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HUMAN REPRODUCTIVE CLONING, HERITABLE GENOME EDITING, AND THE FUTURE OF NOVEL REPRODUCTIVE TECHNOLOGIES

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This Article compares human reproductive cloning (HRC) and heritable genome editing (HGE) to identify factors that encourage bans on novel reproductive technologies. HRC drew legislative opposition in part because it involved asexual reproduction and was incorrectly associated with copying. HGE and other technologies that involve sexual reproduction do not have those problematic qualities. HRC also became entangled with research in which human embryos were cloned to be harvested for their stem cells. HGE did not because scientists learned how to create and edit pluripotent stem cells without creating embryos. However, the legal history of HRC predicts that reproductive technologies strongly associated with embryo destruction will face fierce opposition. Targets for future prohibition may include: pronuclear transfer, a subtype of mitochondrial replacement therapy in which two fertilized eggs are destroyed to reconstruct one; and in vitro gametogenesis, a futuristic process in which couples create hundreds of embryos while discarding the vast majority based on their genetic profiles.

HGE has not been banned, in part because an appropriations rider has prevented the Food and Drug Administration (FDA) from authorizing clinical trials. If the rider were amended to permit consideration of applications to correct mutations that cause serious monogenic diseases, this Article predicts that legislators would not enact bans. However, if genetic enhancements became feasible in the future, difficult policy issues, including impacts on future generations, would arise. Rather than debate these issues, Congress might keep the rider in place, thereby obviating the need for bans on HGE for enhancement.

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I. INTRODUCTION

In 1997, Ian Wilmut and Keith Campbell announced they had cloned a lamb named Dolly from the somatic cell of an adult sheep.[1] In 1998, the United States Food and Drug Administration (FDA) claimed authority over human reproductive cloning (HRC) and stated that it would not grant permission for clinical trials.[2] The United States Congress then tried for years to outlaw HRC but failed to achieve a political consensus.[3] Meanwhile, seventeen states banned HRC.[4] Thus, even though no baby has ever been born through cloning,[5] legislators have reacted strongly against HRC.

Compare heritable genome editing (HGE), in which technicians edit human gametes or embryos before using them to conceive a baby[6] who can pass the edit to descendants through her own

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[1] *See* Ian Wilmut et al., *Viable Offspring Derived from Fetal and Adult Mammalian Cells*, 385 NATURE 810 (1997). For a detailed account of the experimental process, *see* IAN WILMUT & ROGER HIGHFIELD, AFTER DOLLY: THE USES AND MISUSES OF HUMAN CLONING 107–25 (2006).

[2] *See* Elizabeth C. Price, *Does the FDA Have Authority to Regulate Human Cloning?*, 11 HARV. J. L. & TECH. 619, 625 (1998).

[3] *See* KERRY LYNN MACINTOSH, HUMAN CLONING: FOUR FALLACIES AND THEIR LEGAL CONSEQUENCES 180–85 (2013) [hereinafter MACINTOSH, HUMAN CLONING]. For more on these efforts, *see infra* text accompanying notes 14–21.

[4] *See id.* at 185–86. For a fuller discussion of state laws, *see infra* text accompanying notes 24–31, 34–35.

[5] *See* Henry T. Greely, *Human Reproductive Cloning: The Curious Incident of the Dog in the Night-time*, STAT (Feb. 21, 2020), https://www.statnews.com/2020/02/21/human-reproductive-cloning-curious-incident-of-the-dog-in-the-night-time/ [hereinafter Greely, *Human Reproductive Cloning*]. In 2002, Brigette Boisselier, a member of the Raelian religious sect, boasted that she had cloned a human baby. *See* Emma Young, *First Cloned Baby "Born on 26 December"*, NEWSCIENTIST (Dec. 27, 2002), https://www.newscientist.com/article/dn3217-first-cloned-baby-born-on-26-december/. Even though she provided no proof, the media published her claim, *see* Stephen S. Hall, *Eve Redux: The Public Confusion over Cloning*, 33 HASTINGS CENT. REP, 11 (2003), thereby encouraging the public to believe that cloning was either a reality or an inevitability. *See* Art Caplan, *Media Bungled Clone Claim Coverage*, NBC NEWS (Nov. 17, 2003), https://www.nbcnews.com/id/wbna3076566.

[6] This Article does not discuss other forms of human genome editing. Thus, it does not cover the FDA's recent approval of a treatment for sickle cell disease that involves the genome editing of bone marrow stem cells. *See FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease*, FDA (Dec. 8, 2023),

gametes.[7] Congress has adopted an appropriations rider that bars the FDA from acknowledging receipt of applications to conduct clinical trials of HGE.[8] However, Congress has not enacted a permanent ban,[9] nor have any states.[10] Thus, even though babies with edited genomes have been born in China,[11] legislators have not reacted as powerfully against HGE.

Congress has the power to amend or eliminate the appropriations rider and allow the FDA to receive applications for

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https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease; *see also* Sara Reardon, *FDA Approves First CRISPR Gene Editing Treatment For Sickle Cell Disease*, SCI. AM. (Dec. 8, 2023), https://www.scientificamerican.com/article/fda-approves-first-crispr-gene-editing-treatment-for-sickle-cell-disease/.

[7] *See* NAT'L ACAD. OF SCIS. & NAT'L ACAD. OF MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 52 (2017) [hereinafter "2017 Report"].

[8] *See* KERRY LYNN MACINTOSH, ENHANCED BEINGS: HUMAN GERMLINE MODIFICATION AND THE LAW 124–25 (2018) [hereinafter "MACINTOSH, ENHANCED BEINGS"]. The rider, which is enacted along with the annual appropriations bill, appeared most recently in the Consolidated Appropriations Act, 2023. *See* Consolidated Appropriations Act, 2023, 117 Pub. L. No. 328, tit. VII, § 737, 136 Stat. 4459, 4504 (2022). It provided:

> None of the funds made available by this Act may be used to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product under Section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or Section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)) in research in which a human embryo is intentionally created or modified to include a heritable genetic modification. Any such submission shall be deemed to have not been received by the Secretary, and the exemption may not go into effect.

Id.

[9] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 123.

[10] *See id.* at 132. On October 3, 2023, searches for the term "genome" or "germline" returned no state laws in the Genome Statute and Legislative Database of the National Human Genome Research Institute. *See Genome Statute & Legislation Database*, NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/about-genomics/policy-issues/Genome-Statute-Legislation-Database (last visited Oct. 3, 2023).

