAMA 104 (2019).

22. Hank Greely, *Human Germline Genome Editing: An Assessment*, 2 CRISPR J. 253 (2019).

23. *See* Sonia M. Suter, *In Vitro Gametogenesis: Just Another Way to Have a Baby?*, 3 J. L. & BIOSCIENCES 87 (2016) [hereinafter Suter, *IVG*] (describing the theoretical possibility of using IVG for human reproduction); I. Glenn Cohen et al., *Transatlantic Lessons in Regulation of Mitochondrial Replacement Therapy*, 348 SCI. 178 (2015) [hereinafter Cohen, *Transatlantic Regulation*] (comparing the regulation of mitochondrial replacement therapy in the US and UK); César Palacios-González, *A Third*

II. ETHICAL/SOCIAL CONCERNS REGARDING GGE AND PGT

Genetic modifications, whether through CRISPR-Cas9 or other technologies, are relatively uncontroversial when used to treat disease and when they affect only the specific individual involved. The National Academy of Sciences concluded in 2017 that "basic research involving both somatic and germline cells is essential to the advancement of science and should continue with existing regulatory structures."[24] When used to affect reproductive material, especially for clinical purposes, however, it is particularly controversial.[25] And although PGT is increasingly used in the context of infertility treatment or when individuals are at risk for passing on heritable genetic conditions,[26] it is not without its opponents.

Critics have raised objections against both GGE and PGT. Some find the technologies per se problematic. For example, the "hubris" criticism views GGE or PGT as transgressing ethical boundaries by interfering in life creation.[27] Most objections are not that the technologies are per se problematic, however.[28] Indeed, many point out their potential to prevent

MRT-Baby is on the Way, PRACTICAL ETHICS (Jan. 22, 2019), http://www.bioethics.net/2019/01/a-third-mrt-baby-is-on-its-way/ [https://perma.cc/X6Q9-HPP3] (describing the third conception of a child by mitochondrial replacement therapy).

24. Nat'l Acads., *Human Genome Editing*, *supra* note 5, at II. With respect to the second category, the Committee did conclude that somatic "genome editing for purposes other than treatment or prevention of disease and disability should not proceed at this time." *Id.* Yet "perhaps the theoretically sharp distinction between germline modification and somatic cell editing is somewhat idealistic." Alexandra L. Foulkes et al., *Legal and Ethical Implications of CRISPR Applications in Psychiatry*, 97 N.C. L. Rev. 1359, 1394 (2019). An alternative means of classifying gene editing is by function, such as whether it is "therapeutic," designed to treat or prevent diseases, "or enhancement and heritability involving somatic or germline cells." Cribbs & Perera, *supra* note 14, at 629.

25. It is also controversial when it comes to enhancing somatic cells. *See, e.g.*, KERRY LYNN MACINTOSH, ENHANCED BEINGS: HUMAN GERMLINE MODIFICATION AND THE LAW (2018) (discussing some of the main objections). At a global level, the World Health Organization observed "it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing." *Statement on Governance and Oversight of Human Genome Editing* WORLD HEALTH ORGANIZATION (July 26, 2019), https://www.who.int/news-room/detail/26-07-2019-statement-on-governance-and-oversight-of-human-genome-editing [https://perma.cc/8BGM-FEQG]. On the other hand, "perhaps the theoretically sharp distinction between germline modification and somatic cell editing is somewhat idealistic." Foulkes, *supra* note 24, at 1394. Even the alternative means of classifying gene editing by function, such as whether it is "therapeutic," designed to "treat or prevent diseases or enhancement and heritability involving somatic or germline cells," Cribbs & Perera, *supra* note 14, at 629, may draw an untenable line, as discussed *infra*.

26. Sigal Klipstein, *Preimplantation Genetic Diagnosis: Technological Promises and Ethical Perils*, 83 FERTILITY & STERILITY 1347, 1348 (2005).

27. MACINTOSH, *supra* note 25, at 30–38; Rick Weiss, *Building a New Child*, WASH POST (June , 30, 2001), https://www.washingtonpost.com/archive/politics/2001/06/30/building-a-new-child/11adfcea-d3cb-4492-91d4-106bac66c054/ [https://perma.cc/HQ6L-933W] (some describe PGT as "a tool for human hubris.").

28. *See* Rosalind Scott & Stephen Wilkinson, *Germline Genetic Modification and Identity: The Mitochondrial and Nuclear Genomes*, 37 OXFORD J. LEGAL STUD., 886, 909 (2017) (noting that there '"[i]s not in general anything morally troubling about altering qualitative identity" through GGE).

disease and suffering.[29] Instead, the objections are that they have problematic consequential effects in certain contexts.[30]

The consequentialist concerns range from the fear of "designer babies" to concerns about the riskiness of the technologies, with some worries especially heightened for GGE. They include: (1) "the manufacture objection": that GGE or PGT will be used to "improve" or "perfect" reproduction by designing or selecting embryos to produce babies with specific qualities, such as enhanced intelligence[31] or in some cases, without disabilities like hearing loss or dwarfism;[32] (2) "the stratification objection": that these technologies will exacerbate economic inequality, with serious concerns about equitable access to editing therapies or PGT;[33] (3) "the disability critique": that, using GGE and PGT to avoid having children with

29. Christopher Gyngell et al., *Moral Reasons to Edit the Human Genome: Picking Up from the Nuffield Report*, 45 J. MED. ETHICS 514, 517 (2019) (GGE); Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 120–121, 123–124 (GGE); Suter, *IVG*, *supra* note 23, at 115 (PGT); Klipstein, *supra* note 26, at 1349.

30. *See* MACINTOSH, *supra* note 25 (contextualizing the objections); Sonia M. Suter, *A Brave New World of Designer Babies?,* 22 BERK. TECH. L.J. 897 (2007) [hereinafter Suter, *Brave New World*] (noting the importance of context); Suter, *Tyranny of Choice*, *supra* note 1, at 270.

31. MACINTOSH, *supra* note 25, at 39–47 (describing this objection with respect to GGE); Jackie L. Scully, *Choice, Chance, and Acceptance, in* HUMAN FLOURISHING IN AN AGE OF GENE EDITING 143, 150 (Erik Parens & Josephine Johnston eds., 2019) (arguing that "reproductive control needs to be carefully and constantly (self-) limited . . . because it's *wrong for an adult to behave like that* . . . . Too much control risks compromising a fundamental feature of parenthood, one that parents benefit from as much as the future child."); Suter, *Tyranny of Choice*, *supra* note 1, at 270 (describing this objection with respect to PGT); Klipstein, *supra* note 26, at 1348–49 (PGT). Philosopher Michael Sandel identified the danger of "hyperagency—a Promethian aspiration to remake nature . . . to serve our purposes and satisfy our desires," which includes these first two objections. Michael J. Sandel, *The Case Against Perfection*, ATLANTIC (Apr. 2004), https://www.theatlantic.com/magazine/archive/2004/04/the-case-against-perfection/302927/ [https://perma.cc/3Y75-XS96]. Of course, the "dividing line between prevention of disease or disability and the improvement or enhancement of physical and mental traits is not always very clear." Maartje Schermer, *Reprogenetic Technologies Between Private Choice and Public Good*, *in* HUMAN FLOURISHING IN AN AGE OF GENE EDITING, 212, 220 (Erik Parens & Josephine Johnston eds., 2019). *See also* Nicole A. Vincent & Emma A. Jane, *Parental Responsibility and Gene Editing,* in HUMAN FLOURISHING, *supra*, at 120; Drabiak, *supra* note 14, at 991 (expressing skepticism about the rhetoric of treatment).

32. Kalena R. Kettering, Note, "*Is Down Always Out?": The Right of Icelandic Parents to Use Preimplantation Genetic Diagnosis to Select for a Disability*, 51 GEO. WASH. INT'L L. REV. 1, 7 (2020) (describing the view of some future parents that certain traits, like deafness or achondroplasia are not "defects" or disabilities, but instead are "defining characteristics of a community" or culture).

33. Laura Hercher & Anya E.R. Prince, *Gene Therapy's Field of Dreams: If You Build It, Will We Pay?*, 97 N.C. L. REV. 1463, 1464 (2019) (describing concerns generally about equitable access to therapeutic genetic editing generally); *Genetically Modified Humans? Seven Reasons to Say "No,"* BIOPOLITICAL TIMES (May 7, 2015), https://www.geneticsandsociety.org/biopolitical-times/genetically-modified-humans-seven-reasons-say-no [https://perma.cc/YLB6-MEZB] [hereinafter Centers for Genetics and Society] (describing this objection with respect to GGE); The President's Council on Bioethics*, Chapter Three: Screening and Selection for Genetic Conditions and Traits,* in REPRODUCTION AND RESPONSIBILITY: THE REGULATION OF NEW BIOTECHNOLOGIES 89–103, (2004), *available at* https://bioethicsarchive.georgetown.edu/pcbe/reports/reproductionandresponsibility/chapter3.html [https://perma.cc/5JPH-ASES] [hereinafter The President's Council].

disabilities diminishes and fosters discrimination against individuals with disabilities;[34] (4) the embryo-risk problem: that because genetic manipulation of embryos is dangerous, it may destroy embryos or create unintended harms in the future children;[35] (5) "the threats to the gene pool objection": that, decisions involving GGE and PGT could alter the gene pool in potentially problematic ways;[36] and (6) the "ignorance" problem: that much is not understood about how genes affect disease.[37]

For parents, the possible use of CRISPR-Cas9 raises a set of distinct legal, ethical, and moral challenges.[38] Such issues overlap with other concerns raised above, including how the law allocates reproductive-related decision-making to potential parents about any potential offspring,[39] the potential consequences of gene-editing for the resulting children, and the rights children might have (when gene editing is used against the parents or the physician.[40] While, as a general matter, parents are legally entitled to

34. *See* Adrienne Asch & David Wasserman, *Where is the Sin in Synecdoche? Prenatal Testing and the Parent-Child Relationship?*, *in* QUALITY OF LIFE AND HUMAN DIFFERENCE: GENETIC TESTING, HEALTH CARE, AND DISABILITY 172 (David Wasserman et al., eds. 2005) (describing this concern with respect to prenatal testing); Schermer, *supra* note 31, at 220 (describing this concern with respect to reprogenetics – prenatal testing, PGT, and GGE); Suter, *IVG, supra* note 23, at 115 (describing this concern with respect to PGT).

35. MACINTOSH, *supra* note 25, at 4 (GGE and any form of genetic manipulation); Drabiak, *supra* note 140 (GGE); Scott, *supra* note 28, at 910 (noting GGE's "potential to introduce into future people characteristics that are fully 'designed' or 'artificial', unlikely to occur naturally"); The President's Council, *supra* note 33 (expressing this concern regarding PGT). *Cf.* Lei Huang, *Noninvasive Preimplantation Genetic Testing for Aneuploidy in Spent Medium May Be More Reliable than Trophoectoderm Biopsy*, 116 PNAS 14105 (2019) (describing research on a noninvasive version of PGT that would avoid the potential damage to embryos through invasive biopsies). *But see* Desmyttere et al., *Neonatal Follow-Up of 995 Consecutively Born Children After Embryo Biopsy for PGT*, 27 HUMAN REPROD. 288 (2012) (finding that the "[e]mbryo biopsy for PGT does not introduce extra risk to the overall medical condition of newborn children," although "[m]ultiples born following embryo biopsy appear to be at lower risk for low birthweight compared with multiples born following ICSI"). Although risks are inherent to any form of embryo manipulation, MACINTOSH, *supra* note 25, at 4, they are, particularly important to GGE because the technology still has so many unknown risks. Similar concerns were raised in the early days of PGT. *See* President's Council, *supra* note 33. GGE might nevertheless be riskier than PGT because the latter "involves merely choosing between" embryos, "all of which already exist 'in nature' and could easily have gone on to play a role in 'natural' reproduction in any event." Scott, *supra* note 28, at 910.

36. Centers for Genetics and Society, *supra* note 33 (GGE); Schermer, *supra* note 31, at 214 (GGE); Suter, *IVG*, *supra* note 23, at 116 (PGT).

37. Tanya Lewis, *Scientists Seek Better Guidelines for Editing Genes in Human Embryos*, SCI. AM. (Aug. 15, 2019), https://www.scientificamerican.com/article/scientists-seek-better-guidelines-for-editing-genes-in-human-embryos/ [https://perma.cc/39KE-8JF9] ("[N]ot a single complex disease or trait is completely understood").

38. Naomi Cahn, *CRISPR Parents and Informed Consent*, 23 SMU SCI. & TECH. L. REV. 3, 9 (2020) [hereinafter Cahn, *CRISPR Parents*].

39. *Id.*

40. Barbara Pfeffer Billauer, *Wrongful Life in the Age of CRISPR-CAS: Using the Legal Fiction of "the Conceptual Being" to Redress Wrongful Gamete Manipulation*, 124 PENN. ST. L. REV. 435 (2020) (proposing a novel remedy for children harmed by "wrongful genetic manipulation").

deference in their decisions about their children's upbringing and care,[41] the state can infringe upon those rights where there are significantly important governmental interests.[42] Beyond the decisions of individual parents are questions about changing parenting norms. The concern is that using these technologies will alter our view of parenting by creating social pressures to use them,[43] and perhaps even limit meaningful choice.[44]

Many of these objections also have strong counterarguments. For example, traits like intelligence do not depend on one single gene but are also related to interaction with the environment.[45] In addition, parents make many decisions regarding their children, which affect their children's future in long-lasting ways.[46] Nevertheless, we recognize that some of these concerns—including the effects on social norms, the risk of unequal access, the potential for discrimination, and the challenges to informed consent—are legitimate. While the tendency is to evaluate these technologies in terms of "the potential risks and benefits for individuals"—whether they be parents, children, or families—we must also consider how the technologies "can both undermine and promote the flourishing of communities and societies."[47] Thus, we take seriously the societal harms that can arise from individual decisions that may accrue to the benefit of the individuals, but in the aggregate be harmful to society.

III. EXISTING REGULATIONS

Although PGT and GGE are both forms of ART, the story of the legal regulation of each technology is quite different in the United States. Whereas PGT has developed with very little governmental oversight, GGE has emerged in the midst of many layers of sometimes redundant governmental regulation and restrictions. These distinctions reflect the fact that PGT grew directly out of reproductive technologies relating to fertility, specifically prenatal testing and IVF. The relatively thin regulatory oversight of these

41. *See* June Carbone, *Legal Applications of the "Best Interest of the Child" Standard: Judicial Rationalization or a Measure of Institutional Competence*?, 134 PEDIATRICS S111 (2014), https://pediatrics.aappublications.org/content/pediatrics/134/Supplement_2/S111.full.pdf [https://perma.cc/V44L-EDFB].

42. Cahn, *CRISPR Parents*, *supra* note 38; Barbara Atwood, *Marriage as Gatekeeper: The Misguided Reliance on Marital Status for Third-Party Standing*, 58 FAM. CT. REV. 971 (2020).

43. Vincent & Jane, *supra* note 31, at 133–35; Suter, *Tyranny of Choice*, *supra* note 1, at 264 (PGT)

44. Schermer, *supra* note 31, at 222 (GGE); Suter, *Tyranny of Choice*, *supra* note 1, at 271 (PGT).

45. *E.g*., Kerry Lynn MacIntosh, *Heritable Genome Editing and the Downsides of a Global Moratorium*, 2 CRISPR J. 272, 276 (2019); Julia D. Mahoney & Gil Siegal, *Beyond Nature? Genomic Modification and the Future of Humanity*, 81 L. & CONTEMP. PROBS. 197, 203–10 (2018).

46. Suter, *Brave New World*, *supra* note 30.

47. Schermer, *supra* note 31, at 212–213.

reproductive technologies continued with the emergence of PGT. In contrast, GGE developed from the research and clinical development of recombinant DNA technology and somatic cell gene therapy, areas that were heavily regulated from the start.

Despite the fact that PGT and GGE each emerged within very different kinds of regulatory frameworks, because each involves IVF, we begin with an overview of the scant regulation of ART and IVF. We next explore the unique regulatory framework for genetic modification that would apply to GGE. The real regulatory distinctions between PGT and GGE arise in the law's different treatment of genetic analysis versus genetic modification of embryos, even though both are part of the ART world. The question explored later is whether their regulation should be similarly aligned.

A. IVF and ART

Commentators regularly bemoan the limited regulation of ART,[48] which has led some to describe our country as the "'the wild west of the fertility industry.'"[49] Commentators attribute the scant regulation to "the incendiary politics surrounding the creation and destruction of embryos,"[50] to the fact that ART has "evolved as a business, not a research enterprise,"[51] and to the "U.S. emphasis on personal autonomy and the sanctity of privacy."[52]

48. Alicia Ouellette et al., *Lessons Across the Pond: Assisted Reproductive Technology in the United Kingdom and the United States*, 31 AM. J. L. & MED., 419, 419–46 (2005); Ellen S. Fischer, *The 'Wild West' of Medicine: An Argument for Adopting the United Kingdom's 'HFEA' Framework, to Improve the Market for Assisted Reproduction in the United States*, 39 NW. J. INT'L L. & BUS. 201 (2019); Yaniv Heled, *The Regulation of Genetic Aspects of Donated Reproductive Tissue – the Need for Federal Regulation*, 11 COLUM. SCI. & TECH. L. 243 (2010); Sonia Suter, *Giving In to Baby Markets: Regulation Without Prohibition*, 16 MICH. J. GENDER & L. 217, 221–23 (2009) [hereinafter "Suter, *Giving In*"]; Naomi Cahn, *Do Tell! The Rights of Donor-Conceived Offspring*, 42 HOFSTRA L. REV. 1077, 1088 (2014) ("Over the past several decades, the federal government has taken a few tentative steps towards the regulation of reproductive technology. The regulations fall into two categories: safety testing and truth in advertising.").

49. Fischer, *supra* note 48, at 202 (quoting Marcy Darnovsky).

50. Michelle Bayefsky, *Who Should Regulate Preimplantation Genetic Diagnosis in the United States?*, 20 AMA J. ETHICS 1160, 1163 (2018), https://journalofethics.ama-assn.org/article/who-should-regulate-preimplantation-genetic-diagnosis-united-states/2018-12 [https://perma.cc/JKC2-NLLG]. Fischer, *supra* note 48, at 202.

51. Michael Ollove, *Lightly Regulated In Vitro Fertilization Yields Thousands of Babies Annually*, WASH. POST (Apr. 13, 2015), https://www.washingtonpost.com/national/health-science/lightly-regulated-in-vitro-fertilization-yields-thousands-of-babies-annually/2015/04/13/f1f3fa36-d8a2-11e4-8103-fa84725dbf9d_story.html [https://perma.cc/EEV6-BX6S].