[11] *See* THE NAT'L ACADS. OF SCIS., ENG'G, AND MED., SECOND INTERNATIONAL SUMMIT ON HUMAN GENOME EDITING: CONTINUING THE GLOBAL DISCUSSION 2 (2019), https://doi.org/10.17226/25343 [hereinafter "NASEM 2018"].

clinical trials of HGE or other novel reproductive technologies. Suppose it does so, placing the FDA in a position to approve such trials. Even then, trials cannot be held in a state where the legislature bans the technology—or in *any* state if Congress (perhaps in a later session with a different political majority) enacts a ban. Thus, it would be helpful to know which factors are likely to inspire bans of such technologies. To identify such factors, this Article compares HRC and HGE and their legal histories.

Part II theorizes that HRC was banned because legislators had not yet developed confidence in FDA regulation of novel reproductive technologies. Part III explains that legislators were hostile to HRC because society viewed asexual reproduction via cloning as a more radical departure from human norms than HGE or other forms of sexual reproduction. Part IV contends that legislators overlooked HRC's potential as an infertility treatment due to dismissive attitudes that had softened by the time HGE came along. Lastly, Part V argues that HRC was banned because it became entangled in the politics of stem cell research and the destruction of human embryos—a quandary that HGE avoided due to scientific advances that made it possible to generate pluripotent stem cells without embryos.

This Article then applies the foregoing analysis to predict the legal futures of several novel reproductive technologies. It concludes that legislators may ban pronuclear transfer, a subtype of mitochondrial replacement therapy in which two fertilized eggs are destroyed to reconstruct one. Legislators may also eschew in vitro gametogenesis, a futuristic process in which couples create hundreds of embryos while discarding the vast majority based on their genetic profiles. However, legislators are unlikely to ban HGE when it is used to correct genetic mutations that cause serious monogenic diseases. Genetic enhancements would be more controversial; however, if they become feasible in the future, Congress may use the appropriations rider to prevent clinical trials while sidestepping messy policy debates and bans.

II. FDA REGULATION

This Part reviews the history of HRC and HGE, in that order. It then discusses the possibility that legislative activity against HRC declined as confidence in FDA regulation grew. Such confidence might also have inspired the appropriations rider that made it possible to halt clinical trials of HGE without the need for bans.

A. *Human Reproductive Cloning*

The federal war on HRC commenced in earnest in 1998. In January of that year, physicist Richard Seed declared he would become the first to clone a human being.[12] The Biotechnology Industry Organization (BIO) wrote to the Secretary of Health and Human Services inviting federal regulation; a few days later, the FDA claimed authority over HRC and asserted that Seed could not proceed without its permission.[13]

Nevertheless, in February 1998, Senate Majority Leader Trent Lott (R-Miss.) pushed the Senate to criminalize all human cloning without committee review or public debate.[14] If this bill had become law, scientists convicted of cloning human embryos for lab research (research cloning) would have been felons and sent to prison for ten years.[15] Senators Ted Kennedy (D-Mass.) and Dianne Feinstein (D-Ca.) led a filibuster and Senator Lott's bill failed.[16] Finally, in October 1998, the FDA sent a letter to the institutional review boards of medical and research institutions, warning them not to conduct clinical trials of HRC without its permission, but simultaneously asserting that it would not grant permission due to unresolved safety concerns.[17]

Congress could have decided that the FDA had HRC under control and that no further action was necessary. However, that did not happen. In 2001 and 2003 the U.S. House of Representatives passed bills to impose a total ban on all human cloning, including research cloning.[18] These bills did not become law because some members of the U.S. Senate wanted to protect research cloning.[19] In 2007, the House voted on a different bill that would have prohibited HRC but allowed research cloning.[20] This bill failed to garner a majority because

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[12] *See* Price, *supra* note 2, at 623.

[13] *See id.* at 624–25.

[14] *See Senators Stumble in Rush to Outlaw Cloning*, SCIENCE (Feb. 11, 1998), https://www.science.org/content/article/senators-stumble-rush-outlaw-cloning.

[15] *See* Human Cloning Prohibition Act, S. 1601, 105th Cong. (1998).

[16] *See* Lizette Alvarez, *Senate, 54-42, Rejects Republican Bill to Ban Human Cloning*, N.Y. TIMES (Feb. 12 1998), https://www.nytimes.com/1998/02/12/us/senate-54-42-rejects-republican-bill-to-ban-human-cloning.html.

[17] *See* Stuart L. Nightingale, Associate Commissioner, *Letter about Human Cloning*, FDA (Mar. 15, 2018), https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/letter-about-human-cloning.

[18] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 181.

[19] *See id.*

[20] *See id.* at 184.

conservative members opposed research that destroyed cloned human embryos.[21]

Why did Congress pursue legislation for several years when the FDA had already claimed jurisdiction over HRC? The answer may lie in the limited scope of FDA authority. In 2001, the Director of the Center for Biologics Evaluation and Research (CBER), an FDA Center that regulates biological products,[22] was forced to admit before a Congressional subcommittee that the FDA would not stop clinical trials if HRC were proven safe for the child and gestational mother.[23] Given the political climate, there was little chance the FDA would reach such a conclusion; but the Director's admission may have invigorated efforts to enact a federal ban.

State legislatures also acted against HRC, but with greater success. For example, in 1997, the California State Legislature enacted an HRC moratorium that was scheduled to sunset in 2003.[24] In 2002, a blue-ribbon commission issued a report (California Report) recommending that HRC be banned permanently.[25] The California State Legislature heeded this recommendation; it eliminated the sunset provision[26] and banned HRC.[27] Connecticut, Illinois, Iowa, Maryland, Massachusetts, Missouri, Montana, New Jersey, and Virginia also enacted laws that prohibited HRC only.[28]

Meanwhile, in 1998, Michigan became the first state to enact a comprehensive ban on all human cloning,[29] including lab research on cloned human embryos.[30] Following Michigan's example, Arizona, Arkansas, Indiana, North Dakota, Oklahoma, and South Dakota

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[21] *See id.* at 185.

[22] *See About CBER*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/about-cber (last updated Jan. 31, 2024).

[23] *See Issues Raised by Human Cloning Research: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 107th Cong., Serial No. 107-5, 78, 90 (2001) (statement of Dr. Kathryn C. Zoon, Director, Center for Biologics Evaluation and Research, FDA) [hereinafter "Zoon testimony"].

[24] *See* KERRY LYNN MACINTOSH, ILLEGAL BEINGS: HUMAN CLONES AND THE LAW 86 (2005) [hereinafter MACINTOSH, ILLEGAL BEINGS].

[25] *See* CALIFORNIA ADVISORY COMMITTEE ON HUMAN CLONING, CLONING CALIFORNIANS? REPORT OF THE CALIFORNIA ADVISORY COMMITTEE ON HUMAN CLONING 1 (2002) [hereinafter CALIFORNIA REPORT].

[26] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 86.

[27] *See* CAL. HEALTH & SAFETY CODE §§ 24185, 24187 (2023).

[28] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 186.

[29] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 85–86.

[30] *See* MICH. COMP. LAWS §§ 333.16274, 333.16275, 333.20197, 750.430a (2023).

prohibited all human cloning, including research cloning.[31] Thus, the same ideological divide over research cloning that prevented Congress from enacting anti-cloning legislation produced a legislative split among states.

Despite the political furor over research cloning, reputable scientists did not report success in deriving embryonic stem cell lines from cloned human blastocysts until 2013.[32] Ironically, by then, interest in legislating against human cloning had waned. In 2015, a member of the House of Representatives introduced the last federal bill to ban all human cloning.[33] Rhode Island enacted the last state ban on HRC in 2013,[34] but its law expired in 2017.[35]

B. *Heritable Genome Editing*

Now, compare the history of HGE. In 2015, Chinese scientists announced that they had used the CRISPR/Cas 9 molecular editing tool to modify the genomes of human embryos.[36] Only three years later, in November 2018, He Jiankui of China declared that he had edited the genomes of human embryos and transferred those embryos to women.[37] Twin girls had been born and a third child was in gestation.[38] His experiment was immediately condemned as unsafe and unethical.[39] Some reacted by demanding an international moratorium on HGE for

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[31] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 185–86.

[32] *See* Masahito Tachibana et al., *Human Embryonic Stem Cells Derived by Somatic Cell Nuclear Transfer*, 153 CELL 1228 (2013). In 2004 and 2005, Korean scientist Hwang Woo Suk claimed to have cloned human blastocysts and derived embryonic stem cell lines from them. *See* Woo Suk Hwang et al., *Patient-specific Embryonic Stem Cells Derived from Human SCNT Blastocysts*, 308 SCIENCE 1777 (2005); *see also* Woo Suk Hwang et al., *Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst*, 303 SCIENCE 1669 (2004). His data were fabricated and his publications were retracted. *See generally Editorial Retraction*, 311 SCIENCE 335 (2006), https://www.science.org/doi/10.1126/science.1124926. The Hwang affair led scientists to discuss how to prevent future frauds. *See* David B. Resnik, Adil Shamoo & Sheldon Krimsky, *Fraudulent Human Embryonic Stem Cell Research in South Korea: Lessons Learned*, 13 ACCOUNTABILITY RSCH. POL'YS AND QUALITY ASSURANCE 101 (2006).

[33] *See* Human Cloning Prohibition Act of 2015, H.R. 3498, 114th Cong. (2015).

[34] *See* R.I. Gen. L. § 23-16.4-2 (2013).

[35] *See id.* at § 23-16.4-4.

[36] *See* Puping Liang et al., *CRISPR/Cas9-mediated Gene Editing in Human Tripronuclear Zygotes*, 6 PROTEIN & CELL 363 (2015).

[37] *See* NASEM 2018, *supra* note 11, at 2.

[38] *See id.*

[39] *See id.* at 3, 8.

a set time, with individual nations moving forward thereafter only if a broad societal consensus emerged in favor of a specific use.[40] Others worried that allowing any modifications to the human germline would open the door to human enhancement.[41]

Yet, the scientific community maintained an open mind. In 2020, the U.S. National Academy of Medicine, U.S. National Academy of Sciences, United Kingdom Royal Society, and International Commission on the Clinical Use of Human Germline Genome Editing issued a report on HGE (2020 Report).[42] Their charge was to define a responsible pathway if a nation decided to permit clinical use of HGE.[43] The 2020 Report reviewed the science and concluded that HGE was not yet safe for clinical use.[44] However, it reasoned that some carriers of genetic mutations for serious[45] monogenic diseases were either unable to create unaffected embryos or made so few that they had already failed to conceive following one cycle of in vitro fertilization (IVF) with preimplantation genetic testing (PGT).[46] Accordingly, it created a pathway detailing all the scientific and regulatory steps that must be completed in order to transition HGE from basic research to clinical use for those carriers.[47] This translational pathway mandated that the genetic mutations be changed to a common genetic sequence that did not cause disease.[48]

In 2023, the U.S. National Academy of Sciences, United Kingdom Royal Society and Academy of Medical Sciences, and UNESCO's World Academy of Sciences convened the Third International Summit on Human Genome Editing.[49] At the end of this

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[40] *See* Eric Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, 567 NATURE 165 (2019).

[41] *See* Roberto Andorno et al., *Geneva Statement on Heritable Human Genome Editing: The Need for Course Correction*, 38 TRENDS BIOTECH. 351, 353 (2020).

[42] *See generally* NAT'L ACAD. OF MED. ET AL., HERITABLE HUMAN GENOME EDITING (2020) [hereinafter "2020 Report"].

[43] *See id.* at xi. The 2020 Report considered the societal and ethical issues surrounding HGE to be beyond its charge and thus did not provide an analysis of them. *See id.* at 93. However, it acknowledged that a nation must discuss and resolve such issues before deciding to validate a particular use of the technology. *See id.* at 161.

[44] *See generally id.* at 89–93.

[45] The 2020 Report defined "serious" to mean "a life-shortening disease that causes severe morbidity or premature death." *Id.* at 124.

[46] *See* 2020 Report at 101–04, 108–10.

[47] *See generally id.* at 123–38.

[48] *See id.* at 124.

[49] *See* National Academies, *Third International Summit on Human Genome Editing: Expanding Capabilities, Participation, and Access:*

event, the Organizing Committee for the Summit issued a statement cautioning that clinical use of HGE was still unacceptable and would remain so until there was further public discussion, establishment of governance frameworks and ethical principles for responsible use, and proof of safety and efficacy.[50] However, the important point here is that reputable scientists continue to entertain the possibility that HGE may one day be put to clinical use.