52. Ouellette et al., *supra* note 48, at 433.

The only federal law that specifically regulates IVF and ART is the U.S. Fertility Clinic Success Rate and Certification Act of 1992 ("FCSRCA").[53] This statute requires fertility clinics to report their pregnancy success rates and mandates that the Centers for Disease Control ("CDC") publish an annual ART success report.[54] While most clinics comply, there is no legal consequence for failing to report. In fact, the only negative consequence is the possibility of being listed as a non-responder in that annual report.[55]

The FCSRCA also requires the CDC to develop—albeit it does not require compliance with—a model licensing program for embryo laboratories.[56] Accordingly, the certification process of laboratories varies considerably.[57] Even if states had been required to adopt the model program,

53. Fertility Clinic Success Rate and Certification Act of 1992, Pub. L. No. 102–493, 106 Stat. 3146 (codified at 42 U.S.C. §§ 263a–1 to a–7 (2000)).

54. *Id.* at § 263a–2(a)(1); *id.* at § 263a–5(1)(A); Fischer, *supra* note 48, at 201; Ouellette, *supra* note 48, at 420.

55. "These programs will be identified as non-reporters in HHS/CDC's annual Assisted Reproductive Technology Fertility Clinic Success Rates Report." *Reporting of Pregnancy Success Rates from Assisted Reproductive Technology (ART) Programs*, 80 Fed. Reg. 51,811, 51,814 (2015). *See also Seventeenth Annual Review of Gender and Sexuality Law: Annual Review Article: Assisted Reproductive Technologies*, 17 GEO. J. GENDER & L. 83, 84 (2016) (The "only real consequence of non-reporting of the data is a sort of public shaming where the Act requires the non-reporting clinic's name be included in the annual report."); HENRY T. GREELY, THE END OF SEX AND THE FUTURE OF HUMAN REPRODUCTION 155 (2016) (noting that the act "does not provide any sanctions beyond requiring the CDC to publish the names of the scofflaws," which "scarcely counts as 'regulation'"). However, not all non-reporters are listed as such. Ouellette et al., *supra* note 48, at 427–28. In 2017, 448 fertility clinics fulfilled the reporting requirements, but 50 clinics did not. The CDC estimates that "ART surveillance covered 98% of ART cycles performed in the United States in 2017." CDC, 2017 ASSISTED REPRODUCTIVE TECHNOLOGY FERTILITY CLINIC SUCCESS RATES REPORT 4–5, ftp://ftp.cdc.gov/pub/Publications/art/ART-2017-Clinic-Report-Full.pdf#page=17 (last visited Dec. 7, 2020). Ouellette, *supra* note 48, at 419–20. And indeed not all non-reporters are listed as such. *Id.* at 427–28.

56. *Id.*; Fertility Clinic Success Rate and Certification Act of 1992, Pub. L. No. 102–493, 106 Stat. 3146 (codified at 42 U.S.C. §§ 263a–2(a)(1) (2000)); *Id.* at 263a–5(1)(A); Fischer, *supra* note 48, at 201; Ouellette et al., *supra* note 48, at 420–21.

57. Ouellette et al*., supra* note 48, at 430. *See* Implementation of the Fertility Clinic Success Rate and Certification Act of 1992; Proposed Model Program for the Certification of Embryo Laboratories, 63 Fed. Reg. 60178 (1998) for a discussion of the clinic certification program. Until 2021, certification of embryo laboratories was done by one of three nonfederal laboratory accreditation programs: (1) the College of American Pathologists External/ American Society for Reproductive Medicine (CAP/ASRM), (2) the Joint Commission on Accreditation of Healthcare Organizations (JACHO) External, and (3) the New York State Tissue Bank certification for ART laboratories (NYSTB)." CDC, *Assisted Reproductive Technology*, https://www.cdc.gov/art/nass/policy.html [https://perma.cc/NMX2-PD2A] (last visited May 18, 2021). The College of American Pathologists has certified more than 100 reproductive laboratories in the U.S. For example, Virginia has eight certified reproductive labs. *See* College of American Pathologists, *Accredited Laboratory and Biorepository Directory*, https://www.cap.org/laboratory-improvement/accreditation/accredited-laboratory-and-biorepository-directory/ [https://perma.cc/2YTZ-HLYW] (last visited Sept. 17, 2021). Some IVF centers have been certified by the Joint Commission. *See., e.g.,* Shady Grove Fertility, *Shady Grove Fertility (SGF) Maintains Highest Standards in Laboratory Accreditation Established By The Joint Commission* (Sept. 26, 2017), https://www.shadygrovefertility.com/newsroom/Shady-Grove-Fertility-Lab-Accreditation [https://perma.cc/PF9Z-5HR8]. In New York, the "state department of health has extensive policies that laboratories must follow in order to be accredited to operate within New York state." Every state

it sets no minimum safety requirements for the various ART techniques.[58] Ultimately, neither embryo laboratories nor infertility clinics are required to undergo federal licensing or accreditation. Although many do "follow practice standards and apply for accreditation from private agencies,"[59] programs that are not accredited suffer no legal consequence.[60] As one commentator states, this statute offers inadequate regulation of ART because it fails to create "any oversight body" or "enforcement mechanism."[61]

The final piece of federal regulation concerns testing standards for gametes. The FDA's regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products includes, by regulatory definition, donor gametes and embryos. These regulations impose requirements for record-keeping and screening, with the screening focused on communicable diseases. In addition, they require entities that handle gametes and embryos to register.[62] As of May 8, 2020, 1091 establishments were listed as handling semen and 974, oocytes.[63]

department of health provides "oversight and regulation of ART laboratories" to "varying degrees" with New York's and California's departments "particularly active in regulating ART laboratories and their personnel." ANIL K. DUBEY, INFERTILITY: DIAGNOSIS, MANAGEMENT AND IVF 479 (2012). As of 2021, however, the New York state tissue bank is no longer one of the potential sources of accreditation. *See Certification of Embryo Laboratories*, CDC (Dec. 14, 2020), https://www.cdc.gov/art/nass/policy.html#certify [https://perma.cc/SV57-PEWJ].

58. Fischer, *supra* note 48 at 211. *Subpart B - Procedures for Registration and Listing*, 21 C.F.R. 1271.21-37 (describing the registration and reporting requirements); FDA, *Instructions for Using the Electronic Human Cell and Tissue Establishment Registration System (eHCTERS)*, https://www.fda.gov/media/109160/download (last viewed Oct. 8, 2021); *Establishment Registration and Listing for Human Cells, Tissues and Cellular and Tissue-Based Products (HCT/Ps) Questions and Answers*, FDA, https://www.fda.gov/vaccines-blood-biologics/biologics-establishment-registration/establishment-registration-and-listing-human-cells-tissues-and-cellular-and-tissue-based-products [https://perma.cc/UW7U-7K9N] (FAQs, which include the ongoing registration information).

59. Ouellette et al., *supra* note 48, at 420. The College of American Pathologists, the Joint Commission of Accreditation of Healthcare Organizations, and (until 2021), the New York State Tissue Bank Accreditation Program have provided accreditation of laboratories and, as nonfederal programs, they are not overseen by the CDC. *Id.* at 430.

60. *Id.* While data collection is tied to licensing in other countries, it is not in the United States. *Id.* at 425. Accreditation has been increasing since the late 1990s, in part under SART's campaigns to build consumer confidence and their requirement that their members are accredited. *Id.* at 430–31.

61. Fischer, *supra* note 48, at 211.

62. 21 CFR § 1271.1 (2016); *Donor Eligibility Final Rule and Guidance and Questions and Answers*, FDA (March 22, 2018), https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/donor-eligibility-final-rule-and-guidance-questions-and-answers [https://perma.cc/56BV-3NZF].

63 Listed establishments are those that either currently or previously registered with the FDA as distributing, testing, labeling, packaging, processing, recovering, screening, and/or storing semen or oocytes. *Human Cell and Tissue Establishment Registration - Public Query 2020,* FDA, https://www.accessdata.fda.gov/scripts/cber/CFAppsPub/tiss/index.cfm [https://perma.cc/Z9R2-Q6LJ] (last visited June 29, 2020) (select "Semen" under the "Product" parameter, and then click "Continue" to get results). Cahn, *Do Tell!, supra* note 48, at 1089.

Congress's funding restrictions of embryo research also indirectly impact ART developments. In 1996, as part of its approval of the federal budget, Congress passed the Dickey Wicker Amendment, a rider that prohibits DHHS from using appropriated funds for research that creates, destroys, discards, or harms human embryos.[64] This rider has been attached to the appropriation bills for DHHS every year since then.[65]

At the state level, as is typical of health care in America, regulation of ART is a patchwork of highly variable laws. Some states have laws that regulate the use of embryos for research, that ban particular reproductive technologies like cloning,[66] or that regulate the disposition of embryos. Louisiana is unique in defining the embryo as a juridical person, and is so far the only state that prohibits the destruction of human embryos.[67] Arizona enacted a law that requires, in case of disagreement about disposition of the embryos, that they go to the "spouse who intends to allow the in vitro human embryos to develop to birth."[68] In most states, disposition of embryos depends on the common law, with various approaches, most of which tend to default to the party trying to avoid procreation.[69]

In addition, fertility clinics and their providers are subject to state medical licensing standards as a form of indirect regulation.[70] States have developed a series of inconsistent approaches, including those relating to laboratory certification, laboratory standards, and accreditation,[71] as well as restrictions on who can use the technology.[72] In some states, insurance laws

64. Balanced Budget Down Payment Act of 1996, Pub.. L. 104-9, 110 Stat. 26. Two years earlier, the NIH Human Embryo Research Panel had issued a report articulating the special nature of embryos compared to ordinary tissue and suggested various limitations on human embryo research, including using them at the earliest stages of development and in the service of important scientific information that could not be obtained in other ways. Nat'l Acads., *Human Genome Editing*, *supra* note 5.

65. *Id.*

65. Nat'l Acads., *Human Genome Editing, supra* note 5, at 42 n.10.

66. Ouellette et al., *supra* note 48, at 423 (citing NCSL on human cloning).

67. LA. STAT. ANN. § 9:129 (1991) ("A 'human embryo' for the purposes of this Chapter is an in vitro fertilized human ovum, with certain rights granted by law, composed of one or more living human cells and human genetic material so unified and organized that it will develop in utero into an unborn child."). *See* Greer Gaddie, *The Personhood Movement's Effect on Assisted Reproductive Technology: Balancing Interests Under a Presumption of Embryonic Personhood*, 96 TEX. L. REV. 1293, 1295–96 (2018) (noting that although several "states have enacted general personhood laws," only Louisiana has "a personhood law [that] specifically addresses embryos created using ART.").

68. ARIZ. REV. STAT. § 25-318.03(A)(1) (LexisNexis 2018).

69. I. Glenn Cohen & Eli Y. Adashi, *Embryo Disposition Disputes: Controversies and Case Law,* 46 HASTINGS CTR. REP. 13, 13–14 (2016).

70. Lewis, *supra* note 37, at 65.

71. *Id.* at 63. These laboratory safety standards are set by private organizations (although they may require compliance with governmental regulations), and the sanctions are limited. *See* Heled, *supra* note 48, at 272 (discussing AATB sanctions as comprising only decertification).

72. Fischer, *supra* note 48, at 212.

indirectly regulate ART.[73] Fifteen states mandate insurance coverage of infertility treatment, including IVF in some states.[74] And while Texas and California mandate *the offer* of such insurance, California excludes IVF coverage.[75] The laws vary considerably in terms of the requirements for IVF coverage, including age restrictions, numbers of IVF cycles covered, number of embryos that can be transferred per cycle or in total.[76]

At both the federal and state level, therefore, most aspects of IVF are largely unregulated. Whether and under what circumstances one can undergo IVF is not directly governed by state or federal law, although state law establishes parenthood. Legislation at most indirectly affects access to the technology through insurance coverage (or lack thereof) and rules affecting disposition of embryos.

Finally, professional guidelines by such organizations as the American Society for Reproductive Medicine ("ASRM")[77] function as a form of quasi-regulation. For example, the ASRM issues both Ethic and Practice Committee recommendations covering various aspects of reproductive technology.[78]

B. PGT

Once embryos are created through IVF, PGT involves genetic analysis of the embryos and decisions about which embryos to implant based on the results. No state or federal law directly addresses decisions about what kinds of tests may be conducted on the embryos or which embryos to implant,[79] although professional societies have established various guidelines, including with respect to sex selection and implantation of embryos with

73. *Id.*

74. Arkansas, Connecticut, Delaware, Hawaii, Illinois, Louisiana, Maryland, Massachusetts, Montana, New Hampshire, New Jersey, New York, Ohio, Rhode Island, and West Virginia mandate the coverage of infertility treatment, but Louisiana and New York exclude IVF from the coverage requirements. Three limit the mandate to IVF: Arkansas, Hawaii, and Maryland. National Council of State Legislators, *State Laws Related to Insurance Coverage for Infertility Treatment*, (Mar. 12, 2021), https://www.ncsl.org/research/health/insurance-coverage-for-infertility-laws.aspx [https://perma.cc/Q3XD-3TTS] (last visited Aug. 27, 2021).

75. *Id.*

76. Fischer, *supra* note 48, at 212.

77. The ASRM is a nonprofit organization "dedicated to the advancement of the science and practice of reproductive medicine." ASRM, *ASRM's Mission, Vision, and Values* (2021), https://www.reproductivefacts.org/about-asrm/history-of-asrm/.

78. *E.g.*, Ethics Committee Opinions, AM. SOC. REPRODUCTIVE MED., https://www.asrm.org/news-and-publications/ethics-committee-documents/ [https://perma.cc/B663-SJPF]; *Practice Committee Documents*, AM. SOC. REPRODUCTIVE MED., https://www.asrm.org/news-and-publications/practice-committee-documents/ [https://perma.cc/HF54-ZCKY]. These guidance and recommendations cover topics ranging from egg freezing to the number of embryos to be transferred.

79. Bayefsky, *supra* note 50.

genetic anomalies.[80] The FDA has not asserted authority over PGT. This may be because it is outside the FDA's statutory authority. The Public Health Service Act, enacted in 1944, expanded the FDA's authority beyond food and drugs to include regulation concerning the transmission of communicable diseases.[81] Because PGT does not inherently present risks of communicable disease, it does not seem to fall within the FDA's broader authority.[82]

In addition, the ASRM has established a "Preimplantation Genetic Testing Special Interest Group and issued guidance in the area.[83] Although laws affecting disposition of embryos may have an indirect effect on such decisions, they do not specifically determine how PGT will be used.

While states regulate clinical practice, they have generally left decisions about prenatal testing to the individual and health care provider. A growing number of states have, however, begun to enact laws intended to affect termination decisions in the context of prenatal genetic testing decisions. So far, at least nine states have passed laws prohibiting abortions based on fetal anomalies.[84] Four of these laws have been temporarily or permanently enjoined.[85] Louisiana, in a similar vein, prohibits doctors from offering information about abortion after the fetus has been diagnosed with a fetal anomaly.[86] The justification for such laws is to prevent discrimination

80. Ethics Comm. of the Am. Soc'y for Reproductive Med., *Transferring Embryos with Genetic Anomalies Detected in Preimplantation Testing: An Ethics Committee Opinion*, 107 FERTILITY & STERILITY 1130 (2017); Ethics Comm. of the Am. Soc'y for Reproductive Med., *Use of Reproductive Technology for Sex Selection for Nonmedical Reasons*, 103 FERTILITY & STERILITY 1418 (2015); Ethics Comm. of the Am. Soc'y for Reproductive Med., *Use of Preimplantation Genetic Testing for Monogenic Defects (PGT-M) for Adult-Onset Conditions: An Ethics Committee Opinion*, 109 FERTILITY & STERILITY 989 (2018).

81. Public Health Service Act, 42 U.S.C. § 264 (a) (2002).

82. *See* BRUCE JENNINGS & MICHELLE BAYEFSKY, REGULATING PREIMPLANTATION GENETIC DIAGNOSIS IN THE UNITED STATES: THE LIMITS OF UNLIMITED SELECTION 70 (2015); GREELY, *supra* note 55, at 156–57 (2016) (noting the uncertainty of the FDA's authority to regulate PGT).

83. *See Preimplantation Genetic Testing Special Interest Group (PGTSIG)*, AM. SOC. REPRODUCTIVE MED., https://www.asrm.org/membership/asrm-member-groups/special-interest-groups/groups/preimplantation-genetic-testing-special-interest-group-pgdsig/ [https://perma.cc/2QQW-P53S] (last visited Nov. 17, 2020).

84. As of August, 2021, eleven states—Arkansas, Indiana, Kentucky, Louisiana, Mississippi, Missouri, North Dakota, Ohio, South Dakota, Tennessee, and Utah —had enacted such laws. *Abortion Bans in Cases of Sex or Race Selection or Genetic Anomaly*, GUTTMACHER INST. (Aug. 1, 2021), https://www.guttmacher.org/state-policy/explore/abortion-bans-cases-sex-or-race-selection-or-genetic-anomaly [https://perma.cc/Y4N6-VXSX].

85. *Id.*

86. Center for Reproductive Rights (CRR), *Shifting the Frame on Disability Rights for the U.S. Reproductive Rights Movement* (2017) at 31, https://www.reproductiverights.org/document/shifting-the-frame-on-disability-rights-for-the-us-reproductive-rights-movement [https://perma.cc/CAB6-XL68].

against those with disabilities.[87] Although there are moral and legal distinctions between embryos and fetuses, one could imagine the enactment of similar legislation with respect to PGT, particularly by those who believe that life begins at conception.[88] To date, however, no such law exists.

C. GGE

In contrast to PGT, which is routinely used and lightly regulated, GGE is not yet used and is so highly regulated in the United States that it is effectively banned. The history of GGE regulation is intertwined with the development of recombinant DNA technology ("rDNA") and somatic cell gene therapy. Accordingly, this section begins with an overview of the development of somatic cell gene therapy regulation before describing the regulation of GGE.

1. Somatic Cell Gene Therapy Regulation

Two entities were central to the development of gene therapy regulation: the Recombinant DNA Advisory Committee ("RAC") and the FDA, which have each played both distinct and overlapping roles.

The FDA has existed for more than a century, whereas the RAC was created less than half a century ago, based on concerns about the novelty and ethics of being able to alter genetics. As a result, the sole focus of the RAC was evaluating research related to recombinant DNA. As this next section describes, although the FDA ultimately became the primary regulatory body for somatic cell genetic modification, its role was initially not so prominent. Instead, the RAC first shaped the regulation of this new technology and, for several decades, it was integral to the oversight of its research and development. This subsection describes the waxing and waning roles of the RAC and FDA regarding somatic cell gene therapy, including the entities' similarities and differences.

87. *See, e.g.,* Miss. Code § 41-41-403(b) (2020) (describing the purpose of a reason-based abortion ban as consistent with the American with Disabilities act and "numerous state laws [that] prohibit discrimination against individuals on the basis of a real or perceived physical or mental impairment that substantially limits one or more major life activities"); Tenn. Code § 39-15-214(a)(63) (2020) ("The use of abortion as a means to prefer . . . to discriminate based on disability . . . is antithetical to the core values equality, freedom, and human dignity enshrined in both the United States and Tennessee Constitutions.") (preliminarily enjoined by Memphis Ctr. for Reprod. Health v. Slatery, No. 3:20-cv-00501, 2020 WL 4274198 (M.D. Tenn. 2020), aff'd No. 20-5969, 2021 WL 4127691 (6th Cir. Sept. 10, 2021)).