To be sure, that day will not come anytime soon in the United States. The FDA has regulatory oversight of HGE.[51] However, since 2015, Congress has enacted an annual appropriations rider that prevents the FDA from acknowledging receipt of any application to conduct clinical trials of HGE.[52] The legislative history is sparse, but indicates Congress was concerned about safety and ethical issues.[53] Yet, Congress has not pursued legislation to prohibit or control HGE in a more direct and durable manner.[54] Nor has any state legislature outlawed HGE.[55]

C. *Possible Explanation*

Federal attempts to ban HRC have subsided and the last state ban was enacted a decade ago.[56] Biological limitations do not explain this decline in legislative interest. Scientists have cloned many species,[57] including primates,[58] suggesting human births remain possible. Nor has public opinion changed: in Gallup polls conducted

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Proceedings of a Workshop in Brief 1 (2023), [hereinafter "National Academies, *Third International Summit"*].

[50] *See id.* at 13.

[51] *See* Francis S. Collins, *Statement on NIH Funding of Research Using Gene-editing Technologies in Human Embryos*, NAT'L INSTS. OF HEALTH (April 29, 2015), http://www.nih.gov/about/director/04292015_statement_gene_editing_technologies.htm.

[52] *See supra* text accompanying note 8.

[53] *See* H.R. Rep. No. 114-205, at 69 (2015).

[54] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 123.

[55] *See id.* at 132; *see also supra* text accompanying note 10.

[56] *See supra* text accompanying notes 32–34.

[57] Animals that have been cloned include cattle, goats, sheep, pigs, horses, dogs, cats, mice, rats, rabbits, among others. *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 7.

[58] *See* Zhen Liu et al., *Cloning of Macaque Monkeys by Somatic Cell Nuclear Transfer*, 172 CELL 881 (2018) (describing the cloning of macaque monkeys from fetal fibroblasts).

from 2002 to 2023, over eighty percent of respondents have consistently deemed HRC morally unacceptable.[59]

What factor accounts for this decline in anti-cloning legislation? As explained above, after the Director of the CBER admitted that the FDA would not block clinical trials if HRC were safe,[60] anti-cloning legislation may have seemed necessary. However, when decades passed and no human clones were born, federal and state legislators may have realized that the FDA had managed to dissuade scientists from performing clinical trials in the United States. In other words, federal regulation eventually did what the BIO hoped it would do: calm legislators down while bringing HRC to a halt.

Federal regulation may also explain HGE's sparse legislative track record. Long before the first babies were born in China, Congress had adopted the appropriations rider, thereby ensuring that the FDA could not grant permission for clinical trials of HGE.[61] With the FDA in charge, yet unable to approve trials, Congress did not have to engage in the contentious policy debates that had marked HRC.[62] Likewise,

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[59] *See Moral Issues*, GALLUP, https://news.gallup.com/poll/1681/Moral-Issues.aspx (last visited Sept. 23, 2023); *see also* David Masci, *20 Years After Dolly the Sheep's Debut, Americans Remain Skeptical of Cloning*, PEW RSCH. CTR. (Feb. 22, 2017), https://www.pewresearch.org/short-reads/2017/02/22/20-years-after-dolly-the-sheeps-debut-americans-remain-skeptical-of-cloning/#:~:text=Still%2C%20a%20majority%20of%20adults,no%20change%20in%20these%20numbers.

[60] *See supra* text accompanying notes 22–23.

[61] *See supra* text accompanying notes 52–53.

[62] Today, the appropriations rider may further guard against HRC by preventing the FDA from acknowledging receipt of applications for clinical trials. HRC creates an embryo by merging the nuclear DNA of one person with a donor egg that carries its own mitochondrial DNA. *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 47, 50. If a child results from that embryo, she could pass nuclear and mitochondrial DNA to future offspring, so this process is arguably one "in which a human embryo is intentionally created or modified to include a heritable genetic modification." Consolidated Appropriations Act, 2023, 117 Pub. L. No. 328, tit. VII, § 737, 136 Stat. 4459, 4504 (2022). Moreover, the FDA believes the rider covers a similar technology known as mitochondrial replacement therapy (MRT). *See Advisory on Legal Restrictions on the Use of Mitochondrial Replacement Techniques to Introduce Donor Mitochondria into Reproductive Cells Intended for Transfer into a Human Recipient*, U.S. FOOD AND DRUG ADMIN. (Mar. 16, 2018), https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/advisory-legal-restrictions-use-mitochondrial-replacement-techniques-introduce-donor-mitochondria?source=govdelivery. [hereinafter *Advisory on Legal Restrictions on the Use of Mitochondrial*

some state legislatures might not have bothered to outlaw HGE because they were reasonably certain that scientists would not use HGE without FDA permission—a permission that could not be granted.

If this line of reasoning is correct, two inferences can be drawn. First, FDA regulation has emerged as a significant barrier to the implementation of novel reproductive technologies. This barrier becomes impenetrable when Congress uses purse strings to keep the FDA from carrying out its mission. Second, when federal and state legislators are confident that the FDA will not or cannot allow clinical trials, they may be lulled into a state of complacency and not bother to ban reproductive technologies.

Legislative inactivity is desirable because it creates breathing room for novel reproductive technologies. Even if FDA regulation prevents clinical trials, basic scientific research has time to advance and societal attitudes have an opportunity to evolve. Eminent scientific organizations may feel emboldened to create a translational pathway, as they have done for certain medical uses of HGE.[63] Later, if a reproductive technology advances to the point where it is reasonably safe for gestating parents and children, Congress may amend or lift the rider, and the FDA may grant permission for clinical trials. The trials may then proceed in the absence of federal or state bans.

III. HRC IS PERCEIVED AS A RADICAL DEPARTURE FROM STANDARD HUMAN REPRODUCTION

Lawmakers may also have treated HRC and HGE dissimilarly because the technologies themselves are different. Specifically, lawmakers may have perceived HRC as a more radical departure from standard human reproduction than HGE. This Part examines three possible reasons for this perception: HRC is a form of asexual reproduction; HRC is falsely believed to be a method of making human copies; and HRC is incorrectly framed as a manufacturing process.