88. Bayefsky, *supra* note 50.

a. The Dual Role of the RAC and the FDA

In the early 1970s, scientists discovered the ability to use special enzymes that could cut and recombine strands of DNA. Concerns about the potential biohazards of recombinant DNA (rDNA) inspired the creation of a National Academy of Sciences panel charged with evaluating the safety of, and issuing recommendations for, such research.[89] In mid-1974, the panel called for the voluntary moratorium of recombinant DNA research until the risks could be better understood and contained as well as the creation of an advisory committee to oversee such research and establish safety guidelines.[90] Both recommendations were heeded. Despite strong debates about the wisdom of a moratorium, scientists across the world universally halted rDNA research with calls for an international conference to assess the nature and magnitude of its risks. In early 1975, on the final day of the now-famous Asilomar Conference on Recombinant DNA,[91] the participants agreed to allow rDNA research to continue, but only under "stringent" restrictions.[92] Those restrictions became the basis for federal guidelines issued in 1976,[93] just two years after the NIH director created the Recombinant DNA Advisory Committee, or the RAC, an interdisciplinary group of scientists, lawyers, bioethicists, and other "public members."[94] This group was charged with creating guidelines for and reviewing all federally funded rDNA experiments. The first NIH guideline on rDNA research also

89. Specifically, the panel—called the "Recombinant DNA Advisory Committee"—was created in response to a recombinant DNA protocol that scientist Paul Berg and some colleagues had proposed, which would have involved inserting viral DNA into a common bacterium, *E. Coli.* Interestingly, Paul Berg himself was not only on the committee, but also named its Chair. Joseph M. Rainsbury, *Biotechnology on the RAC—FDA/NIH Regulation of Human Gene Therapy*, 55 FOOD & DRUG L.J. 575, 575–76 (2000).

90. Paul Berg et al., *Potential Biohazards of Recombinant DNA Molecules*, 185 SCI. 303 (1974). As noted *supra* note 89, Paul Berg was the Chair of the Committee on Recombinant DNA Molecules, Assembly of Life Sciences, National Research Council, National Academy of Sciences. *Id.*

91. This was actually the second of two conferences at Asilomar. "The "First" Asilomar Conference was held in January 1973, where roughly 100 scientists considered "laboratory safety and containment issues and discuss[ed] evidence on the risk of cancer from genetically modified viruses." At the second Asilomar conference, participants considered whether the research moratorium should continue and ultimately proposed that it proceed with appropriate safeguards. INSTITUTE OF MEDICINE; BOARD ON HEALTH SCIENCES POLICY; COMMITTEE ON THE INDEPENDENT REVIEW AND ASSESSMENT OF THE ACTIVITIES OF THE NIH RECOMBINANT DNA ADVISORY COMMITTEE, OVERSIGHT AND REVIEW OF CLINICAL GENE TRANSFER PROTOCOLS: ASSESSING THE ROLE OF THE RECOMBINANT DNA ADVISORY COMMITTEE (Rebecca N. Lenzi, Bruce M. Altevogt, & Lawrence O. Gostin, eds., 2014).

92. Paul Berg, *Asilomar 1975: DNA Modification Secured*, 455 NATURE 290 (2008). The conference comprised roughly 140 participants, including not just scientists, but also lawyers, journalists and government officials. *Id.*

93. *Id.*

94. Rainsbury, *supra* note 89, at 575–76 (citing 41 Fed. Reg. at 27,903 and the source of the RAC's statutory authority, Public Health and Welfare Act, 42 U.S.C. § 282(b)(6) (2018)); Recombinant DNA Molecules, 41 Fed. Reg. 27,901, 27,902 (Jul. 7, 1976).

required every institution involved in such research to create an Institutional Biohazard Committee (IBC) to evaluate the safety of research protocols to humans and the environment.[95]

As concerns about the biohazards of rDNA research eventually waned, the role of the RAC shifted from focusing on laboratory and animal experiments to reviewing protocols for human gene-transfer research.[96] In 1985, NIH issued *Points to Consider in the Design and Submission of Human Somatic Protocols*,[97] which was the first time the RAC expressed its willingness to consider protocols for human gene-transfer protocols.[98]

At the same time, the FDA began to flex its regulatory muscles, announcing its intention to regulate rDNA products in 1984, including gene therapies,[99] and specifically asserting its jurisdiction over human gene transfer experiments in 1986.[100] By 1990, after receiving both RAC and FDA approval, the first human gene transfer clinical trial began.[101]

For a period, all protocols conducted within institutions that received federal dollars for rDNA research had to be reviewed by both the RAC and the FDA.[102] The result was two layers of oversight for human gene-transfer experiments. The growing number of protocols, however, began to tax the capacity of the RAC, which met only a few times a year. Furthermore, many applications presented routine issues for review, not the novel ethical or safety issues for which the RAC had been developed.[103] Pressure from investigators, frustrated by what they viewed as a redundant, duplicative, and inefficient review process, led to various measures to streamline the process.[104] Ultimately, both the NIH and FDA agreed that the FDA would

95. Recombinant DNA Molecules, 41 Fed. Reg. at 27,903. Rainsbury notes that several guidelines still persist. Rainsbury, *supra* note 89, at 576. Initially, the RAC drafted guidelines for rDNA research. Although these guidelines did not have "the legal force of regulations," they did "have an enormous influence on practices for preventing the unintended release of or human exposure to genetically modified organisms and material." Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 48.

96. *Id.; see* LORI B. ANDREWS ET AL., GENETICS: ETHICS, LAW AND POLICY 409 (West Acad. 4th ed. 2015) [hereinafter "G&L 4th"]. It did so, however, without any protocols ready for review. As one scholar notes, it "was an odd case of a bureaucratic panel outpacing the technology it was charged with reviewing." Rainsbury, *supra* note 89, at 581.

97. Recombinant DNA Research, 50 Fed. Reg. 2,940 (Jan. 22, 1985).

98. G&L 4th, *supra* note 96, at 418.

99. Statement of Policy for Regulating Biotechnology Products, 49 Fed. Reg 50,878 (Dec. 31, 1984).

100. Rainsbury, *supra* note 89, at 581.

101. *Id.* at 584.

102. For a period, they also had to be reviewed by both the Human Gene Therapy Subcommittee and the full RAC. In 1992, the NIH director "merge[d] the subcommittee into the full RAC." *Id.* at 586.

103. *Id.* at 585–86.

104. G&L 5th, *supra* note 3, at 262; Rainsbury, *supra* note 89, at 586–87.

be the principal regulatory body for this technology.[105] As a result, the NIH Director scaled back the RAC's regulatory authority and the RAC primarily became a venue for consideration of "novel scientific, safety, social and ethical issues" and matters "deserving of public discussion."[106] Although the RAC still retained the authority to review controversial protocols on a case-by-case basis, it became a "pale ghost of its former self" as the FDA retained the authority to approve protocols.[107]

The final nail was placed in the RAC's regulatory coffin in 2019 when the NIH eliminated RAC review and reporting requirements to the NIH for human gene transfer protocols. It explained this decision by pointing to recent advances in translating research into clinical practice, including FDA approval for licensed gene transfer products.[108] Moreover, it emphasized the "duplications in the approval process and special oversight" that do not apply to "other areas of clinical research." With existing "oversight mechanisms" that can "keep pace with new discoveries in this field,"[109] the NIH left full regulatory authority over gene transfer to the FDA.[110] This meant that the special oversight that had been accorded to genetic modification no longer existed.[111]

The RAC did not completely disappear, however. In response to concerns that without the RAC there would not be a "transparent forum for discussion on various scientific, ethical, legal and social issues related to emerging biotechnologies," the NIH transitioned the RAC into the Novel and Exceptional Technology and Research Advisory Committee (NExTRAC).

105. *Id.* at 590–92.

106. *See generally* Recombinant DNA Research, 61 Fed. Reg. 35,774 (Jul. 8, 1996) (describing the NIH Director's proposed changes regarding the roles and responsibilities of NIH oversight); Recombinant DNA Research: Actions Under the Guidelines, 62 Fed. Reg. 59,032 (Oct. 31, 1997) (formally describing the changed policy). The Director's initial plans to dissolve the RAC were met with criticisms, including the concern that it "would shield controversial research from public scrutiny." Rainsbury, *supra* note 89 at 591. As a result, he decided instead to scale back the RAC's role. *Id.* The Director was influenced by several concerns: the science was sometimes "too shoddy" for human testing; too few experiments focused on genetic diseases, and instead addressed cancers and AIDS; and biotech companies treated RAC approval as "some kind of N.I.H. imprimatur" to tout in the business pages. Stolberg, *supra* note 3, at 137.

107. Rainsbury, *supra* note 89, at 591.

108. *See* Katherine A. High & Maria G. Roncarolo, *Gene Therapy*, 381 NEW ENG. J. MED. 455, 461 (2019) (listing FDA approval of five gene therapies as of 2019).

109. *See* Recombinant or Synthetic Nucleic Acid Research, 83 Fed. Reg. 41,082 (Aug. 17, 2018) (noting that similar observations had been made in a 2014 Institute of Medicine report that had recommended limiting RAC review to "exceptional HGT protocols that meet certain criteria and that would significantly benefit from RAC review" and suggesting that modifying the "roles of IBCS in reviewing HGT to be consistent with review of other covered research").

110. *See* Final Action for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, 84 Fed. Reg. 17,858, 18,860 (Apr. 26, 2019) (granting regulatory to FDA).

111. The creation of NExTRAC did not fully replace this oversight because it fills merely an advisory, rather than regulatory, role. *See infra* text accompanying nn. 112–114..

NExTRAC has no regulatory authority. Instead, it exists as an advisory body for the NIH "regarding issues of emerging biotechnologies, biosafety, or when proposing changes to the *NIH Guidelines* or other relevant policies."[112] As the NIH noted, the transition allegedly brought the renamed RAC closer to its "original mandate – a transparent forum for science, safety, and ethics of emerging biotechnologies"[113]—although its purview was no longer limited to rDNA.[114]

112. Final Action for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, 84 Fed. Reg. at 17,860; s*ee also Novel and Exceptional Technology and Research Advisory Committee*, Nat'l Inst. Health, https://osp.od.nih.gov/biotechnology/main-nextrac/ [https://perma.cc/KC3H-B36Z] ("The purpose of the committee is to provide recommendations to the NIH Director and serve as a public forum for the discussion of the scientific, safety, and ethical issues associated with emerging biotechnologies.") (last visited Dec. 9, 2020).

Public comments varied in their reactions to the change, with some who fully opposed it, some who fully supported it, and some who were generally in favor of reducing duplication but worried about the lack of information as to what this would really mean for IBCs. Almost every commenter applauded the effort to minimize duplication, regardless of position. Companies, whether for-profit or not, generally seemed to favor the change, with some commenters suggesting that oversight by IBCs and IRBs would be effective, though some asked for further details on the practicality of shifting to IBCs and IRBs. As a comment from Biotechnology Innovation Organization noted, "BIO believes that there is currently sufficient and robust regulatory framework in place for safe and effective development of gene therapy products. We encourage the Agency to define more clearly the transfer of responsibilities, as well as the IBC review process." Aug162018_AllComments, https://osp.od.nih.gov/wp-content/uploads/Aug162018_AllComments_r508.pdf [https://perma.cc/9CE4-N7DS] (last viewed Dec. 9, 2020).

On the other hand, universities generally were either entirely against the change or were somewhat against the change. *Id.* Their comments cited major concerns about the practicality of IBCs and IRBs. *Id.* One concerned commenter asked, "What will protect scientific decisions from the influences of politics and personal bias?" *Id.* Some comments expressed apprehension about putting too much power into the hands of IBCs, which were viewed as lacking the necessary expertise and which they feared would struggle to manage the burdens of approval. *Id.* Others worried about insufficient guidance to IBCs as to the nature of the review process and their responsibilities. *Id.* In addition, some comments worried about the loss of a unique public forum and backstop for emerging technologies. *Id.* As one comment noted, the change would "end the most prominent forum for the public discussion of recombinant DNA technology we have had over the last 40 years." And as another said, "[r]eview by one body such as the RAC for ethical, scientific, and risk assessment of HGT research is outside the FDA purview, and would remain beneficial." *Id.*

Comments from four taxpayers were divided in their views. Two supported the change and two opposed the elimination of RAC, including the father of Jesse Gelsinger, the young man who died participating in a gene therapy protocol in 1999. *See supra* note 3. As Mr. Gelsinger said:

> Little has been done to place firewalls between the money and the research. The swinging door between the FDA and industry remains wide open. . . . At the time of Jesse's death the role of the RAC had been subordinated to what they want to do again; they were not getting the information on the ongoing OTC clinical trial. That second level of oversight may have saved Jesse's life. . . . Please do not let history repeat itself. The death of innocence is something that we all must carry, and is an almost overwhelming burden. Everybody failed Jesse Gelsinger, at every level, and all he wanted to do was help.

Id.

113. *NIH Guidelines*, NATIONAL INSTIT. HEALTH (2019), https://osp.od.nih.gov/biotechnology/nih-guidelines/ [https://perma.cc/C7KM-WESF].

114. Daniel Kavanagh, *NIH Launches NExTRAC to Advise on Emerging Biotechnologies*, WCG Institute (Dec. 10, 2019), https://www.wcgclinical.com/insights/blog/nih-launches-nextrac-to-advise-on-emerging-biotechnologies [https://perma.cc/LET7-8R5X].

b. Comparing the RAC and the FDA

Given the long history of the dual role of the RAC and FDA in reviewing gene therapy protocols, it is worth noting some key distinctions between their regulatory frameworks. First, the scope of their regulatory authority has always been different. The RAC was developed specifically to oversee research using a particular technology, rDNA. Thus, its oversight of the development of new technologies, like gene therapy, was limited to technologies that used rDNA. In contrast, the FDA's scope was always much broader. Its oversight of gene therapy included any technology used for that purpose.

This distinction between the breadth of the regulatory scope of the two entities was illustrated by their different reactions to a technique to treat female infertility caused by problems with the cytoplasm in a woman's eggs. In the 1990s, researchers developed a treatment, ooplasmic transfer, which involved the transfer of the nucleus of the egg from the affected women into an enucleated donor egg to remove the deficiency. Although this technique resembled germline gene therapy by genetically modifying the egg, it did not fall within the purview of the RAC because it did not involve recombinant DNA.[115] By contrast, the FDA viewed the research, which resulted in a live birth in 1997, as falling under its jurisdiction. While it did not take a position on whether such research should go forward, it sent a letter to several fertility clinics warning them that such clinical experiments were subjected to the FDA regulatory process.[116]

Second, whereas the creation of the RAC subjected most forms of gene therapy or genetic modification to a special level of oversight and review, the FDA saw no need to develop a particular approach for each technology. In its 1984 policy statement, the FDA indicated that it would subject "[n]ucleic acids used for human gene therapy trials . . . to the same requirements for other biological drugs."[117] In other words, it adopted the framework it still uses today, which does not subject biotechnology products and processes, including rDNA products, to "special review." Instead, it subjects them to the same level and types of oversight as all other products or processes.[118]

115. Erik Parens & Eric Juengst, Editorial, *Inadvertently Crossing the Germ Line*, 292 SCI. 397 (2001).

116. Leila Abboud, *FDA Seeks Rigorous Review of New Fertility Treatments,* WALL ST. J. (Oct. 7, 2002), https://www.wsj.com/articles/SB1033940987332846993 [https://perma.cc/8RBP-2Y8B].

117. 49 Fed. Reg 50,878 (1984).

118. G&L, 5th *supra* note 3, at 260. This is similar to how it treats donated gametes, assimilating them into an existing structure. Human Cells, Tissues, and Cellular and Tissue-based Products, 21 C.F.R. § 1271 (2020).

A third distinction is the role of ethics in the review process. From the beginning, ethical concerns were an important part of the RAC's review of gene therapy protocols. Indeed, the Committee included not just scientists to evaluate the environmental and medical risks but also ethicists and lawyers to consider the societal implications of the technology.[119] Such concerns have never been part of the FDA's review process, whose primary focus is to monitor the safety and effectiveness of gene therapy products. For example, in guidance documents issued in the 1990s, the Center for Biologics Evaluation and Research ("CBER") focused only on the technical aspects of the technology.[120] They offered no indications that FDA review would include ethical considerations.[121] That generally remains true today in the multiple guidance documents for manufacturers developing gene therapies.[122]

Fourth, the two entities interact differently with the public. The FDA, as a regulatory agency, allows for public input with respect to the rules it promulgates regarding its regulatory process.[123] But the public cannot participate in the actual deliberations.[124] By contrast, the RAC review process provided a public venue. As a public advisory committee under the Federal Advisory Committee Act of 1972,[125] the RAC was required to provide advance notice of meetings open to the public, allow the public to participate, and provide transcripts of the meetings.[126] Overall, the RAC offered multiple benefits in (a) considering not only the health and safety concerns with respect to genetic modification but also the ethical issues it

119. *See* The President's Council on Bioethics, *Reproduction and Responsibility: The Regulation of New Biotechnologies* (Mar. 2004) (in Kelly, *infra* note 158, at 336–37).

120. *See* FDA, POINTS TO CONSIDER IN HUMAN SOMATIC CELL THERAPY AND GENE THERAPY (1998) ("This guidance document updates and replaces the 1991 PTC with new information intended to provide manufacturers with current information regarding regulatory concerns for production, quality control testing, and administration of recombinant vectors for gene therapy; and of preclinical testing of both cellular therapies and vectors.").

121. Rainsbury, *supra* note 89, at 590.

122. *Cellular & Gene Therapy Guidances*, FDA (Feb. 14, 2020), https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances [https://perma.cc/7VJY-NVGL] (last viewed Aug. 28, 2021).

123. *Comment on Proposed Regulations and Submit Petitions*, FDA, https://www.fda.gov/regulatory-information/dockets-management/comment-proposed-regulations-and-submit-petitions [https://perma.cc/57E6-T3RX] (last updated Aug. 16, 2019) (noting that the public can comment on rules by responding to proposed rules during the public comment period or by petitioning the FDA to "issue, change or cancel" a regulation).

124. *See infra* text accompanying note 165 (discussion of IBCs and Institutional Review Boards).

125. 5 U.S.C. Appendix–Federal Advisory Committee Act; Pub. L. No. 92-463.