Replacement Techniques]. MRT resembles HRC in that it combines the nuclear DNA of intended parent(s) with the mitochondrial DNA of an egg donor. *See infra* text accompanying notes 176–78. The FDA would probably choose to expand its own authority and reason by analogy that the rider must also extend to HRC.

[63] *See supra* text accompanying notes 42–48.

A. *Cloning Is Asexual Reproduction*

In sexual reproduction, sperm joins with egg to create an embryo with its own unique blend of chromosomes and genes.[64] If the embryo is gestated and born, the baby will have two genetic parents.[65] Sexual intercourse is the traditional method of bringing gametes together.[66] IVF is a newer method of sexual reproduction in which technicians unite sperm and eggs in the lab to create embryos for transfer to a patient seeking to get pregnant.[67] HGE is also sexual reproduction: technicians edit the genomes of gametes before combining them in the lab to create embryos for transfer; or technicians combine unmodified gametes to create embryos, and then edit the genomes of those embryos prior to transfer.[68]

By contrast, in HRC, a scientist may begin by fusing a somatic cell to an enucleated egg to create a cloned human blastocyst.[69] The next step in the process—which has not yet been performed successfully—is to transfer that embryo for gestation to an intended parent, who gives birth to a baby nine months later.[70] Because HRC does not combine gametes, HRC is a type of asexual reproduction in which a single person—the somatic cell donor—passes nuclear DNA down to the resulting child.[71]

Asexual reproduction is not uncommon on Earth. For example, a bacterium reproduces by dividing into two cells, or clones.[72] Some

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[64] *See Sexual Reproduction*, BIOLOGY ONLINE, https://www.biologyonline.com/dictionary/sexual-reproduction (June 16, 2022).

[65] *See id.*

[66] *See id.*

[67] *See* PRESIDENT'S COUNCIL ON BIOETHICS, HUMAN CLONING AND HUMAN DIGNITY: AN ETHICAL INQUIRY 59 (2002) [hereinafter HUMAN CLONING AND HUMAN DIGNITY]. For a detailed description of the steps involved in the IVF process, *see* SHERMAN J. SILBER, HOW TO GET PREGNANT 174–79, 201–02, 222–23, 233–35, 238–39 (Little, Brown & Co. rev. ed. 2005, paperback ed. 2007).

[68] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 11–12.

[69] *See* Tachibana, *supra* note 32 (describing the experiment that created embryonic stem cells derived from cloned human blastocysts).

[70] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 47.

[71] *See* Katheryn D. Katz, *The Clonal Child: Procreative Liberty and Asexual Reproduction*, 8 ALB. L.J. SCI. & TECH. 1, 14 (1997). The child inherits mitochondrial DNA from the person who provided the egg for the procedure. *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 47, 50.

[72] *See, e.g.*, *Bacteria*, MICROBIOLOGY SOC'Y, https://microbiologysociety.org/why-microbiology-matters/what-is-microbiology/bacteria.html#:~:text=Most%20bacteria%20reproduce%20by

plants can reproduce asexually and sexually, including onions,[73] potatoes,[74] and aspen trees. [75] Certain animals can also reproduce asexually and sexually, including worms,[76] wasps, ants, starfish, and some sharks. [77] However, mammals, including human beings, generally reproduce sexually; thus, HRC deviates from the reproductive norm for our species.[78] In light of these facts, some conclude HRC is "unnatural,"[79] while others assert asexual reproduction does not deserve the same constitutional protection as sexual reproduction.[80]

B. *Cloning Is Falsely Believed to Be Copying*

As indicated above, sexual reproduction produces a baby who inherits a unique blend of chromosomes and genes.[81] HGE does not alter that basic fact. To be sure, scientists may edit gametes before using them to conceive an embryo, or use unmodified gametes to conceive an embryo that is then edited.[82] But either way, the process of combining gametes still yields a nuclear genome that no other person has.

%20binary,divides%20into%20two%20 (replicates) (last visited Nov. 9, 2023).

[73] *See How Do Onions Reproduce?*, HOME GARDEN VEGETABLES (June 8, 2021), https://homegardenveg.com/how-do-onions-reproduce/.

[74] *See* BENNY ORDONEZ, MATILDE ORRILLO, & MERIDETH BONIERBALE, INT'L POTATO CTR., POTATO REPRODUCTIVE AND CYTOLOGICAL BIOLOGY 7 (2017), https://potatoassociation.org/wp-content/uploads/2018/05/Potato-reproductive-and-cytological-biology.pdf.

[75] *See Quaking Aspen*, NAT'L WILDLIFE FED'N, https://www.nwf.org/Educational-Resources/Wildlife-Guide/Plants-and-Fungi/Quaking-Aspen#:~:text=Quaking%20aspens%20can%20reproduce%20via,from%20a%20single%20root%20system (last visited Nov. 9, 2023).

[76] *See* Steven A. Ramm, *Exploring the Sexual Diversity of Flatworms: Ecology, Evolution, and the Molecular Biology of Reproduction*, 84 MOL. REPROD. & DEVELOP. 120, 123–24 (2017).

[77] *See* Katherine Gallagher, *12 Animals that Reproduce Asexually*, TREEHUGGER (Dec. 13, 2022), https://www.treehugger.com/animals-that-reproduce-asexually-5112566.

[78] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 14.

[79] *E.g.*, CALIFORNIA REPORT, *supra* note 25, at 31.

[80] *See* Lori B. Andrews, *Is There a Right to Clone? Constitutional Challenges to Bans on Human Cloning*, 11 HARV. J. L. & TECH. 643, 666 (1998).

[81] *See supra* text accompanying notes 64–65.

[82] *See supra* text accompanying note 68.

HRC differs in that a child shares nuclear DNA with a single parent.[83] For that reason, the media have often depicted human clones as identical multiples.[84] Science fiction movies and television series have done the same, serving up menacing images of clone armies,[85] Hitler clones,[86] doppelgangers,[87] and so on.[88] Such portrayals are not harmless fun; research indicates that narratives, including fictional ones, hold the power to shift the beliefs and attitudes of those who consume them into alignment with those narratives.[89]

Science tells a different story. Since Dolly was born, animal experiments have shown that clones have bodies and personalities that differ from those of their somatic cell donors.[90] Genetic mutations, mitochondria inherited from the egg, epigenetic changes, and environmental factors may account for these differences.[91] A human clone would be subject to the same influences[92] and more: she would grow up within a family, school, and community, all of which would shape her intellect, values, and beliefs.[93]

Unfortunately, politicians often seem to be unaware of these facts. For example, after Dolly was born, President Bill Clinton said, "Each human life is unique, born of a miracle that reaches beyond laboratory science. I believe we must respect this profound gift and resist the temptation to replicate ourselves."[94] When Congress debated HRC, members complained that HRC was a threat to individuality and described clones as replicas or duplicates.[95] Governmental advisory bodies stacked with experts did little better: they admitted human

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[83] *See supra* text accompanying note 71.

[84] *See* Patrick D. Hopkins, *Bad Copies: How Popular Media Represent Cloning as an Ethical Problem*, 28 HASTINGS CTR. REP. 6-9 (Mar.–Apr. 1998).

[85] *See* STAR WARS II: ATTACK OF THE CLONES (Twentieth Century Fox 2002).

[86] *See* THE BOYS FROM BRAZIL (Twentieth Century Fox 1978).

[87] *See* THE SIXTH DAY (Columbia Pictures 2000); MULTIPLICITY (Columbia Pictures 1996).

[88] For an account of these and other stories with similar themes, *see* MACINTOSH, HUMAN CLONING, *supra* note 3, at 78–81, 131–33, 148–51.

[89] *See* Kurt Braddock & James Price Dillard, *Meta-analytic Evidence for the Persuasive Effect of Narratives on Beliefs, Attitudes, Intentions, and Behaviors*, 83 COMMC'N MONOGRAPHS 446, 460–63 (2016).

[90] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 33–37.

[91] *See id.*

[92] *See id.* at 47–53.

[93] *See id.* at 54–55.

[94] Hopkins, *supra* note 84, at 9.

[95] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 93.

clones would not be copies,[96] but speculated that human clones would suffer from impaired individuality, diminished autonomy, or both.[97] This concern for uniqueness is specific to cloning and may account for much of the legislative animus towards HRC.

C. *Cloning Is Incorrectly Framed as Manufacture*

Critics have long argued that IVF treats children as manufactured products.[98] This derogatory characterization is inapt. The word "product" denotes an item manufactured or grown for sale, often in large quantities.[99] IVF cannot manufacture a specific child; rather, it brings gametes together in the lab to form embryos.[100] When a baby is born from one of these embryos, she is not fungible or multitudinous in the way that a toothbrush or microwave oven is. Rather, she is a human being with a random and unique nuclear genome.[101]

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[96] *See* NAT'L BIOETHICS ADVISORY COMM'N, CLONING HUMAN BEINGS, REPORT AND RECOMMENDATIONS OF THE NATIONAL BIOETHICS ADVISORY COMMISSION 67 (1997) [hereinafter "NBAC REPORT"] (describing concern that cloning yields identical bodies and personalities as "scientifically inaccurate"); *see also* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 102 (conceding that "our genetic makeup does not by itself determine our identities").

[97] *See* CALIFORNIA REPORT, *supra* note 25, at 25; *see also* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 102–04; NBAC REPORT, *supra* note 96, at 66–69.

[98] *See, e.g.*, James McTavish, *Why the Church Says "Yes" to Life and "No" to IVF*, 89 THE LINACRE Q. 450, 452 (2022).

[99] *See Product*, CAMBRIDGE DICTIONARY, https://dictionary.cambridge.org/us/dictionary/english/product (last visited Dec. 17, 2023).

[100] *See supra* text accompanying note 67.

[101] To be sure, some parents screen their IVF embryos and discard the ones that contain chromosomal abnormalities or genetic mutations that cause disease. *See* Michelle Bayefsky, *Who Should Regulate Preimplantation Genetic Diagnosis in the United States?*, 20 AMA J. ETHICS E1160, 1160, 1162–63 (2018). However, the technology is not novel enough to enable them to screen and select an IVF embryo that carries desirable but complex traits such as intelligence or height. *See* Jocelyn Kaiser, *Screening Embryos for IQ and Other Complex Traits Is Premature, Study Concludes*, SCIENCE (Oct. 24, 2019), https://www.science.org/content/article/screening-embryos-iq-and-other-complex-traits-premature-study-concludes. Even if they could select for such traits, their choices would be limited to embryos within their own combined gene pool. *See* PRESIDENT'S COUNCIL ON BIOETHICS, REPRODUCTION AND RESPONSIBILITY: THE REGULATION OF NEW BIOTECHNOLOGIES 95 (2004) [hereinafter REPRODUCTION AND RESPONSIBILITY].

HGE may occur within an IVF cycle, but differs in that it makes deliberate changes to gametes or embryos that will be carried into the bodies of any children who result. In assessing legislative reactions to date, the current state of HGE is most relevant; and the only realistic potential use in the near term is to protect offspring against disease.[102] Several reputable scientific organizations have developed a translational pathway to clinical applications in which genetic mutations that cause serious diseases would be corrected to ensure the birth of healthy children.[103] If these clinical applications are perfected and children are born, the edits to their genomes will be minute. To characterize this type of HGE as manufacture would be overreach.

HRC begins with a somatic cell donor.[104] By selecting the donor, one selects the entire nuclear genome of the child.[105] However, as explained above, a child conceived through HRC will differ from the somatic cell donor in many ways.[106] Thus, HRC is not a manufacturing process and cannot deliver a specific child, but many people seem not to understand that fact. Human clones manufactured in multiple identical copies are a common science fiction trope.[107] Governmental advisory bodies have expressed concern that HRC could cause parents and society to view children as manufactured products,[108] and members of Congress have voiced similar concerns while debating anti-cloning legislation.[109] Relative to other novel reproductive technologies, HRC entails a greater degree of genetic selection, and

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[102] This Article does not include He Jiankui's experiment within this category. He intended to create babies resistant to infection with human immunodeficiency virus (HIV). *See* Henry T. Greely, *CRISPR'd Babies: Human Germline Genome Editing in the 'He Jiankui Affair'*, 6 J.L. & BIOSCIENCES 111, 117 (2019). However, the babies did not receive the natural genetic variant that confers some protection against infection. *See id.* at 156–59. Of course, there are easier and safer ways to protect against HIV infection, which is one of many reasons this experiment was unethical. *See id.* at 156. For a review of additional ethical problems with the experiment, *see id.* at 151–69.

[103] *See supra* text accompanying notes 42–48.

[104] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 47.

[105] *See* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 106.