126. REBECCA N. LENZI ET AL., OVERSIGHT AND REVIEW OF CLINICAL GENE TRANSFER PROTOCOLS: ASSESSING THE ROLE OF THE RECOMBINANT DNA ADVISORY COMMITTEE 5 (2014); Foundation on Economic Trends v. Heckler, 756 F.2d 143 (D.C. Cir. 1985).

presented, and (b) the involvement of the public. On the other hand, the more expansive focus of the FDA provides a different set of benefits.[127]

2. The Regulation of Germline Genetic Modification

Although the regulatory structure for gene therapy involves the same entities with respect to both somatic and germline gene editing, the regulation of germline modification has followed a very different path from that of somatic cell gene therapy. In stark contrast to the continued efforts to nurture the development of the latter has been the long-standing resistance—both direct and indirect—to germline genetic modifications. As early as 1985, the FDA announced that it would not approve any protocols for germline therapy and that the RAC would "not entertain" such proposals.[128] Just over a decade later, with the passage of the Dickey Wicker Amendment,[129] Congress used the power of the purse to limit human embryo research. While not directed specifically at germline editing, this prohibition of federal funding for research that creates, destroys, or harms human embryos effectively bars federally funded research on germline genetic modification.

The general opposition to germline genetic modification continued as technologies evolved, including the development of CRISPR-9 and other gene editing techniques. In 2015, echoing the calls by researchers to halt rDNA research four decades earlier, scientists published commentaries urging a voluntary moratorium of human germline modification.[130] That same year, NIH Director Francis Collins issued a statement on gene-editing technologies in embryos. He observed that the "concept of altering the human germline in embryos for clinical purposes has been debated over many years from many different perspectives, and has been viewed almost universally as a line that should not be crossed." As a result, he declared that the NIH would "not fund any use of gene-editing technologies in human embryos."[131] He also indicated that the RAC, which still had some authority

127 The RAC's focus on a particular technology, as we discuss *infra*, may have been unduly myopic, as evidenced by the ooplasm transfer matter. *See supra* text accompanying notes 115–116.

128. Recombinant DNA Research, 50 Fed. Reg. 33,462, 33,464 (Aug. 13, 1985).

129. *See supra* text accompanying notes 64–65.

130. Edward Lanphier et al., *Don't Edit the Human Germ Line*, 519 NATURE 410 (2015); David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCI. 36 (2015).

131. Francis S. Collins, *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT'L INST. HEALTH (Apr. 28, 2015), https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos [https://perma.cc/D95G-KVVM].

at that time to review novel gene therapy trials, would not "entertain proposals for germ line [sic] alteration."

Although the NIH Director discouraged such technology, he asserted that it was within the FDA's jurisdiction as part of its authority to regulate gene therapy products as biological products and/or drugs. As a result, he noted, the development of human germline modification, which could be pursued without federal funds, was still subject to the FDA regulatory process.[132]

The prospect of such research going forward so troubled Congress that, in 2016, it once again used its budgetary authority, this time explicitly, to limit germline modification. Although federally funded research of this technology was already prohibited under the Dickey-Wicker Amendment, Congress passed the Consolidated Appropriations Act to address all such research.[133] The statute prohibited the Department of Health and Human Services ("DHHS"), including the FDA, from using federal funds "to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product under . . . the Federal Food, Drug, and Cosmetic Act . . . or the Public Health Service Act . . . in research in which a human embryo is intentionally created or modified to include a heritable genetic modification."[134] In other words, the FDA could not review any germline modification protocols, even if privately funded. This limitation remains in effect today: Congress has carried forward this provision in the appropriations bills every year since then.[135]

3. GGE Regulation Going Forward

Although Congress has precluded the FDA from reviewing germline genetic modifications, it has not challenged the underlying framework that would otherwise give the FDA the same regulatory control over this technology that it has over somatic cell genetic modification. In other words, should Congress and the NIH relax their resistance to the development of GGE for clinical purposes, many believe the FDA would be the body to oversee the process,[136] especially with its claim of regulatory authority over

132. *Id.*

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

134. *Id.*

135. *See* Consolidated Appropriations Act, 2017, Pub. L. No. 115-31 §736, 131 Stat. 135, 173 (2017); Consolidated Appropriations Act, 2018, Pub. L. No. 115-141, §734, 132 Stat. 348, 389 (2018); Consolidated Appropriations Act 2019, Pub. L. No. 116-6, §731, 133 Stat. 13, 81 (2019).

136. Evita V. Grant, *FDA Regulation of Clinical Applications of CRISPR-CAS Gene Editing Technology*, 71 FOOD & DRUG L. J. 608, 626 (2016); Eli Y. Adashi & I. Glenn Cohen, *The Lumbering Crawl Toward Human Germline*, 46 L. MED. & ETHICS 1010 (2018) [hereinafter Adashi & Cohen,

somatic cell genetic modification.[137] Indeed, at least one circuit court has set a basis for including GGE within FDA authority.[138] This Section discusses how GGE might fit within the regulatory structure of the FDA along with objections to that claim of authority.

The FDA has the power to regulate drugs and medical devices under the Food, Drug, and Cosmetic Act[139] and biologics under the Public Health Service Act.[140] The regulation of drugs, devices, and biologics has some similarities.[141] For example, manufacturers (or "sponsors") must show that their product is both safe and efficacious before it can be shipped across state lines.[142] This requires an extensive approval process, including the submission of the results of human clinical trials. But the details of the regulations of each type of product differ. Manufacturers of drugs or biologics must submit an Investigational New Drug Application ("IND") in order to undergo clinical trials for those products. The application is deemed

Lumbering]; Paul Enriquez, *Editing Humanity: On the Precise Manipulation of DNA in Human Embryos*, 97 N.C. L. REV. 1147, 1197 (2019) (noting the FDA has "strong footing to assert its jurisdiction over" human germline genome editing). The FDA claims that the procedures are biological products and/or drugs within its purview: "Gene therapy products are defined for the purpose of this statement as products containing genetic material administered to modify or manipulate the expression of genetic material or to alter the biological properties of living cells. Some gene therapy products . . . fall within the definition of biological products . . . [Some] gene therapy products, such as chemically synthesized products, meet the drug definition but not the biological product definition." Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248 (Oct. 14, 1993).

137. *See supra* text accompanying notes 99–100.

138. *See* United States v. Regenerative Scis., 741 F.3d 1314, 1322 (D.C. Cir. 2014) (stating that the company failed to meet its burden of showing stem-cell product was only minimally manipulated because "the culturing process [was] designed to 'determine the growth and biological characteristics of the resulting cell population" and "appellants add[ed] substances to the cell culture that affect[ed] the differentiation of bone marrow cells"); Hallie A. Hamilton, Note, *Three-Parent Babies and FDA Jurisdiction: The Case for Regulating Three-Party in Vitro Fertilization as a Drug and Biologic*, 53 CREIGHTON L. REV. 427, 451–52 (2020).

139. 21 U.S.C. §9.

139. MACINTOSH, *supra* note 25, at 109.

140. *Id.*

140. *Id.*

141. The definition of a drug under the Food, Drug, and Cosmetic Act includes: "(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals." 21 U.S.C.A. § 321 (2020); see *Classification of Products as Drugs and Devices and Additional Product Classification*, FDA (2017), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/classification-products-drugs-and-devices-and-additional-product-classification-issues#drug [https://perma.cc/V997-JLHX] (FDA Guidance Document on the distinction between drugs and medical devices). "The term 'biological product' means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings." *Id.*

142. G&L 5th, *supra* note 3, at 262.

approved unless the FDA objects to the protocol within 30 days.[143] In contrast, for clinical trials of medical devices, manufacturers must seek Investigational Device Exemption applications.[144]

If the clinical trials are successfully completed, the manufacturers must then file an application for approval to market the product. For drugs, they must seek a New Drug Application ("NDA") and for biologics,[145] they must seek a biologics License Application ("BLA").[146] Marketing approval for medical devices is more complex because such products are divided into three classes. Only Class III devices, "significant risk devices," require an approved Premarket Approval Application ("PMA"), which is the analogue of an NDA or BLA.[147]

Although the FDA was eager to assert its authority in this domain in the mid-1980s, it took some time for it to clarify the basis of its authority and articulate how this technology fits into its regulatory structure. The challenge was, as one commentator described it, that the products of gene transfer defied "easy classification under the existing regulatory schemata of drugs, devices or biologics."[148] Neither the 1984 nor the 1991 FDA policy statement addressed whether "a medical intervention based on modification of the genetic material of living cells" was a biological product or drug.[149] Finally, in 1993 the FDA explicitly declared that the viral or retroviral vectors used to insert natural DNA in gene therapy were biologics,[150] and that "a synthetic polynucleotide sequence intended to alter a specific genetic sequence in human somatic cells after systemic administration" was a drug.[151] In 1998, the FDA categorized somatic cell gene therapy as a biological drug under the authority of what today is the Center for Biological Evaluation and Research ("CBER").[152] With the recent success in somatic cell gene therapies, there is

143. 21 C.F.R. § 312.20(c).

144. 21 C.F.R. § 812.1(a).

145. 21 C.F.R. § 314.

146. FDA Modernization Act of 1997, 21 U.S.C. §§ 355-397.

147. G&L 5th, *supra* note 3, at 263.

148. Rainsbury, *supra* note 89, at 589.

149. G&L 5th, *supra* note 3, at 264. It did imply that "[n]ucleic acids used for human gene therapy trials" were biological drugs in noting that the "same requirements" would apply to them as to "other biological drugs." *Id.* at 260 (citing 49 Fed. Reg. 50,878 (1984)).

150. Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248, 53,251 (Oct. 14, 1993). Before they had to obtain both a product and establishment license. G&L 5th, *supra* note 3, at 263.

151. *Id.* The FDA did not justify its interpretation, it merely asserted it. Rainsbury, *supra* note 89, at 589.

152. *Oversight of Gene Transfer Research*, *supra* note 126; U.S. FOOD & DRUG ADMIN., GUIDANCE FOR HUMAN SOMATIC CELL THERAPY AND GENE THERAPY: GUIDANCE FOR INDUSTRY (1998); REBECCA N. LENZI ET AL., OVERSIGHT AND REVIEW OF CLINICAL GENE TRANSFER PROTOCOLS 45 (2014); G&L 5th., *supra* note 3, at 264.

no longer any dispute that the FDA is the agency that regulates and approves products used for gene modification, at least with respect to somatic cell modifications.[153]

It is worth noting, however, that some scholars are skeptical about the certainty of the FDA's authority with respect to GGE. One view is that genetic modification for clinical uses could be argued to be a practice of medicine, which most believe the FDA lacks the authority to regulate.[154] Some argue that the FDA has been regulating other reproductive technologies like ooplasmic transfer "through letters for over twenty years," without providing "proof of jurisdiction" and contrary to "researchers' and attorneys' understanding of what the FDA regulates."[155] Others point out that the FDA has "explicitly excluded modification of germline cells from its definition of gene therapy over the last three decades," raising some question as to whether the agency actually believes it has the authority to regulate GGE at all.[156]

Others suggest that the FDA's authority to regulate this technology may be limited based on the language of the governing statute as well as the suitability of FDA procedures. For example, some have suggested that GGE would need to be "manipulated and jerry-rigged to fit the FDA's current and outdated three-category framework" of drug, biological product, or medical device because GGE products and research may not always neatly fit into those categories.[157] This would leave uncertain the FDA's jurisdiction with respect to some new technologies in this area.[158] A few point out that the FDA only has authority over products used on human subjects, but because

153. Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 51.

154. G&L 5th, *supra* note 3, at 261.

155. Myrisha S. Lewis, *How Subterranean Regulation Hinders Innovation in Assisted Reproductive Technologies*, 39 CARDOZO L. REV. 1239, 1288–90 (2018) [hereinafter "Lewis, *Subterranean*']

156. Enriquez, *supra* note 136, at 1180. Ultimately, Enriquez thinks it is unlikely that the FDA does not believe it has such authority, especially given that GGE techniques are "likely to overlap extensively with those used in present gene-therapy approaches that are in preapproval stages or have already been approved." *Id.*

157. Bob Zhao, *Mitochondrial Replacement Therapy and the Regulation of Reproductive Genetic Technologies in the United States*, 15 DUKE L. & TECH. REV. 121, 132 (2017).

158. *Id.* (suggesting this regulatory challenge "creates an environment of uncertainty" and "confusion," which "may have a chilling effect among scientists and investors who shy away from potential breakthroughs due to the unpredictability of whether the FDA will exert jurisdiction over new technologies and under which category it will be classified"); *see also* Girard Kelly, Comment, *Choosing the Genetics of Our Children: Options for Framing Public Policy*, 30 SANTA CLARA HIGH TECH. L. J. 303, 338–341 (2014); Sarah Ashley Barnett, Comment, *Regulating Human Germline Modification in Light of Crispr*, 51 U. RICH. L. REV. 553, 578 (2017). That is, the FDA may not "technically have the authority to regulate products and research protocols related to human germline modification. In other words, scientists may perform experiments on human embryos and genetic material as long as the items are not "aimed at the development of a 'product' subject to its approval.'" Eric E. Williams, *CRISPR: Redefining GMOs—One Edit at A Time*, 39 U. ARK. LITTLE ROCK L. REV. 437, 453 (2017).

genetic material, gametes, and embryos are "not technically 'human subjects,'" the FDA has no authority to regulate research or products used to genetically modify these entities.[159] Finally, some question whether "the FDA's narrowing of the scope of gene therapy to treat or cure disease could create a deep regulatory void" with respect to nontherapeutic uses of GGE.[160] Under this view, modifications for enhancement or "off-use" interventions, as opposed to treatment or prevention of disease, would not be within the FDA's purview, even if it does include other aspects of GGE.[161] Although the FDA has asserted its authority to regulate "all products related to diseases or conditions in human beings," which would include even nontherapeutic uses of such products, some believe this argument has not been persuasive.[162] Questions about FDA authority surface whenever a new gene-editing or related technology, such as cloning, develops.[163]

If the FDA does have the authority to regulate the development of GGE,[164] researchers using federal funds would first have to obtain approval at the local level from the Institutional Review Board ("IRB"),[165] which

159. Williams, *supra* note 158, at 453. *See also* Barnett, *supra* note 158, at 578; Kelly, *supra* note 158, at 338; Enriquez, *supra* note 136, at 1179–80. "Technically, the FDA has no general authority to regulate research and products related to HGM [Human Germline Modification] because gametes and embryos are not 'human subjects.'" Barnett, *supra* note 158, at 578.

160. Enriquez, *supra* note 136, at 1181.

161. "[O]nce the technology is approved for disease uses scientists could engage in "off-label" enhancement applications of germline gene therapy." Emily Marden & Dorothy Nelkin, *Displaced Agendas: Current Regulatory Strategies for Germline Gene Therapy*, 45 MCGILL L.J. 462, 476 (2000). *See* David Orentlicher, *Off-Label Drug Marketing, the First Amendment, and Federalism*, 50 WASH. U. J.L. & POL'Y 89, 91 (2016) (noting questions about the FDA's authority over off-label uses); Brooke Elizabeth Hrouda, Comment, *"Playing God?": An Examination of the Legality of CRISPR Germline Editing Technology Under the Current International Regulatory Scheme and the Universal Declaration on the Human Genome and Human Rights*, 45 GA. J. INT'L & COMP. L. 221, 230 (2016) (noting that "the FDA is required to oversee articles intended to 'diagnose, cure, mitigate, treat, or prevent disease,' but enhancements do not fit within these categories"); Zhao, *supra* note 157, at 130 (noting that "the FDA's mandate is limited to issues related to safety and efficacy, considerations regarding the 'well-being' of the research participants and of society will be neglected under the FDA's authority"); Enriquez, *supra* note 136, at 1181. This distinction may be illusory, however, because of the difficulty of drawing lines between enhancements and treatments.

162. Hrouda, *supra* note 161, at 230 (citing *Oversight and Review of Clinical Gene Transfer Protocols*, *supra* note 126).

163. *See, e.g.*, Gregory Rokosz, *Human Cloning: Is the Reach of FDA Authority Too Far a Stretch*, 30 SETON HALL. L. REV. 464, 492 (2000); Elizabeth Foley & Elizabeth C. Price, *Does the FDA Have Authority to Regulate Human Cloning?,* 11 HARV. J. L. TECH. 619 (1998); Richard A. Merrill & B.J. Rose, *FDA Regulation of Human Cloning: Usurpation or Statesmanship?*, 15 HARV. J. L. TECH 85 (2001); Gail H. Javitt & Kathy Hudson, *Regulating (For the Benefit of) Future Persons: A Different Perspective on the FDA's Jurisdiction to Regulate Human Reproductive Cloning*, 2003 UTAH L. REV. 201 (2003).

164. *See* Enriquez, *supra* note 136, at 1192–93, 1198–99.

165. *See* Institutional Review Boards, 21 CFR part 56, https://www.ecfr.gov/cgi-bin/text-idx?SID=e7ecfefdc4380c6cf81ee5b7b0af006a&mc=true&node=pt21.1.56&rgn=div5 [https://perma.cc/73QF-A3EJ] (last visited August 29, 2021).

oversees human subjects research, and from the Institutional Biosafety Committee ("IBC"), which oversees biohazard risks.[166] In addition, as described earlier,[167] manufacturers developing GGE would need to submit an IND application to undergo the clinical trials for those products. And if those trials are successful, they would then have to seek an NDA. If the products are considered biologics,[168] they would be required to seek a BLA.[169] No longer, however, is there any type of a RAC-like level of review and approval. While the NExTRAC serves as an advisory body when called upon to address issues involving emerging biotechnologies,[170] it no longer has regulatory authority. Thus, barring the creation of additional levels of oversight, GGE would be subject to the typical FDA regulatory oversight for drugs or biologics.

IV. CONTINUUM OF REGULATORY APPROACHES

Turning to the potential regulation of PGT and GGE, possible approaches range from no regulation to a complete moratorium. This section briefly explores the approaches and their benefits and drawbacks. Regulation raises questions about just what will be proscribed (which, if any, forms of PGT and GGE are permissible) and the source of regulation[171]—professional societies, state, federal, or international. As noted earlier, in the United States, reproductive technologies, such as in vitro fertilization, the use of donor gametes, or PGT, are subject to comparatively little mandatory regulation at the state and federal levels, with professional societies providing recommended standards about when and how to use the

166. U.S. FOOD & DRUG ADMIN., NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (2019).

167. *See supra* text accompanying notes 143–146.

168. Enriquez, *supra* note 136, at 1195 (focusing on the regulation of GGE as drugs or biological products, because GGE is unlikely to be deemed a "medical device"). If some forms of GGE were to be deemed medical devices, specifically Class III, "significant risk devices," they would require an approved Premarket Approval Application ("PMA"), the analogue of an NDA or BLA. *See supra* note 146.

169. 21 C.F.R. 601.2; G&L 5th, *supra* note 3, at 263.

170. National Institutes of Health, *Amended Charter*: *Novel and Exceptional Technology and Research Advisory Committee*, DEPARTMENT OF HEALTH & HUMAN SERVICES (Apr. 1 2019), https://osp.od.nih.gov/wp-content/uploads/NExTRAC_Charter_041219_508.pdf [https://perma.cc/JM3V-FJHP]. See *supra* text accompanying note 112.