[106] *See supra* text accompanying notes 90–93.

[107] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 109.

[108] *See* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 104–07; *see also* CALIFORNIA REPORT, *supra* note 25, at 1175; NBAC REPORT, *supra* note 96, at 72–73.

[109] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 92–93; *see also* MACINTOSH, HUMAN CLONING, *supra* note 3, at 181–85.

that element of selection may explain some of the legislative backlash against it.

D. *Summary*

Legislators may have treated HRC more harshly than HGE due to features that are specific to cloning. Because HRC enables asexual reproduction, it may be perceived as a radical change from the human reproductive status quo. HRC has also been incorrectly associated with copying and human manufacture. If this line of analysis is correct, HRC bans are *sui generis* and do not predict bans on HGE or other novel reproductive technologies that involve sexual reproduction.

IV. DISMISSIVE ATTITUDES TOWARD INFERTILITY

Disparate legislative reactions to HRC and HGE may also arise from differences in the underlying purposes of these technologies. To explain, after Dolly's birth was announced, some infertility patients and their doctors expressed an interest in HRC.[110] As the late Professor John Robertson recognized, men and women with nonviable gametes could clone themselves to have genetic offspring.[111] For such men and women, asexual reproduction had a medical purpose: it enabled them to procreate.[112] Robertson also suggested that carriers of genetic diseases might choose to clone themselves rather than risk transmitting the diseases to offspring via sexual reproduction, particularly if they were morally opposed to fetal screening and abortion.[113] Similarly, carriers could employ HRC rather than screening and discarding in vitro embryos via PGT.[114]

Despite these potential benefits, the American public has consistently opposed HRC.[115] Medical professionals and scientists have also been hostile to HRC. For example, in 2001, the American Society for Reproductive Medicine (ASRM)[116] opposed HRC as

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[110] *See, e.g.*, Gina Kolata, *For Some Infertility Experts, Human Cloning Is a Dream*, N.Y. TIMES (June 7, 1997), https://www.nytimes.com/1997/06/07/us/for-some-infertility-experts-human-cloning-is-a-dream.html.

[111] *See* John A. Robertson, *Liberty, Identity and Human Cloning*, 76 TEX. L. REV. 1371, 1379–80, 1391 (1998).

[112] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 46.

[113] *See* Robertson, *supra* note 111, at 1379.

[114] *See* MACINTOSH, ILLEGAL BEINGS, *supra* note 24, at 37.

[115] *See supra* text accompanying note 59.

[116] According to its website, "[t]he American Society for Reproductive Medicine (ASRM) is dedicated to advancing the science and practice of reproductive medicine. The Society accomplishes its mission by pursuing

unsafe.[117] By doing this, the ASRM distanced itself from charlatans who prematurely offered cloning services to desperate patients,[118] but missed an opportunity to acknowledge the therapeutic potential of HRC for infertile men and women in the long term. Similarly, in 2002, the National Academies issued a report that condemned HRC as unsafe and declared it should be banned.[119]

Turning to HGE, that technology is also unsafe and not ready for clinical use.[120] Yet, the public and scientists have reacted more positively to it. According to a recent poll, most Americans approve the correction of genetic mutations to spare babies from disease.[121] And as Part II discussed, the U.S. National Academy of Medicine, U.S. National Academy of Sciences, United Kingdom Royal Society, and International Commission on the Clinical Use of Human Germline Genome Editing issued a 2020 Report that established a translational pathway to correct genetic mutations that lead to serious monogenic diseases.[122] Few will benefit from the pathway because it is limited to couples who create no unaffected embryos or so few that one cycle of

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excellence in evidence-based, life-long education and learning, growing and supporting innovative research, developing and disseminating the highest ethical and quality ethical and quality standards in patient care, and advocating for physicians and affiliated healthcare providers and their patients." *About Us*, AM. SOC'Y FOR REPROD. MED., https://www.asrm.org/about-us/ (last visited Oct. 4, 2023).

[117] *See* American Society for Reproductive Medicine, *Safety Concerns Render Any Attempt at Human Cloning Unethical*, ASRM PRESS RELEASE (March 28, 2001), http://fbaum.unc.edu/lobby/_107th/121_Human_Cloning/Organizational_Statements/ASRM/ASRM_Unethical_03_28_01.htm.

[118] For example, Dr. Panos Zavos claimed to have transferred cloned embryos to several women, but achieved no pregnancies. *See* Sarah Boseley, *Human Cloning Claims Condemned by Leading Scientists*, GUARDIAN (Apr. 22, 2009), https://www.theguardian.com/society/2009/apr/22/human-cloning-panayiotis-zavos.

[119] *See* THE NAT'L ACADS., SCIENTIFIC AND MEDICAL ASPECTS OF HUMAN REPRODUCTIVE CLONING 2 (2002).

[120] *See Third International Summit*, *supra* note 49, at 13.

[121] In a 2020 poll, sixty-six percent of respondents approved changing a baby's genes to avoid a serious disease or condition at birth. *See* Cary Funk et al., *Biotechnology Research Viewed with Caution Globally, but Most Support Gene Editing for Babies to Treat Disease*, PEW RSCH. CTR. 19 (Dec. 10, 2020), https://www.pewresearch.org/science/2020/12/10/biotechnology-research-viewed-with-caution-globally-but-most-support-gene-editing-for-babies-to-treat-disease/.

[122] *See supra* text accompanying notes 42–48.

IVF with PGT has already failed.[123] Yet, these organizations still invested time and effort in establishing this pathway for potential future use. Nothing of the sort has ever been done for HRC.

Dismissive attitudes towards infertility might account for the cold reception HRC received. As Professor David Orentlicher has noted, "despite the level of suffering and the presence of a real bodily dysfunction, many policymakers and scholars do not treat infertility as a disability. Although infertile persons may be deprived of the opportunity to procreate, such a deprivation, it is argued, is the loss of a lifestyle option."[124]

However, public attitudes toward infertility may be evolving. In 2000, twenty-three percent of United States respondents agreed that infertility was a disease, and sixty percent disagreed.[125] By 2020, however, sixty-nine percent of United States respondents agreed that it was appropriate to research new technologies to help women get pregnant.[126] If opposition to HRC was rooted in dismissiveness, one would expect it to decline over time as sympathy for the infertile increased. Lawmakers did stop legislating against HRC around ten years ago.[127] But opinion polls show that public opposition to HRC remains high at over eighty percent.[128]

There is a way to reconcile increased sympathy for the infertile with these poll results. Humans tend to resist change—a predilection known as the status quo bias.[129] Suppose people initially decided that HRC was morally unacceptable because they did not consider infertility to be a disease or an important problem to be solved. This initial decision would have become the status quo opinion on HRC. Years later, people might still cling to that opinion even though sympathy for the infertile had increased in the meantime. Few would be motivated to reevaluate their opinion; doing so would take mental energy,[130] and admitting error could be psychologically

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[123] *See supra* text accompanying notes 45–47.