171. "[T]he regulatory regime does not need to respond to germline gene editing as if it were an exceptional technology requiring substantially different regulation than traditional ART or products the FDA regulates." Myrisha Lewis, *Is Germline Gene Editing Exceptional?*, 51 SETON HALL L. REV. 735, 766 (2021) [hereinafter "Lewis, *Exceptional*"]; Heled *supra* note 48, at 296–297.

technologies.[172] By contrast, as discussed above, GGE is subject to federal administrative regulation and Congressional funding oversight.[173]

A. Laissez-Faire Through a Free Market

At one end is the possibility of a free market, or a "genetic supermarket," that would allow consumers free choice and producers to offer whatever technologies they can.[174] Such a market would be open to any consumer and any provider, in recognition of American values of autonomy and freedom.[175] Similar to the proposal of Richard Posner and Elisabeth Landes for an adoption baby market that would allow infants to be bought and sold,[176] such a market need not operate unconstrained. With respect to the adoption market, for example, Landes and Posner argued that child abuse and neglect laws should remain in place, along with some "minimal" background checks.[177] Posner suggested the possibility of additional limitations in a later article, including a prohibition on some of the normal remedies for breach, such as a prohibition by the purchasers on rejection of a baby "not in conformity with their expectations" nor requiring specific performance by the birth mother.[178]

Translating that concept to PGT and GGE would mean that the goal of regulation would be to prevent abuse of the market, such as through truth in advertising, rather than to manage the use of the technology by imposing, for example, standards based on safety testing, anti-discrimination, or other principles.[179] The underlying concept is that the market itself would self-

172. *See supra* text accompanying notes 78, 80. Surrogacy is more highly regulated than other forms of ART: it is prohibited in some states, encouraged in others. Naomi Cahn & June Carbone, *United States of America,* in EASTERN AND WESTERN PERSPECTIVES ON SURROGACY 307 (Jens Scherpe et al, eds. 2019). The regulation, however, is not in the form of safety or health standards but is instead focused on parentage determinations and, in some states, moral concerns about nonmarital individuals. *See* Courtney Joslin, (*Not) Just Surrogacy*, CAL. L. REV. (forthcoming 2021).

173. *See supra* text accompanying notes 128–170.

174. Schermer, *supra* note 31, at 10.

175. In the donor gamete context, Martha Ertman has praised an "open market in which a large number of people can participate, and a free market that flourishes because of its comparative freedom from regulation." Martha M. Ertman, *What's Wrong with A Parenthood Market? A New and Improved Theory of Commodification*, 82 N.C. L. REV. 1, 16 (2003).

176. Elisabeth Landes & Richard Posner, *The Economics of the Baby Shortage*, 7 J. LEGAL STUD. 323 (1978); Richard A. Posner, *The Regulation of the Market in Adoptions*, 67 B.U.L. REV. 59 (1987).

177. Landes & Posner, *supra* note 176, at 343–44.

178. Posner, *supra* note 176, at 67 (Posner does suggest the possibility of specific performance if harm would otherwise occur to the baby).

179. To some extent, a free market already exists with respect to editing an embryo's genome for research purposes, albeit without potential federal funding. I. Glenn Cohen & Eli Adashi*, The FDA is Prohibited from Going Germline*, 353 SCI. 545, 546 (2016). On the other hand, genome editing "followed by intrauterine transfer is precluded." *Id.* In terms of discrimination, as discussed *supra* text accompanying notes 33–34, we are concerned about two different line-drawing exercises: preventing

regulate, ensuring responsible and efficient use of the technology, and also preventing the emergence of an extralegal market, in which prices are high, but quality is low.[180] As a result, in order to market a desirable product, providers themselves would ensure the quality of gene-editing; and the market, based on supply and demand, would regulate the price.[181] It would also prevent government-sanctioned discrimination among users based, for example, on marital status or sexual orientation.[182] And, in responding to the market, suppliers would allow consumers to choose the traits they wanted. The market could be policed, not by onerous government regulation, but through tort suits brought, for example, on the basis of reproductive negligence.[183]

The value of a market system is that it would promote autonomy, patient choice, efficiency, and innovation. And the types of players who enter and survive in the market would provide useful data on the viability of the technologies and attitudes towards their use, potentially replacing the extensive process of public comments.[184] The existence of a market might result in broader awareness and acceptance of the technologies.[185]

Balanced against these potential benefits are a series of drawbacks.[186] First, even if a market system results in competitive prices, the technology will still be financially infeasible for many people. This will increase the

discrimination among users based on finances or sexual identity, for example, and ethical consideration of potential uses of the technology (if it is used to edit in ways that encourage/discourage the birth of certain kinds of people).

180. Posner, *supra* note 176, at 62 (defining a black market).

181. "[T]he paramount importance of reproductive freedom should outweigh potential concerns about access, especially in light of the fact that competition and insurance should eventually drive the price down." Deborah Zalesne, *The Intersection of Contract Law, Reproductive Technology, and the Market: Families in the Age of Art*, 51 U. RICH. L. REV. 419, 423–24 (2017).

182. *See, e.g.*, Ertman, *supra* note 175 (dangers of regulation).

183. *See e.g.*, DOV FOX, BIRTH RIGHTS AND WRONGS: HOW MEDICINE AND TECHNOLOGY ARE REMAKING REPRODUCTION AND THE LAW (2019), Dov Fox, *Causation and Compensation for Intergenerational Harm*, 96 CHI.-KENT L. REV. 139 (forthcoming 2021). Of course, such lawsuits would be available regardless of the regulatory choice.

184. *See* Mahoney & Siegal, *supra* note 45, at 212 ("The sorts of markets that emerge or fail to materialize in human germline modification services will provide crucial information about the moral judgment that actual individuals who face hard choices make in real life."). *See infra* text accompanying note 214 (addressing public comments during FDA processes).

185. *See id.*

186. *See* Ertman, *supra* note 175, at 16 (noting "quality control" and access). Many of these have been developed in response to the Landes and Posner original proposals. E.g., Kimberly D. Krawiec, *Price and Pretense in the Baby Market, in* BABY MARKETS: MONEY AND THE NEW POLITICS OF CREATING FAMILIES 42 (Michele Goodwin ed. 2009). "Baby markets may support a regime in the near future that integrates prenatal genetic screening into social welfare systems so that everyone, including low-income women of color, is encouraged to filter out certain disfavored traits." Dorothy E. Roberts, *Why Baby Markets Aren't Free*, 7 UC IRVINE L. REV. 611, 620 (2017).

economic inequities associated with gene editing or PGT.[187] Market mechanisms themselves, without further government oversight on availability of the technologies (such as through an insurance requirement) will not ensure access to those without the resources to pay.[188]

Second, the goal of many in the fertility market is profit, which does not necessarily produce incentives that are aligned with the interests of either the patients or their potential children.[189] Indeed, regardless of whether regulation requires testing to ensure the technologies are safe, patients might be willing to take risks based on the medical providers' representations about the promises of the technology.[190] This could then cause even more pressure to create or select the "perfect baby," increasing societal inequality. While "the perfect baby" might mean a child with hearing disabilities for some parents and an Olympic athlete for others, for reasons discussed earlier, such choices may not be socially or ethically desirable. A final concern is that markets commodify things of value, and reproduction and family creation are "integral to personhood."[191]

B. Guidelines Through Professional Organizations

An intermediary step towards more regulation would subject gene editing and PGT to guidelines from professional organizations,[192] or even professional societies, supplemented by a limited patchwork of state regulations with minimal oversight similar to that which typically applies to reproductive technology.[193]As Michelle Bayefsky has suggested in the context of PGT, health professionals who work in the field will have an enhanced and accurate understanding of the risks of the technology and the

187. *See supra* text accompanying note 33.

188. *See* Schermer, *supra* note 31, at 11 ("The public good of social justice, which entails that sufficient genuine opportunities to flourish are open to all, requires that [] access to reprogenetic technologies should be available for everyone equally"). Individual choice in a market could thus, on this critique, outweigh the public good. To be sure, some IVF practitioners have reduced prices for patients willing to share gametes. *E.g.*, Bourn Hall Fertility Clinic, *Egg and Sperm Sharing* (2021), https://www.bournhall.co.uk/fees-funding/free-ivf-options/free-ivf-cycle-for-egg-sharers/ [https://perma.cc/9SSE-NHFV]; Arizona Reproductive Medicine Specialists, *Shared Hope IVF Program* (2021), Gene editing does not have the same spillover benefits for other patients, however, so such an innovation is unlikely.

189. Heled, *supra* note 48, at 277; *see* Jennifer L. Rosato, *The Children of ART (Assisted Reproductive Technology): Should the Law Protect Them from Harm?*, 2004 UTAH L. REV. 57, 69 (2004) (both discuss the dangers of self-regulation).

190. Or they may not be adequately informed. *See* Cahn, *CRISPR Parents, supra* note 38, at 25–26; Ouellette et al., *supra* note 48, at 446.

191. Suter, *Giving In*, *supra* note 48.

192. Bayefsky, *supra* note 50.

193. Lewis, *Exceptional*, *supra* note 171, at 795.

needs of patients.[194] Rather than entrust the decisions concerning when GGE or PGT should be permitted to an entity that may not have the same expertise and that may be subject to political influences, a professional organization might be better suited to handle the differing interests.

Although, as discussed earlier, the ASRM has not (as of August 2021) issued guidelines concerning germline editing, it does have both practice and ethical committee guidance on aspects related to PGT.[195] Because gene-editing would presumably become one part of the add-on services offered by a reproductive endocrinology practice, according to this perspective, ASRM is well-suited to handle the relevant regulatory issues, just as it has offered guidelines with other add-on procedures.[196] That is, because it has experience providing guidance for ART practices, ASRM (or another professional organization) could apply its expertise as new reproductive technologies develop. Based on the assumption that PGT and GE are just the start of new developments in the field, ASRM would have the flexibility and knowledge to offer guidelines for future reproductive technologies. ASRM would support the existing self-regulatory norms that have developed among practitioners.[197]

The ASRM approach might range from granting discretion to individual practitioners to use their best judgment based on a number of factors, to providing more structured and definitive guidance based on ethical as well as medical considerations.[198] This more definitive guidance could help maintain a standard of best practices that might prevent a race to the bottom as clinicians felt pressure to compete for market share.[199] Moreover, because the ASRM is relatively nimble, it could initially develop stringent recommendations that might be relaxed as gene-editing technology (or other new forms of ART) becomes more established and common. In addition, the ASRM could adopt reporting requirements that would allow for the ability

194. Bayefsky, *supra* note 50, at 1164.

195. *See supra* text accompanying note 83.

196. *See, e.g.*, *Intracytoplasmic Sperm Injection (ICSI) for Non-Male Factor Infertility: A Committee Opinion*, AM. SOC'Y REPROD. MED. (Aug. 2020), https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/practice-guidelines/for-non-members/intracytoplasmic_sperm_injection_icsi_for_non-male_factor.pdf [https://perma.cc/6VXX-L53X].

197. See Lewis, *Exceptional*, *supra* note 171, at 813.

198. Bayefsky critiques the ASRM's regulation of PGT because it provides too much discretion to each clinician, resulting in "essentially limitless use of PGT." Bayefsky, *supra* note 50, at 1164.

199. *Id.* For example, as private equity firms pour into the fertility market, some physicians "worry that the new ethos of treating fertility medicine as a cash cow may lead to clinics pushing patients toward unnecessary tests and services." Rebecca Robbins, *Investor See Big Money in Infertility. And They're Transforming the Industry*, STAT (Dec. 4, 2017), https://www.statnews.com/2017/12/04/infertility-industry-investment/ [https://perma.cc/RRJ8-B5R6].

to gather data and evaluate the safety, efficacy, and usage of the technology over time. Fertility practitioners are unaccustomed to oversight beyond state medical licensing requirements and professional society recommendations, but they are familiar—and comfortable—with professional society standards and with developing individual ethical approaches to difficult issues.

Treating GGE in the same manner as other reproductive technologies would make it less exceptional (and potentially stigmatizing),[200] and might enhance innovation as well as patient choice, without the extensive supervision of a federal authority. It would ensure the development of guidelines and responsible compliance.[201]

Just as it is problematic to rely solely on the free market system, there are also downsides to relying solely on professional organizations. These drawbacks relate to development of appropriate standards and to compliance. First, establishing appropriate standards requires not just information about the technology but also consideration of the role of that technology more generally as a public good. Reporting requirements allow for evaluation over time, and the reporting interests of a professional organization may differ from those of the public. For example, the organization may be more interested in success rates of the technology. In contrast, the public might also be interested in long-term information as to health of future generations, which could be less accessible to practitioners because of the need to maintain extensive records and engage in follow-up. In addition, with a focus on protecting the market or even on the safety of the technology, professional regulation may overlook ethical issues or broader societal impacts. Moreover, even if such issues are considered, their resolution may reflect the preferences of those within the professional society, which might differ from those of patients, their children, or the public.

Second, professional organizations have no enforcement authority; they depend on voluntary compliance.[202] Relatedly, they are not accustomed to directly overseeing safety with their own members, but instead rely on the diligence and accuracy of those regulated to self-report and self-monitor any

200. *See* Lewis, *Exceptional*, *supra* note 171, at 813 (advocating for treating gene-edited children in the same manner as children born without third party interventions).

201. Although the ASRM does not know how many members comply with its recommendations, there are ways of checking, such as analyzing the decrease in number of multiple-embryo transfers or reported malpractice actions. Independent surveys have found relatively high rates of compliance with professional standards, but a 20-25% noncompliance rate. Heled, *supra* note 48, at 273–75.

202. *E.g.*, Naomi Cahn & Jennifer Collins, *Fully Informed Consent for Prospective Egg Donors*, 10 AM. MED. ASS'N J. ETHICS 49, 50–51 (2014).

problems.[203] While most practitioners will comply, and while clinics are likely to move towards best practices,[204] not all will do so. And finally, the same concerns with equity in a free market arise with professional societies. Although the technologies may be generally available, economic constraints will limit who can actually access them, and professional societies cannot overcome those barriers.[205]

To be sure, because it reflects the experiences and interests of practitioners themselves, professional society guidance provides a useful source of information,[206] regardless of which regulatory approach is chosen.

C. Oversight Through the FDA

One step further along the regulatory continuum would be relying on the combined FDA system.[207] Assuming that funding restrictions are lifted for GGE, the current system could ensure the safety and effectiveness of the procedures.[208] Given that the FDA has claimed jurisdiction over somatic cell genetic modification[209] and mitochondrial replacement therapy,[210] for example, GGE oversight could be a straightforward fit, with comparable procedures applicable.[211] In light of the FDA's mandate to advance public health, the FDA could use its authority over drugs and biological products to set appropriate uses of GGE.[212] Because the FDA does not seem to have authority to regulate PGT,[213] congressional action would be necessary to include PGT in the FDA's purview.

A variety of possibilities could be used for this approach. For example, the FDA could continue applying the current model of public consultation

203. Heled, *supra* note 48, at 277.

204. *See supra* text accompanying notes 198–199 (discussing SART reporting compliance).

205. While they can recommend insurance coverage, they cannot require it.

206. *See, e.g.*, Heled, *supra* note 48, at 305. Note that, even though they lack enforcement authority, "ASRM conducts research, publishes reports, sponsors educational outreach programs, and drafts policy guidelines for ART." Alicia J. Paller, Note, *A Chilling Experience: An Analysis of the Legal and Ethical Issues Surrounding Egg Freezing, and a Contractual Solution*, 99 MINN. L. REV. 1571, 1586 (2015).

207. Heled, *supra* note 48, at 289 (the FDA "is the natural and most promising candidate" for regulating donor reproductive tissues).

208. Schermer suggests the installation of "government programs to promote certain applications of the technology while discouraging others," such as through incentives or subsidies, and certifying centers eligible to use gene editing. Schermer, *supra* note 31, at 11.

209. *See supra* text accompanying note 110.

210. Zhao, *supra* note 157, at 129–30.

211. Mahoney & Siegal, *supra* note 45, at 212. On the other hand, there are existing "large gaps in the gene-therapy regulatory scheme," including that the FDA "has explicitly excluded modification of germline cells from its definition of gene therapy over the last three decade." Enriquez, *supra* note 136, at 1180–81.

212. *See supra* text accompanying notes 132–138; 42 U.S.C. § 262 (2020).

213. *See supra* text accompanying notes 81–82.

regarding general regulatory rules[214] and the comparatively slow but rigorous testing. Alternatively, it could use a model that provides less "top down command and control regulation" and more transparency to researchers.[215] In either case, the FDA would seek to effectuate goals of protecting consumers and promoting rigorous data collection.[216] It could continue to follow its current procedures requiring an IND and BLA.[217]

The FDA is not, however, without its critics. First, some point to the FDA's increasing lack of independence from presidential oversight and related politics.[218] As the 2011 consideration of Plan B showed, FDA new drug approval or nonapproval recommendations are subject to such oversight, even of its consideration of scientific data.[219]

Second, the FDA has a multi-step, potentially cumbersome, and sometimes secretive approach to regulation that may stifle innovation in developing new techniques.[220] During the 2020 Covid-19 pandemic, the FDA was frequently faulted for its slow response.[221] Moreover, the FDA has numerous other priorities and is not a specialized agency with a focus on reproductive or germline technology.[222]

Third, federal regulation could interfere with the doctor/patient relationship by imposing one-size-fits-all oversight.[223] This could "limit flexibility in utilizing innovative" procedures and techniques.[224] It might also infringe on the patient's procreative rights.[225] This objection is particularly salient with respect to PGT. That technology (for reasons discussed earlier)

214. As discussed *supra* text accompanying notes 123–126, the FDA's consultation regarding general rules of regulation is different from the RAC's consultation processes that focused on the approval of a particular protocol. The FDA has been criticized for its lack of public debate with respect to mitochondrial replacement therapy. Zhao, *supra* note 157, at 131.

215. Mahoney & Siegal, *supra* note 45, at 213.

216. Enriquez, *supra* note 136, at 1198–99.

217. *Id.* at 1197.

218. Eli Adashi et al., *When Science and Politics Collide: Enhancing the FDA*, 364 SCI. 628 (2019) [hereinafter "Adashi et al., *Science and Politics*"]; Myrisha S. Lewis, *Innovating Federalism in the Life Sciences*, 92 TEMP. L. REV. 383, 411, 412 (2020).

219. Adashi et al., *Science and Politics*, *supra* note 218, at 629.

220. *E.g.*, Lewis, *Subterranean*, *supra* note 155; Zhao, *supra* note 157, at 128–29, 131 (FDA not taking adequate steps to foster safe and productive research).

221. *E.g.*, Glenn E. Roper, *COVID-19 Testing Missteps Illustrate Failures of the Regulatory State*, (Apr. 7, 2020), https://thehill.com/opinion/finance/491326-covid-19-testing-missteps-illustrate-failures-of-the-regulatory-state [https://perma.cc/9G9J-B37L].

222. Accordingly, its jurisdiction may be too "broad." Zhao, *supra* note 157, at 132.

223. Ouellette et al., *supra* note 48, at 433.

224. *Id.*

225. *See* Rokosz, *supra* note 163. *But see* Christine Willgoos, Note and Comment, *FDA Regulation: An Answer to the Questions of Human Cloning and Germline Gene Therapy*, 27 AM. J.L. & MED. 101, 121–23 (2001) (noting that the FDA would not be regulating the practice of medicine, but recommending a separate advisory body to consider ethical issues).

has been regulated through the ART system, which focuses on physician and patient autonomy.

Fourth, some worry that, with the FDA's focus primarily on safety and effectiveness, it is not sufficiently attuned to considerations of the broader social or ethical implications of certain uses of the technology.[226] As discussed above, such issues fell within the purview of the RAC with respect to genetic modification. And finally, it is unclear when the current limits on FDA consideration of germline editing will be lifted.[227]

D. A Ban with Federal Oversight

The most draconian approach is some variation of a moratorium or total ban, advocated by those who are more concerned about the health risks and potential misuse of the technology, as well as concerns about its ultimate effectiveness.[228] If such a ban were imposed, violations might result in civil sanctions or even criminal sanctions.[229] Enforcing this ban might implicate the FDA, which has various forms of enforcement authority.[230]

The ban might apply to both research and clinical uses of these technologies; alternatively, various groups and scientists have recommended that research proceed, but clinical applications be banned until certain preconditions are met.[231] Alternatively, a ban might apply to GGE, but permit PGT. Or it might ban certain uses of PGT and permit GGE for limited purposes. It might be temporary, until more information is available about the long-term impact, or it might be permanent.

226. *See supra* text accompanying notes 119–122 (discussing the distinctions between the RAC and the FDA); Zhao, *supra* note 157, at 130 (noting that the FDA's focus on safety and efficacy, does not focus on the "wellbeing of research participants and society").

227. Eli Y. Adashi & I. Glenn Cohen, *Therapeutic Germline Editing: Sense and Sensibility*, 36 TRENDS IN GENETICS 315, 316 (2020).

228. "Eric Lander, Françoise Baylis, Feng Zhang, Emmanuelle Charpentier, Paul Berg and specialists from seven countries call for" a moratorium." Eric Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, 567 NATURE 195 (2019).

229. Katherine Drabiak, *supra* note 14, at 1003; Katherine Drabiak, *Emerging Governance of Mitochondrial Replacement Therapy: Assisting Coherence Between Scientific Evidence*, 20 DEPAUL J. HEALTH CARE L. 1 (2018).

230. *See, e.g.*, *Types of FDA Enforcement Actions*, FDA https://www.fda.gov/animal-veterinary/resources-you/types-fda-enforcement-actions [https://perma.cc/B9E2-QWTD] (last visited Nov. 18, 2020).

231. *E.g.*, Lander et al., *supra* note 228; Nat'l Acads., *Human Genome Editing*, *supra* note 5, at 132; Nat'l Acads., *Summit*, *supra* note 19; Press Release, Nat'l Acad. of Sci., Eng'g, & Med., *Statement on Call for Moratorium on and International Governance Framework for Clinical Uses of Heritable Genome Editing* (Dec. 3, 2015), http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a [https://perma.cc/L6T8-FUBJ] [hereinafter "2015 Call for a Moratorium"]; *see* Melanie Hess, *A Call for an International Governance Framework for Human Germline Gene Editing,* 95 NOTRE DAME L. REV. 1369, 1397 (2020).

A moratorium would be based on concerns about not just the safety and medical necessity of the technology, but also the long-term consequences of altering the germline, impact on future generations, and using these technologies not to treat diseases but for genetic enhancement or trait selection.[232]

One problem with banning the technology is that, even if it is global in reach, there will still be a black market.[233] For example, although paid surrogacy is increasingly legal in the United States, a growing number of countries are banning it.[234] The result in some countries, like China, has been a thriving underground market.[235] Second, depending on the strength of the moratorium, it could preclude responsible development of a technology with critical therapeutic benefits.

V. REGULATING ALL FORMS OF ART TOGETHER

As noted above, each of the existing regulatory alternatives presents different problems. We therefore recommend a new system that would build on the strength of the free market, the expertise of professional organizations, the authority of existing structures, and the sensitivity to ethical and moral issues. Such a system might take the form of a new entity, comparable to the Human Fertilisation and Embryology Authority ("HFEA)" in England, or it could be a special section within the FDA. Furthermore, we believe such a regulatory system should apply to all ART for the reasons described below.

A. Why All Forms of ART Should Be Regulated Together

As noted in Part III, the regulatory histories of PGT and GGE are quite different, reflecting the different realms from which they emerged. Whereas PGT developed as part of ART, for which there has been limited regulatory oversight (and none from the FDA), germline genetic modification developed out of recombinant DNA research, for which there has long been

232. Lander, *supra* note 228.

233. It is difficult to enforce a complete ban, given the cost and general availability of gene editing. Niklaus H. Evitt et al., *Human Germline CRISPR-Cas Modification: Toward a Regulatory Framework*, 15 AM. J. BIOETHICS 25, 26 (2015).

234. Christina Caron, *Surrogacy Is Complicated. Just Ask New York*, N.Y. TIMES (Apr. 18, 2020), https://www.nytimes.com/2020/04/18/parenting/pregnancy/surrogacy-laws-new-york.html [https://perma.cc/BJ4U-CJDL] (noting that "[p]aid surrogacy is now banned in Thailand, Cambodia, China and much of Western Europe").

235. Ian Johnson & Cao Li, *China Experiences a Booming Underground Market in Surrogate Motherhood*, N.Y. TIMES, (Aug. 2, 2014), https://www.nytimes.com/2014/08/03/world/asia/china-experiences-a-booming-black-market-in-child-surrogacy.html [https://perma.cc/EWS9-5YDB] (describing a black market in surrogacy, which is illegal in China); *Cf.* Suter, *Giving In*, *supra* note 48, at 297.

extensive regulatory oversight. We argue that this historical distinction based on the spheres in which each developed is no longer a viable way to shape the regulation of any form of ART. Specifically, we challenge the two different lines that have been drawn to justify special regulation for GGE as compared to other reproductive technologies. The first line is largely a historical artifact, which has resulted in arbitrarily different regulatory approaches for GGE involving recombinant DNA and other technologies that also affect the germline of future generations, such as ooplasmic transfer[236] and mitochondrial replacement therapy.[237] If the rationale for special regulation of GGE is that it alters the germline, then regulation should not depend on the manner in which such alterations occur, i.e., whether recombinant DNA is used.

The second line attempts to distinguish between reproductive technologies that directly alter the germline—like GGE, MRT, and ooplasmic transfer—and other reproductive technologies. This Article argues, however, against even that rationale for special regulation of GGE. In other words, we think this second and commonly articulated line is unsustainable as a basis for different regulatory approaches. There may be technical differences between these two types of technologies: GGE, by definition, intentionally changes the genetic makeup of the implanted embryo, while PGT does not. Nevertheless, we do not think that these are meaningful differences from a regulatory perspective because each technology ultimately influences what the germline of the resulting child will be. Indeed, any form of ART or even "natural" reproduction influences the future child's germline, which has generational and heritable impacts. The choice of a partner for reproduction, whether a known sexual partner or unknown gamete donor, will influence which genes are in the future child's germline and potentially, subsequent generations. PGT influences future generations not only in the choice of one's reproductive partner, but also in selecting among the potential progeny from that reproductive union. The choice of which embryo(s) to implant based on a desire to prevent disease or to select for traits has an impact on the genes inherited by future generations. While GGE involves modification of genes in an existing embryo, if the technique works as intended, it can act much like PGT in determining whether future generations will have certain heritable diseases or traits. In short, all reproductive technologies shape which genetic combinations will

236. *See supra* text accompanying note 115.

237. Zhao, *supra* note 157, at 126. Although if MRT was limited only to implantation of male embryos, who do not pass on the mitochondrial DNA, then there would not be a further generational transmission of the genetic modification. Adashi & Cohen, *Lumbering*, *supra* note 136, at 1010.

result in the future child, influencing the child's germline and potentially future generations.

Of course, as an emerging technology, GGE raises understandable concerns about its known risks, such as off-target effects, potential unknown risks, and the fear of passing on errors to future generations. Whether, as GGE advances, it will ultimately be riskier than other forms of ART remains to be seen and depends on the findings from research and long-term follow-up. It is worth noting, however, that when some of the current forms of ART, such as IVF, first emerged, little was known about their risks.[238] Moreover, associated risks may not be apparent when a technology is initially used; some of IVF's potential risks, for example, only emerged after it had been in use for a while.[239]

To be clear, in rejecting the lines used to treat GGE differently from PGT, we propose a regulatory framework that would cover not just GGE and PGT, but all forms of reproductive technologies that involve third parties. Our rationales are several. First, as noted above, all such technologies implicate future generations. Second, we lack important data about the long- and short-term health and societal implications of virtually all of these various technologies. For example, we have limited data about sperm donors, including how often they donate or whether they later develop health conditions that might impact donor-conceived children.[240] Nor do we have good data about health conditions, like genetic diseases, that might be diagnosed in donor-conceived children and therefore relevant to the future children of the donors. Third, to the extent that third-party participants, like egg donors, are subjected to heightened medical risks but may not technically be classified as patients,[241] appropriate oversight is important to protect their well-being.

238. "[E]xperimental reproductive techniques have been rapidly introduced on the market 'without sufficient prior animal experimentation, randomized clinical trials, or the rigorous data collection that would occur in federally funded studies.'" Zhao, *supra* note 157, at 127 (quoting Parens & Knowles, *infra* note 243, at S11). And "innovative therapy in reproductive medicine need not be subject to peer review, may not conform to current standards for informed consent, and may be offering services that have never been fully evaluated for safety and efficiency." *Id.* (quoting Parens & Knowles, *infra* note 243).

239. Ziru Yiang et al., *Genetic and Epigenetic Risks of Assisted Reproduction*, 44 BEST PRACT. RSCH. CLINICAL OBSTETRICS GYNAECOLOGY 90 (2017) (describing evidence related to genetic, especially epigenetic, risks of assisted reproduction).

240. This contrasts with the situation in other countries. In England, for example, the HFEA provides careful oversight of the number of children born per donor. *E.g.*, Naomi Cahn, *Accidental Incest: Drawing the Line – or the Curtain? – for Reproductive Technology*, 32 HARV. J. L. & GENDER 59, 84 (2009).

241. Judith Daar, *Regulating the Fiction of Informed Consent in ART Medicine*, 1 AM. J. BIOETHICS 19 (2001) (querying whether an egg donor is "treated as a patient, quasi-patient, or even non-patient by the physicians monitoring her progress in the donation process").

Technically, we would include under this regulatory umbrella any use of third-party reproductive technologies, whether it involves purchasing sperm from a commercial sperm bank, insemination under the supervision of a physician, or the use of donated sperm from a friend for personal insemination in one's own home.[242] The value of data collection exists in all such instances, but we recognize the practical difficulties of regulating the more informal uses of ART. As a result, our framework only encompasses the use of reproductive technologies that involves entities like commercial gamete and embryo banks or fertility clinics and providers because these actors are already subject to some, albeit a limited, form of regulation.

An approach that provides oversight of all reproductive technologies through one entity will thus have in place standardized systems for review of newly developing technologies. This would be an improvement over the current ad hoc system, under which the technologies are subject to varying and different regulatory systems, even though the same concerns arise as each technology appears. Further, our recommended approach can provide valuable information about existing technologies that are already widely used.

We turn now to a description of what the regulation could look like and what type of entity might exercise regulatory authority.

B. What the Regulation Would Look Like

We propose a regulatory model that would oversee reproductive technologies writ large. It would include oversight of the preclinical and clinical research, comprehensive data collection, a framework for public deliberation, the provision of educational materials, oversight of marketing and advertisements, and efforts to provide wider access to technologies. It would also cover emerging and developing technologies like GGE, MRT, and technologies that are even less ready for clinical application, like in vitro gametogenesis and reproductive cloning. In addition, it would oversee future reproductive developments that have not yet been considered or imagined. Perhaps most controversial, it would also extend to technologies that are not only in the research stage, but that are currently clinically available, like IVF, PGT, and gamete and embryo donation. While the focus would largely be

242. Whether and to what extent surrogacy would be included in such regulation depends on which aspect of surrogacy is at issue. To the extent that surrogacy involves third-party gametes, it would be regulated. Whether or not it should be permissible, however, would be left to the states. In other words, our approach toward the regulation of surrogacy would distinguish the technological aspects (involving IVF, PGT, gamete/embryo donation, etc.), which we believe should be regulated uniformly, and the parentage/commercial aspects of surrogacy, which we believe should be left to the states.

oversight of the clinical development and application of this technology, it would also include oversight of preclinical research, particularly embryonic or gamete research, that would be a necessary precursor to clinical studies.

While these various reproductive technologies are different in terms of their uses, goals, risks, etc., we believe that regulating all of them under one entity offers several benefits. Not only would it provide a tool to protect the safety and efficacy of these technologies for those who use them, those who are necessary to promote their use (like tissue donors), and the children born as a result of them, but it also could offer larger societal benefits from the initial stages of preclinical research to the ultimate clinical use of the technology. Such regulation would allow for short- and long-term data collection, public engagement, oversight of preclinical research and clinical trials, public education, regulation of marketing, and public access to the technology. We describe these types of regulatory mechanisms in more detail below.

First, instead of the current ad hoc approach to clinical innovation in reproductive technology, which often falls outside the definition of "human subjects research" and therefore is not bound by the Common Rule,[243] all developments of new reproductive technologies would be regulated. This would include regulation of research even before clinical trials are done on humans,[244] such as, research on embryos and gametes, when relevant.[245] Although such preclinical research is already required as part of the FDA approval process for any reproductive technology that is considered a drug, device, or biologic, it is not currently required for clinical innovations that fall outside the FDA's purview or that are not considered human subjects research.[246] A centralized regulatory body would address these limitations

243. "In reproductive medicine, more than in most other areas of medical practice, the line between clinical innovation and human experimentation is fuzzy." Erik Parens & Lori P. Knowles, *Reprogenetics and Public Policy: Reflections and Recommendations,* 33 HASTINGS CT. REP. S1, S6 (2003).

244. For example, Adashi and Cohen point out the greater mosaicism rates if GGE occurs in day three cleavage-stage embryos as compared with editing embryos at the time of fertilization. Adashi & Cohen, *Lumbering*, *supra* note 136, at 1011. A regulatory entity could require analysis of such outcomes.

245. Parens & Knowles, *supra* note 243, at S7 (noting that "reprogenetic techniques have been rapidly introduced on the market 'without sufficient prior animal experimentation, randomized clinical trials, or the rigorous data collection that would occur in federally funded studies'" and "that ooplasmic transplantation was advertised on the Internet before the FDA intervened to collect information and conduct hearings on the techniques safety and efficacy") (quoting Institute for Science, Law, and Technology Working Group, *ART into Science: Regulation of Fertility Techniques*, 281 SCI. 651 (1998)); *id.* at S11–12 (noting that "many new interventions in [reproductive medicine] are considered 'innovative application'—not research—by those who offer them. And since they are presented as innovative clinical practice, rather than research, oversight of them is left to the discretion of the individuals or institutions offering them").

246. Other limits on the oversight of research in this area exist. For example, because insurance does not cover many forms of ART, insurance companies "have not insisted on scrutinizing the results of

by ensuring that all innovation in ART would fall under one regulatory umbrella. Such an agency could calibrate the level and scope of regulation for each technology. GGE, for example, which involves the added step of gene editing, on top of IVF and PGT, would arguably necessitate heightened regulation to address the added manipulation that does not exist with PGT. Similarly, PGT, with its added step of genetic analysis, would require greater oversight than IVF.

Second, this broad regulatory framework would provide a central and comprehensive mechanism for data collection of the health effects on the various entities potentially affected—the women who reproduce, the children, and the providers of gametes or embryos—with a focus on both short- and long-term outcomes. At the moment, there is very limited data even with respect to the most widely used form of ART, sperm donation. We do not have consistent or centralized data about the number of cycles any donor provides, how many donations are used for reproduction (successfully or not), in what geographic locales donations are used, etc.[247] Nor do we have a central source of information about the well-being of donor-conceived children, in the short- and long-run, including whether they develop heritable or other conditions, or whether donors themselves later develop heritable conditions. Such information has been collected through informal mechanisms intended to fill this vacuum.[248] The result is that individuals seeking ART do not have complete information that may be highly relevant to selecting a donor.[249] Moreover, donors do not have comparable information either.[250]

reproductive research in the way they scrutinize other forms of medical research." Parens & Knowles, *supra* note 243, at S1, 12.

247. Yaniv Heled, *supra* note 48; Cahn, *supra* note 240, at 59.

248. *E.g.,* DONOR SIBLING REGISTRY, https://www.donorsiblingregistry.com/ [https://perma.cc/U8FZ-A9WF] (last visited May 18, 2021); Naomi Cahn, *The New Kinship*, 100 GEO. L.J. 367, 383 (2012).

249. For example, they do not have information such as how many donor-conceived children were born from a particular donor, in what geographic areas, and with what health outcomes.

250. There is evidence that some donors are interested in such information. *See, e.g.*, Lauren McMah, *Sperm Donor Fathers Reveal Struggle of Not Knowing Who Their Kids Are*, NEWS.COM.AU (July 27, 2015), https://www.news.com.au/lifestyle/parenting/sperm-donor-fathers-reveal-struggle-of-not-knowing-who-their-kids-are/news-story/670e4c0709806303436c6eeba269ae69 [https://perma.cc/9YM6-U29W] (describing the desires of some sperm donors to meet their children, including one who thinks "donors should be legally allowed to contact their offspring, not just the other way around," especially because '[p]eople who have their children up for adoption are allowed to seek their children and it's always been an inequitable issue when it comes to donor conception'"); Sarah Zhang, *The Man With 17 Kids (And Counting)*, ATLANTIC (June 17, 2019), https://www.theatlantic.com/science/archive/2019/06/sperm-donor-17-kids/591178/ [https://perma.cc/R3V7-JAWS] (describing sperm donor chose to get to know his kids and "invites them all out to a lake in California every summer"). *See also* Inez Raes et al., *The Right of the Donor to Information About Children Conceived from His or Her Gametes*, 28 HUMAN REPROD. 560 (2013)

With technologies that specifically alter the germline, such as GGE and MRT using female embryos, long-term data on the generational impacts is extremely important given the possibility of unintended consequences for not only the children born but also future generations. The need for data on generational impacts, however, is not limited to germline modifications. In the context of IVF, such data might be useful to examine, for example, the reproductive capacity of IVF-conceived children or whether potential epigenetic effects of IVF pass down to future generations. Nevertheless, with the current regulatory scheme for ART, where much of the development occurs within private institutions and there is limited interaction between such institutions and regulatory bodies like the FDA,[251] it is next to impossible to gather such data and fully understand the ways in which ART is used. Furthermore, a regulatory entity that oversees all ART would bring together the expertise in divergent scientific disciplines that are converging, but not yet coordinating, as reproductive medicine merges with genetics.[252] The result would likely provide more robust insight into the risks and ramifications of the technologies.

The collection of data would not, however, be limited to information about health, safety, and efficacy of various technologies.[253] Information could also be collected about data relevant to policy considerations regarding the use of ART, including information relevant to questions about "human *well-being*."[254] It might include, for example, data about who uses which technologies, in which contexts, for which purposes, all of which could provide useful information about the demographics and societal impacts of the different technologies, which are relevant to concerns about justice, equity, access, and treatment of those needed to support ART (like egg donors and surrogates).

In a related vein, the regulatory body would create a role for public consultation and democratic deliberation regarding the societal harms and benefits of these technologies, not just with respect to safety and the procedural mechanisms of oversight, but also with respect to public welfare understood more broadly.[255] Given that both PGT and GGE raise public welfare issues, such as exacerbating inequalities, promoting discrimination,

(describing five arguments as to why donors should be granted a right to some information about the offspring conceived by their donations).

251. Parens & Knowles, *supra* note 243 at S7; Zhao *supra* note 157, at 134.

252. Parens & Knowles, *supra* note 243 at S10.

253. Zhao, *supra* note 157, at 130 (noting that FDA's focus is limited to safety and efficacy, not the "wellbeing of research participants and society").

254. *Id.*

255. *See* Parens & Knowles, *supra* note 243, at S14.

changing norms about reproduction and parenting,[256] it makes sense to subject them to the same regulatory framework, even if that doesn't result in the same treatment for them all.

There are models of such forms of public deliberation with the HFEA in England,[257] and even in our own country, with the public hearings held by the RAC.[258] While scientific and clinical experts make up the membership of those entities, they are also interdisciplinary, intentionally including members with training in law and ethics as well as laypeople. A regulatory body with such diverse expertise would reflect the fact that the concerns regarding these technologies are not just about safety, but also concerns about public welfare and societal impacts.

The virtue of public engagement and deliberation is two-fold. First, to the extent that developments of technologies occur in secret, the failure to share data presents a potential threat to innovation,[259] while also undermining safety when information about discovered risks or side effects is not disclosed to other researchers and the public.[260] Second, some of the risks associated with ART are not limited to health and safety, but also include public and societal effects. Experts in science and medicine may be no better equipped to address those concerns than the public. We recognize, however, that there are drawbacks to public engagement, including the injection of politics into scientific decision-making.[261] We hope there are creative ways that prevent politics from swaying the critical analysis that needs to occur.

256. *See supra* text accompanying notes 32–44.

257. Zhao, *supra* note 157, at 134 (citing Cohen et al., *Transatlantic Regulation*, *supra* note 23).

258. *See supra* text accompanying notes 125–126.

259. Zhao, *supra* note 157, at 128–29.

260. After the tragic death of Jesse Gelsinger, it was discovered that a number of adverse events that occurred during gene therapy protocols were not reported to the NIH. Deborah Nelson & Rick Weiss, *Gene Test Deaths Not Reported Promptly: NIH Was Unaware of 'Adverse Events*,' WASH. POST, Jan. 31, 2000, at A1; Jeffrey Fox, *Gene Therapy Safety Issues Come to Fore,* 17 NATURE BIOTECH. 1153 (1999) (noting that although deaths that occurred during gene therapy trials were "apparently . . . reported promptly to the FDA, not all the details were shared immediately with NIH," which "points to an important issue that has dogged both NIH and FDA—how to find an appropriate balance between public disclosure and confidentiality when considering ongoing trials").

261. *See supra* text accompanying notes 218–219 (contraceptive FDA decision-making). We have witnessed the injection of politics in science to a great degree in the context of addressing the Covid-19 pandemic. *See* Joe Palca, *COVID-19 Vaccine May Pit Science Against Politics*, NAT'L PUB. RADIO (Aug. 27, 2020), https://www.npr.org/sections/health-shots/2020/08/27/906240454/covid-19-vaccine-may-pit-science-against-politics [https://perma.cc/YMP5-XDWB]; Anna Edney et al., *FDA Sets Up Vaccine Safeguards to Counter Pressure from Trump*, BLOOMBERG (Sept. 8, 2020), https://www.bloomberg.com/news/articles/2020-09-08/will-a-vaccine-be-politicized-fda-sets-up-safeguards [https://perma.cc/GKL3-PLNJ]; Aaron Blake, *Trump Injects Himself into the Vaccine Approval Process – Yet Again*, WASH. POST. (Dec. 11, 2020), https://www.washingtonpost.com/politics/2020/12/11/trump-injects-politics-into-vaccine-again-most-inopportune-time/ [https://perma.cc/ZP8B-LZ72].

A single regulatory body for all reproductive technologies could also play a pivotal role with respect to public and consumer understanding about the various technologies, including their benefits, risks, and societal implications. For newer technologies, it could also educate the public about their stage of clinical development.[262] The central regulatory body could present relevant data regarding the short- and long-term impacts of the different reproductive technologies in a single, widely publicized location. This would help prevent individuals from pursuing "risky and premature" reproductive technologies in the U.S. and other countries.[263] In addition, it would allow the public to easily compare the technologies and to avoid searching various sources for such information. Because the information might not be provided by entities with a market interest in presenting and packaging data to minimize the significance of certain risks or enhance certain successes,[264] the data would be more consistent and as "neutral" as possible. Any efforts in that regard would help promote meaningful reproductive choices.

Related to the education component of this central body would be its regulation of advertising. One of the concerns of leaving much of the development of reproductive technologies to the marketplace is the societal impact of certain individual choices, including those that might exacerbate inequities, reinforce discriminatory views, or promote unnecessary technologies with unrealistic hopes.[265] Regulation of advertising would not, in and of itself, eliminate individual choice regarding selection for or against certain traits. But it might minimize the market effects of advertising that preys on certain desires or beliefs through advertising campaigns.[266] To "'protect consumers from fraud and deception in the marketplace,'" the FTC generates advertising rules specific to particular industries.[267] In this

262. See Achim Rosemann et al., *Heritable Genome Editing in a Global Context: National and International Policy Challenges*, HASTINGS CTR. REP. 30, 40 (May–June 2019) (noting the importance of involving "multiple stakeholder organizations" in the dissemination of such information).

263. *Id.*

264. *See supra* text accompanying notes 189–190.

265. *See supra* text accompanying notes 33–34. *See* Rosemann, *supra* note 262. The controversy over egg freezing illustrates this tension. Seema Mohapatra, *Using Egg Freezing to Extend the Biological Clock: Fertility Insurance or False Hope?,* 8 HARV. L. & POL'Y REV. 381 (2014); Naomi Cahn, *Is Egg Freezing All It's Cracked Up to Be?,* FORBES (Nov. 8, 2019), https://www.forbes.com/sites/naomicahn/2019/11/08/is-egg-freezing-all-its-cracked-up-to-be/?sh=7c5733dad784 [https://perma.cc/U4AC-QXL3].

266. Suter, *Tyranny of Choice*, *supra* note 1, at 278–79, 293 (discussing both current and potential future types of advertising in "the reproductive realm that preys on certain cultural norms or needs for reassurance").

267. Sheila W. Elston, *Swipe Right for Daddy: Modern Marketing of Sperm and the Need for Honesty and Transparency in Advertising*, 13 J. HEALTH & LIFE SCI. L. 28, 36 (2020) (citing *Truth in Advertising*, FTC, https://www.ftc.gov/news-events/media-resources/truth-advertising/

context, the ART regulatory body could, in conjunction with the FTC, generate such rules for various types of ART. In addition, it would ensure that advertisements regarding various reproductive technologies were "truthful, not misleading, and, when appropriate, backed by scientific evidence."[268] The FTC requires advertisements concerning health and safety claims – which would apply in the context of ART advertising– to be supported by "competent and reliable scientific evidence –tests, studies or other scientific evidence that has been evaluated by people qualified to review it."[269] The need for such regulation of marketing is not just important with respect to new technologies like GGE, but also for all forms of ART. Yet "no FTC industry guide has been created for the marketing of sperm,"[270] despite the fact that sperm donation is the most prevalent form of ART.

One of the common concerns about many forms of ART, not just GGE and PGT, is ensuring equal access to the technology.[271] Regulation can potentially address the risk of market forces limiting access to those with the greatest resources. When access to these technologies is unequal, it promotes and exacerbates existing inequalities, and it reduces the ability to make meaningful reproductive choices for all but a few.[272] Just as professional guidelines can influence insurance coverage for various technologies, guidelines issued by this ART regulatory body could include insurance coverage of ART. At the moment, a federal regulatory body would not have the authority to directly control whether state insurance coverage was required for certain forms of ART, but it could influence decisions by state legislatures and insurance companies.[273] When employers self-insure, however, ERISA preempts state laws that relate to at least some employee

[https://perma.cc/9US8-S5BH] (last visited Nov. 18, 2020)) (noting that the "FTC can exercise notice and comment rule making and establish industry-specific advertising guidance on how particular concerns within an industry should be addressed" and that the "FTC industry guides advise industry members on how to comply with the applicable laws").

268. *Id.* Advertisers must have a "reasonable basis" or "objective evidence that supports" the claims made in advertisements." Elston, *supra* note 267; Rosemann, *supra* note 262.

269. *Advertising FAQ's: A Guide for Small Business*, FTC, https://www.ftc.gov/tips-advice/business-center/guidance/advertising-faqs-guide-small-business [https://perma.cc/EC24-5JHT] (last visited Nov. 18, 2020).

270. Elston, *supra* note 267, at 37.

271. *See supra* text accompanying note 33.

272. Schermer *supra* note 31; Suter, *Tyranny of Choice*, *supra* note 1.

273. In United States v. South-Eastern Underwriters Association, 322 U.S. 533 (1944), the Supreme Court ruled that insurance is part of interstate commerce and subject to the Commerce Clause, overturning an earlier decision, Paul v. Virginia, 75 U.S. 168 (1869), which had held that insurance was not interstate commerce. To resolve any uncertainty about the power of the states to regulate insurance, Congress enacted the McCarran-Ferguson Act of 1956, which delegated the regulation of the "business of insurance" to the states. 15 U.S.C. §§ 1011-1015 (1956). While Congress does have authority to mandate that insurance plans cover various procedures (consider the ACA's birth control mandate), such a mandate requires explicit action, which may not be easy to achieve.

benefit plans, limiting the reach of state laws to expand insurance coverage in this realm. The regulatory body could recommend Medicaid coverage as well as expansion of essential health benefits to include some form of ART under the Affordable Care Act ("ACA").

The issue of increasing access to reproductive technologies is complex, however. First, there is resistance to insurance coverage of many forms of ART.[274] Second, although increased access would reduce disparities with respect to who could use these technologies, expanded access might normalize certain uses of the technology. In one sense, a broadened capacity of all groups to reproduce would be good for the public. But it could also potentially have negative societal impacts, for example, by enabling reproductive choices that reject certain traits and promote discriminatory views.

Finally, a unified regulatory body overseeing reproductive technologies would provide a mechanism to be proactive regarding the development of future embryonic or gamete therapies and treatments. Not only would there be guidelines for necessary preclinical and clinical research based on the development of existing reproductive technologies, but there would also be a central location of regulators familiar with the kinds of issues and concerns that might arise in this context. Such a regulatory body could be tasked with promoting innovation in this area, something that some have criticized the FDA for failing to do.[275]

Although we do not provide the precise regulatory structure for this body, we do note that it could fulfill many of the functions described above by engaging in several functions: (1) licensing entities that provide reproductive technologies, such as fertility clinics, embryo and gamete banks, etc., to engage in ART and for particular uses of ART; (2) monitoring those entities for compliance and quality control; (3) developing practice guidelines and "codes of practices"; (4) collecting and publishing data to

274. Some courts have held that infertility is not a disease, and therefore infertility treatments should not be covered. *See. e.g.*, Krauel v. Iowa Methodist Medical Ctr., 95 F.3d 674, 679 (8th Cir. 1996); Witcaraft v Sundstrand Health and Disability Group Benefit Plan, 420 N.W. 2d 785 (Iowa 1988); Egert v. Connecticut General Life Insurance Co., 900 F.2d 032 (7th Cir. 1990). There is still no federal law mandating insurance coverage for ART (and Medicaid does not cover infertility treatments); however, states are slowly passing legislation that requires private insurance to cover ART. Currently, "sixteen states have laws on insurance coverage for infertility treatment," some of which require insurers to make coverage for some forms of ART available, others require insurance coverage of some infertility treatments. Meghan E. Vreeland, *Artful Dodging: States' Reliance on The Medical Expense Income Tax Deduction as a Failure to Provide Inclusive Coverage for Infertility*, 40 WOMEN'S RIGHTS L. REP. 211, 215–16 (2019).

275. See *supra* text accompanying note 220.

share with the public; and (5) providing mechanisms for public debate and deliberation.[276]

C. Possible Regulatory Entities/Options for ART Regulations?

There are two potential approaches to achieving the centralized regulation of ART in a single entity. The first would be to build on the existing FDA structure. As noted above, many already presume it has the authority to regulate GGE.[277] A trickier issue would be whether the FDA has authority over PGT and the collection, banking, and sale of embryos and gametes beyond the prevention of communicable diseases.[278] Whether those actions would constitute more than minimal manipulation of tissues or whether congressional action would be required to expand the scope of the FDA's regulatory oversight is an unresolved issue.

The virtue of using the FDA is that it already exists, with a structure and system in place for oversight from the research to the marketing phase of ART technologies. However, because many of the regulatory goals we envision include levels of oversight that do not currently exist within the FDA, substantial adjustments would be necessary. First, and most important, the FDA's authority would have to be broadened beyond just oversight of approved products to actual uses of the technology, a dramatic reshaping of the FDA's role.[279] Second, the FDA would need to expand—and in some cases develop—rigorous data collection methods.[280] Third, it would need to be more "efficiently structured to deal with novel fields that are developing as rapidly as reproductive genetics," a problem that arises because its authority is so broad in encompassing "all therapeutics."[281] Fourth, it would have to provide the transparency necessary to deliver the kind of reporting and public education that our regulatory system envisions,[282] which may be inconsistent with its sometimes secretive approach to review.[283] Fifth, it

276. We note that others have recommended similar kinds of oversight for certain types of ART, but not for all ART as we suggest. See Zhao, *supra* note 157, at 133 (focusing on germline genetic modification); Parens & Knowles, *supra* note 243, at S18 (focusing on reprogenetics).

277. *See supra* text accompanying note 136–138.

278. *See supra* text accompanying note 81–82.

279. Kathy L. Hudson, *Preimplantation Genetic Diagnosis: Public Policy and Public Attitudes*, 85 FERTILITY & STERILIZATION 1638, 1639 (2006) (noting that the FDA "could not restrict the actual use of [certain] products by PGT providers); Zhao, *supra* note 157, at 132 (noting the "FDA's authority is too narrow" in extending only to drugs, biologics and devices).

280. Enriquez, *supra* note 136, at 1198–99.

281. Zhao, *supra* note 157, at 132.

282. Mahoney & Siegal, *supra* note 45, at 213.

283. *See supra* text accompanying note 220; Lewis, *Subterranean Regulation*, *supra* note 155; Lewis, *Exceptional*, *supra* note 171, at 43; Zhao, *supra* note 157, at 128–29, 131 (describing the FDA as not taking adequate steps to foster safe and productive research).

would either have to assume a more comprehensive role in advertising, which is currently limited to advertisements for prescription drugs, some medical devices, and procedures[284] , or coordinate with the FTC, to generate advertising rules for the ART community.[285] Sixth, it would have to expand its involvement of the public, which currently only consists of consultation regarding regulatory rules[286] and which tends to focus on the safety and procedural mechanisms of oversight as opposed to the societal harms and benefits.[287] Seventh, because the FDA has not historically issued guidance with respect to matters of access and insurance coverage[288] and other "moral and philosophical issues of the technology,"[289] restructuring would be necessary to create such a role for the FDA. Finally, the FDA would either have to coordinate with NExtTRAC or create such an entity within itself to be proactive with respect to innovation and development of new reproductive technologies and treatments.[290]

Rather than try to restructure the FDA to add types and levels of oversight that do not currently exist, not to mention expanding the breadth of the technologies it reviews,[291] an alternative would be to create a new

284. *Prescription Drug Advertising: Questions and Answers*, FDA (2015), https://www.fda.gov/drugs/prescription-drug-advertising/prescription-drug-advertising-questions-and-answers [https://perma.cc/S578-68KF].
(last visited Nov. 18, 2020). *See also Prescription-Drug Advertisements,* 21 CFR § 202.1.

285. *See supra* text accompanying note 268.

286. *See supra* text accompanying note 214; Zhao, *supra* note 157, at 131. There have been statements from leadership in the FDA, however, hinting that there may be an interest in greater stakeholder inclusion in the FDA's future, at least with respect to "public health objectives." Anna Abram, the FDA's Deputy Commissioner for Policy, Planning, Legislation and Analysis, for example, expressed such an aspiration in September 2017:

> As part of my commitment to help oversee the development and implementation of key policy issues, and to help advance these broader policy efforts, I've been working closely with FDA Commissioner Scott Gottlieb, M.D., and other senior agency colleagues, to explore ways to modernize our regulations in a manner that will benefit all Americans. . . . As part of this process we're asking ourselves and others to think about how current regulations could be reshaped to achieve our public health objectives through more efficient approaches. We are opening a number of public dockets to solicit feedback from patients, consumers, health providers, caregivers, industry, health groups, academia, as well as state, local and tribal governments, and public health partners. We're also exploring other opportunities to solicit input from stakeholders on this effort. We believe that engaging both internal and external stakeholders are critical to focusing our attention on where our policies might need updating; to ensure FDA's work maximizes our public health purpose.

Anna Abram, *FDA's Plan to Engage The Public in The Agency's New Effort to Strengthen and Modernize FDA's Regulatory Framework*, FDA (Sept. 7, 2018) https://www.fda.gov/news-events/fda-voices/fdas-plan-engage-public-agencys-new-effort-strengthen-and-modernize-fdas-regulatory-framework [https://perma.cc/3XVH-7VZP] (last visited Oct. 8, 2021).

287. *See supra* text accompanying note 255; Parens & Knowles, *supra* note 243, at S14.

288. *See supra* text accompanying note 274.

289. Zhao, *supra* note 157.

290. *See supra* text accompanying note 218.

291. Zhao, *supra* note 157, at 131.

entity. One example is the HFEA in England,[292] which licenses, monitors, and inspects fertility clinics; provides comprehensive oversight of the development and uses of new technologies; collects data about fertility treatments; and provides "free, clear and impartial information about fertility treatment, clinics and egg, sperm and embryo donation."[293] The virtue of an entity that focused solely on ART is that it could be structured around, and peopled with, scientific, clinical, and bioethics experts with knowledge of the special issues surrounding reproductive technologies. A regulatory body with such diverse expertise would be well-positioned to evaluate not just the safety and efficacy of new and existing technologies, but also their societal impact. Just as the HFEA offers a form of public deliberation,[294] so too could a new regulatory body.

Whether it would be more difficult to restructure the FDA and challenge some of its existing norms and practices to accommodate the kinds of regulation we envision or to create a new regulatory entity from scratch is an important question, politically and logistically. Ultimately, our focus is less on the body that would provide such regulation and more on the nature of the regulation.

Whatever form the entity ultimately takes, we recommend the creation of an advisory commission, which would include members of professional associations and experts in the various fields.[295] Not only would this provide important expertise, but it would address the industry's desire to play a part in its regulation. While it would not fully satisfy its strong preference for self-regulation, it would avoid the opposite extreme of regulation by a government entity without a seat at the table.

292. *See* Ouelette et al., *supra* note 48. In 2004, Canada enacted the Assisted Human Reproduction Act ("AHR Act"), which establishes a system that closely mirrors England's HFEA. *See* Assisted Human Reproduction Act (S.C. 2004, c. 2); s*ee also* Erin L. Nelson, *Comparative Perspectives on the Regulation of Assisted Reproductive Technologies in the United Kingdom and Canada*, 43 ALBERTA L. REV. 1023 (2006) ("The Canadian response to the burgeoning science of assisted reproduction has paralleled that of the U.K. . . . Once it is in place, the AHRA, like the HFEA, will have the power to issue, suspend, renew, amend and revoke licences for treatments or research involving AHR techniques; inspect clinics and labs to ensure health and safety; maintain confidential personal health information pertaining to donors, patients and offspring born of AHR procedures; advise the Minister of Health and to monitor national and international policy developments; and provide information to the public on the operations of the agency and ART issues, including public reports on outcomes.").

293. *About Us*, HUMAN FERTILISATION & EMBRYOLOGY AUTH., https://www.hfea.gov.uk/about-us/ [https://perma.cc/V4QU-F4CF] (last visited Nov. 18, 2020) describing the functions of the HFEA). *See also* Ouellette et al., *supra* note 48, at 420–24.

294. Zhao, *supra* note 157, at 134 (citing Cohen, *Transatlantic Regulation*, *supra* note 23).

295. Parens & Knowles, *supra* note 243, at S18 (recommending a "Reprogenetics Technologies Advisory Commission" to "engage the public, stakeholder, and expert constituencies in consultation; articulate the ethical commitments that must guide such a regulatory effort; and draft the terms of reference for embryo research, including the limits, restrictions, and prohibitions").

VI. OBJECTIONS TO ANY FORM OF OVERSIGHT

Numerous scholars have raised questions about federal government oversight of forms of ART for a variety of reasons.[296] First, and perhaps most fundamentally, are concerns about reproductive autonomy[297] and the right to use ART. Such concerns are based on assumptions about the existence of a "broad theory of procreative liberty."[298] Such a theory protects not only the right not to reproduce but also the right *to* produce through alternative forms of procreation that include control of an offspring's genes.[299] The basis for procreative liberty is arguably not just constitutional jurisprudence, grounded in historical conceptions of privacy[300] and reproductive rights, beginning with *Griswold,* but also in principles of parental autonomy that accord "special weight" to parental decision-making.[301] Accordingly, new reproductive technologies should be protected from regulation because "'individuals should be free to have children by any means that science permits.'"[302] Based on a conception of procreative rights that focuses on individual autonomy, any limitations would be subject to rigorous (either strict or intermediate) constitutional scrutiny.[303] Even under a strong version

296. *E.g.,* Lewis, *supra* note 218, at 387 (noting that the "FDA does not have exclusive jurisdiction over innovative life sciences techniques and also how the FDA's regime is inadequate to regulate these techniques"); Myrisha S. Lewis, *Halted Innovation: The Expansion of Federal Jurisdiction over Medicine and the Human Body,* 2018 UTAH L. REV. 1073, 1093 (2018) ("Similarly, while CRISPR-Cas9 will likely involve a delivery method (so as to deliver the "product" that will edit the relevant gene(s)), the gene editing itself would not be an "article"; as such the entire technique would not fall within the FDA's jurisdiction."). Of course, some have argued that federal entities, like the FDA, have the authority to regulate in this area. *See supra* text accompanying notes 136-138, 150-153. Hank Greely tartly notes: "The FDA has asserted its power to regulate human reproductive cloning, mitochondrial transfer, and human germline genomic editing by calling the modified human embryos 'drugs' or 'biological products,' but this is probably not what Congress had in mind in the 1938 Federal Food, Drug, and Cosmetics Act or the 1944 Public Health Service Amendments." Henry T. Greely, *The Law of the Tetrapods*, 22 VAND. J. ENT. & TECH. L. 251, 259 (2020).

297. "A right to make reproductive decisions free from state interference arose in response to sterilization and antimiscegenation laws and has since been used to strike down bans on contraception and abortion. The Supreme Court has not considered whether autonomy or privacy rights encompass decisions involving the use of assisted reproductive technologies." Dov Fox, *Racial Classification in Assisted Reproduction*, 118 YALE L.J. 1844, 1881–82 (2009).

298. *See* Suter, *Repugnance Lens*, *supra* note 12, at 1528.

299. *See id.*; John A. Robertson*, Assisting Reproduction, Choosing Genes, and the Scope of Reproductive Freedom,* 76 GEO. WASH L. REV. 1490, 1511 (2008) ("the freedom to screen, identify, and perhaps even alter genes should follow from the standard accounts of reproductive autonomy").

300. *E.g*., Tandice Ossareh, Note, *Would You Like Blue Eyes with That? A Fundamental Right to Genetic Modification of Embryos*, 117 COLUM. L. REV. 729, 754 (2017).

301. Enriquez, *supra* note 136, at 1160 (failing to suggest that the right would be absolute).

302. Suter, *Repugnance Lens*, *supra* note 12, at 1561.

303. Courtney Megan Cahill, *Reproduction Reconceived*, 101 MINN. L. REV. 617, 674 (2016). *See* Susan Frelich Appleton, *Between the Binaries: Exploring the Legal Boundaries of Nonanonymous Sperm Donation*, 49 FAM. L. Q 93 (2015). For an argument that intermediate scrutiny would be appropriate, see

of reproductive autonomy rights, some limitations might be permissible if, for example, potential uses of the technology would infringe the health of any resulting child.[304]

An alternative source of procreative liberty might be equality theory, which emphasizes the social and physical aspects of a woman's choice to control whether and when to become a parent.[305] This decision affects all aspects of a woman's life, beyond her health, such as her education, work, societal expectations.[306] Moreover, parenting obligations continue to fall more heavily on women than men. As a result, for example, caring for a child born with a serious illness would impact the day-to-day life of women more than men. Protecting a right to decide whether and when to become a parent would support, at the least, the right to prevent future offspring from suffering from debilitating illnesses that could affect parenting.[307]

On the other hand, such a right to procreative liberty, regardless of whether it is based on autonomy, equality, or parental rights, is not explicitly based in Supreme Court jurisprudence. This means that objections to regulation on this basis may not serve as a bar. *Skinner v. Oklahoma*, which protected procreation as a "basic civil right," arose long before contemporary assisted reproductive technology became medically possible.[308] Later Court decisions on the right to reproductive liberty focused only on the right not to reproduce[309] and thus provide limited support for an expansive right to reproduce that would include genetic modification.

In addition, although sex equality jurisprudence protects against sex-based discrimination, decisions to modify an embryo do not directly implicate this form of equality. Moreover, while PGT and GGE might promote sex-based equality, a critique based on disability-equality provides "a different kind of equality argument against constitutional protections of these technologies [arguing] that the availability and use of such technologies promotes an attitude that the 'normal' or appropriate response

Fernando Montoya, *Intergenerational Control: Why Genetic Modification of Embryos via CRISPRCas9 is Not a Fundamental Parental Right*, 60 AM. U.L. REV. 1015 (2020).

304. Ossareh, *supra* note 300, at 762–63.

305. Suter, *Repugnance Lens*, *supra* note 12, at 1561–62.

306. *See, e.g.*, JUNE CARBONE & NAOMI CAHN, MARRIAGE MARKETS: HOW INEQUALITY IS REMAKING THE AMERICAN FAMILY (2014) (impact of childbearing on women's economic opportunities); Deborah Widiss, *Equalizing Parental Leave*, 105 MINN. L. REV. 2175 (2021).

307. Suter, *Repugnance Lens*, *supra* note 12, at 1562. Disability theories, of course, provide a counter to this right. *Id.* at 1563.

308. 361 U.S. 535, 541 (1942).

309. Griswold v. Connecticut, 85 U.S. 1678 (1965); Eisenstadt v. Baird, 92 U.S. 1029 (1972); Roe v. Wade, 93 U.S. 705 (1973); I. Glenn Cohen, *The Constitution and the Rights Not to Procreate*, 60 STAN L. REV. 1135, 1150 (2008).

to identifying a defect in the fetus or embryo is to prevent the existence of the future child."[310]

A second, and related, set of objections concerns the imposition of greater oversight for PGT and GGE than for coital reproduction. Sexual behavior and family relationships occur within a constitutionally-protected zone of privacy that includes the bedroom[311] and parental decision-making, which is somewhat insulated (in both positive and negative ways) from mainstream legal doctrines in other aspects of the law, such as tort and contract.[312] By contrast, an individual who wants to use reproductive technologies is subject to public regulation (in part because someone else needs to produce and supply those technologies). The "sex/non-sex binary" is, according to this argument, intrusive,[313] setting extra obstacles for those outside of traditional procreation. Regulation thus exceptionalizes the use of ART, drawing a perhaps untenable distinction between sexual and alternative forms of reproduction.[314] This distinction, accordingly, might be challenged on legal grounds, as infringing protected due process rights to reproduce. Another variation of this argument is that doctors can self-regulate and ensure informed consent for GGE (and other forms of ART) without an extra layer of regulation beyond existing state licensing standards.[315]

The problem with this anti-regulation argument is that there may be significant reasons to treat sex and non-sex forms of reproduction differently. Non-sex forms of reproduction typically involve professionals,[316] who have a fiduciary relationship to their patients, one that is trust-based; an individual consults a medical professional to draw on that professional's expertise. A professional who mispresents the patient's ability to control a child's traits should be sanctioned; an intimate partner who misrepresents a family history

310. Suter, *Repugnance Lens*, *supra* note 12, at 1563.

311. *Griswold*, 85 U.S. at 1678; *Eisenstadt*, 92 U.S. at 1029; Lawrence v. Texas, 539 U.S. 558 (2003).

312. Kaiponanea Matsumura, *Reproductive Exceptionalisms*, FAMILY L. JOTWELL (Jul. 3, 2020), https://family.jotwell.com/reproductive-exceptionalisms/ [https://perma.cc/3HRV-GTEL] (reviewing DOV FOX, BIRTH RIGHTS AND WRONGS: HOW MEDICINE AND TECHNOLOGY ARE REMAKING REPRODUCTION AND THE LAW (2019)) (showing benefits and drawbacks of this "exceptionalism").

313. Cahill proposes a "unitary system of reproductive regulation grounded in intent." Cahill, *supra* note 303, at 689 (Cahill does not address PGT or GGE). She suggests that *Obergefell* is an obstacle to efforts to regulate alternative forms of reproduction if such regulation sets up separate rules for sexual and nonsexual procreation. Courtney Megan Cahill, *Obergefell and the "New" Reproduction*, 100 MINN. L. REV.: HEADNOTES 1, 12 (2016). Attempts to regulate PGT and GGE would, based on this theory, constitute a distinctive, potentially unconstitutional, set of rules.

314. *Id*. at 619.

315. Lewis, *Subterranean*, *supra* note 155, at 1288.

316. While not all third-party sperm use involves a professional, virtually all other forms of non-sex reproduction, including those addressed in this article, require professional involvement.

perhaps should not.[317] Non-sex forms of reproduction, which sometimes rely on third-party tissue donors, constitute a new technology that has not yet been tested. By contrast, sexual reproduction is part of human evolution. Moreover, protecting patients and their children is a core government function.

Third, regulation in this area raises concerns about the potential imposition of majoritarian values on very personal decisions.[318] Particularly in areas involving the intersection of sex, family, and intimacy, there is a healthy skepticism of state regulation, even well-intentioned state regulation designed to ensure safety. Other countries, for example, regulate who is eligible to use in vitro fertilization based on marriage and sexual orientation.[319] Similarly, people in the disability community (as discussed earlier) might feel their interests were not being respected or that regulations discriminate against them.[320] Allowing government intervention in such personal matters as creating a child—regardless of the constitutionality of such action —cannot, according to this argument, adequately consider the differing needs, concerns, and values of potential parents. Not only is the government "both less invested in the well-being of each" potential parent than are the parents themselves, but also "the state has far less appreciation of the relevant factors and information to determine whether" use of PGT or GGE "is in the best interest" of the potential parents and child.[321] Political influences on government regulation can result in less-than-optimal decision-making.[322]

317. Matsumura, *supra* note 312. There are, of course, arguments that sexual partners owe one another some duties. "Some courts have found that a sexual relationship may, but does not always, give rise to a duty of care necessary for a negligence claim, thus creating grounds for liability if a person with an STI fails to take caution to prevent transmission—including notifying their partner of the risk." Alexandra Brodsky, "*Rape-Adjacent": Imagining Legal Responses to Nonconsensual Condom Removal*, 32 COLUM. J. GENDER & L. 183, 198 (2017).

318. "Decisions relying on the public policy doctrine can sometimes obscure the courts' endorsement of specific normative positions." Kaiponanea T. Matsumura, *Public Policing of Intimate Agreements*, 25 YALE J.L. & FEMINISM 159, 215 (2013); *see* Martha M. Ertman, *What's Wrong with A Parenthood Market? A New and Improved Theory of Commodification*, 82 N.C. L. REV. 1, 22 (2003).)

319. For example, in 2010, Germany's Federal Constitutional Court "considered it constitutional that public health insurance covered the costs of in vitro fertilization only for married couples." Anne Sanders, *Marriage, Same-Sex Partnership, and the German Constitution*, 13 GERMAN L.J. 911, 935 (2012). In the United States, a "tax court decision, *Magdalin v. Commissioner*, however, suggests the deductibility of IVF services is limited to medically infertile, married, opposite-sex couple." I. Glenn Cohen & Daniel L. Chen, *Trading-Off Reproductive Technology and Adoption: Does Subsidizing IVF Decrease Adoption Rates and Should It Matter?,* 95 MINN. L. REV. 485, 577 (2010).

320. *See supra* text accompanying notes 34, 310.

321. Suter, *Repugnance Lens*, *supra* note 12, at 1596.

322. For example, "[i]n 1992, the Recombinant DNA Advisory Committee was pressured by a member of Congress to approve a gene transfer intervention for a constituent with advanced brain cancer." Christine Coughlin et. al., *Regenerative Medicine and the Right to Try*, 18 WAKE FOREST J. BUS. & INTELL. PROP. L. 590, 637 (2018); *see supra* text accompanying note 219 (discussion of Plan B).

Rather than "indulg[ing] the misplaced view that, if something important is at stake, law should regulate it," one could argue against regulation in this area. The intent would be to avoid a slippery slope of regulation that begins with a focus on safety and limited interventions (drawing a line between therapy and enhancements, for example) and that might end up determining which patients can use the technologies.[323] It is not just that drawing appropriate lines is difficult and complicated, but also that such lines must be constantly reviewed as the technology advances. Avoiding such a slippery slope with continued reassessment of regulations might be difficult.

On the other hand, it remains important to acknowledge that, even in the absence of explicit regulation, the law still defines the space for development, whether that is hands-off development or highly regulated development.[324] And there is an argument that the government gets the balance of all interests right and therefore "adequately" considers the needs of the parents, even if it is less invested in their well-being. In other words, parents might overstate their needs/interests vis-à-vis all the relevant interests that the government considers. In addition, depending on the normative vision that defines the government's role, the benefits of regulation may justify its costs. A normative vision of promoting fairness, economic equity, anti-discrimination, and other public goods supports one type of regulation, while a normative vision associated with protecting patient autonomy, privacy, and the industry supports a different type of regulation.

Of course, the process of line drawing and selecting which normative framework should govern in this (or any other area) is difficult and potentially risky— lines might be drawn that, in retrospect, stifled innovation or permitted a technology to move forward before proof of its safety.[325] On the other hand, using its police powers to protect the public and ensure responsible use of new technologies is the purpose of government.[326] For the

323. Cahn, *supra* note 248, at 406.

324. *Id.* at 407. As Hank Greely notes, "[n]othing is not regulated, even when some technologies are not regulated by dedicated agencies. The decision to avoid a dedicated agency is not just a decision against one kind of (expert) regulation, it is one in favor of another, more general, kind." Greely, *supra* note 296, at 260. Maxwell Mehlman, *Modern Eugenics and the Law, in* A CENTURY OF EUGENICS: FROM THE INDIANA EXPERIMENT TO THE HUMAN GENOME ERA (Paul Lombardo ed., 2011) ("A number of practices typically are thought of as private rather than public decision making. But the fact that the law permits them to take place indicates a measure of public acquiescence, if not approval").

325. Stolberg, *supra* note 106, at 137.

326. Parens & Knowles, *supra* note 243, at S14 ("One of the government's responsibilities is to promote the public welfare, and how reprogenetic technologies are developed and disseminated will affect the public welfare").

government to fulfill that purpose, it must consider how new assisted reproductive technologies might affect communities "by promoting and exacerbating inequity and [then] balance it against the possible threat to the family of banning genetic enhancement of offspring. Ultimately, we should consider the effects on all relationships, with special attention to those most affected by such regulations, the families themselves."[327]

Finally, and most pragmatically, the reproductive technology industry has resisted further regulation, claiming that it is already highly regulated and that self-regulation is adequate.[328] The involvement of the industry is critical to the success of any regulatory program going forward, so its opposition could be a significant obstacle. That means that the development of a single regulatory structure must include consultation with the industry and then include industry advisers for any entity that is ultimately created.

CONCLUSION

As reproductive technologies advance in new directions, the regulatory structure has not yet developed to respond fully and appropriately.[329] The current sources of regulation are fragmented,[330] leading to some lack of clarity about what entity should be responsible for the regulation. Moreover, there is no consensus about the circumstances under which these new technologies can or should be used, even though these technologies affect not only individuals, but also the public welfare. This paper suggests directions for moving forward, with one entity responsible for future regulation and for developing appropriate scientific and ethical guidelines for all forms of ART.

327. Suter, *Repugnance Lens*, *supra* note 12, at 1597.

328. Michael Ollove, *States Not Eager to Regulate Fertility Industry*, PEW (Mar. 18, 2015), https://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2015/3/18/states-not-eager-to-regulate-fertility-industry [https://perma.cc/MQ4U-545D].

329. Gaia Bernstein, *The Socio-legal Acceptance of New Technologies: A Close Look at Artificial Insemination*, 77 WASH. L. REV. 1035 (2002).

330. PGT and GGE are subject to different schemes, for example. *See supra* Part III.B–C.