[124] David Orentlicher, *Discrimination Out of Dismissiveness: The Example of Infertility*, 85 IND. L.J. 143 (2010).

[125] *See* The Bertarelli Foundation Scientific Board, *Public Perception on Infertility and Its Treatment: An International Survey*, 15 HUM. REPROD. 330, 332, table III (2000).

[126] *See* Cary Funk et al, *supra* note 121, at 19.

[127] *See supra* text accompanying notes 33–35.

[128] *See Moral Issues*, *supra* note 59.

[129] *See* RONALD M. GREEN, BABIES BY DESIGN: THE ETHICS OF GENETIC CHOICE 8–9 (2007).

[130] *See* Scott Eidelman & Christian S. Crandall, *Bias in Favor of the Status Quo*, 6 SOC. & PERSONALITY PSYCH. COMPASS 270, 271 (2012).

uncomfortable.[131] After decades of opposition, people might not be willing to reconsider the possibility that they were wrong and that HRC could relieve human suffering. In other words, HRC may have been the right technology at the wrong time.

In sum, dismissive attitudes towards infertility may have encouraged legislators to ban HRC. It is easier to prohibit a novel technology if society does not acknowledge the need for it. If this line of reasoning is correct, the recent increase in sympathy for the infertile is good news for those who need other novel reproductive technologies to conceive and bear children. Congress and state legislatures might be more inclined to embrace those technologies, or at the very least, leave them alone.

V. THE POLITICS OF HUMAN EMBRYO RESEARCH

Finally, HRC and HGE differ in yet another way that may have contributed to their disparate legal treatment. As this Part will explain, HRC quickly became entangled in the politics of human embryonic stem cell (hESC) research. HGE evaded that fate because it emerged years later, after scientific advances had made it possible to generate and edit pluripotent stem cells without creating or harming human embryos.

In 1998, scientists derived the first stem cell line from a human embryo.[132] Their goal was to facilitate the development of new drugs and transplantable tissues.[133] This development led to the following speculation: scientists could clone an embryo from the somatic cells of a patient; disaggregate the embryo to create a stem cell line; and conduct research, therapy, or both using cells that matched the patient's DNA.[134] Logically, in order to provide such individualized therapies, scientists would have to clone and disaggregate as many embryos as there were patients who needed the therapies. However, one cannot disaggregate an embryo and harvest its stem cells without killing it.[135] From a pro-life perspective, research cloning was tantamount to

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[131] *See* William Samuelson & Richard Zeckhauser, *Status Quo Bias in Decision Making*, 1 J. RISK & UNCERTAINTY 7, 38–39 (1988).

[132] *See generally* James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCIENCE 1145 (1998).

[133] *See id*. at 1146–47.

[134] *See* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 129–33.

[135] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 200–01.

murder.[136] Thus, the pro-life movement wanted a total ban on all human cloning to protect embryonic human life.[137]

The biotechnology industry had a very different point of view. It wanted HRC to be banned so that scientists could pursue grants and engage in research cloning within a stable legal regime.[138] After the Biotechnology Industry Organization (BIO) asked the FDA for help,[139] that agency sent a letter to the institutional review boards of medical and research institutions, asserting authority over HRC while declaring it would not grant permission to proceed with clinical trials due to unresolved safety concerns.[140] But only three years later, the Director of the CBER testified before Congress that the FDA would not stop clinical trials if HRC were proven safe for the child and gestational mother.[141] Congress then tried for years to enact anti-cloning legislation but failed because it was impossible for pro-life and research advocates to reach a consensus on research cloning.[142] Meanwhile, research-friendly states enacted bans on HRC while pro-life states banned all human cloning.[143] So it was research cloning that created much of the energy required to propel cloning bills forward.

After much anti-cloning legislation had been introduced or enacted, two developments undermined interest in research cloning. First, in 2007, Japanese scientists reported that they had derived induced pluripotent stem cells (iPSCs) directly from human fibroblasts.[144] Scientists now had a way to create DNA-matched stem

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[136] *See id.*

[137] *See* Price, *supra* note 2, at 626; *see also*, HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 150–59 (articulating the pro-life position against research cloning).

[138] *See* Lee Silver, *Public Policy Crafted in Response to Public Ignorance Is Bad Public Policy*, 53 HASTINGS L. J. 1037, 1045–1046 (2002) (opining that scientists opposed HRC because they did not care about human infertility but feared cloning hysteria would affect their hESC research).

[139] *See* Price, *supra* note 2, at 623–25.

[140] *See* Nightingale, *supra* note 17.

[141] *See* Zoon testimony, *supra* note 23.

[142] For an account of various Congressional efforts, *see* MACINTOSH, HUMAN CLONING, *supra* note 3, at 180–85.

[143] *See id.* at 185–86.

[144] *See* Kazutoshi Takahashi et al., *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 CELL 861 (2007). In a prior experiment, the scientists transformed murine fibroblasts into pluripotent stem cells. *See* Kazutoshi Takahashi and Shinya Yamanaka, *Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors*, 126 CELL 663 (2006).

cells without cloning and disaggregating human embryos.[145] Second, in 2009, the National Institutes of Health issued guidelines for the federal funding of research on hESC lines derived from donated IVF embryos.[146] These guidelines provided that federal funds were not available for research on cloned human embryos.[147]

Now, let us consider how HGE relates to basic research in which human embryos are edited. Such research destroys the embryos involved[148] but is not undertaken lightly. It could advance knowledge of early human development, improve IVF, and contribute to new birth control methods.[149] Embryo editing also could enable scientists to perfect HGE and prove that it is safe for gestating parents and children.[150]

Experts once expected much more of embryo editing. They thought scientists would clone embryos from the somatic cells of patients, edit out mutations, and generate stem cell lines to achieve cures.[151] Instead, the science moved in a different direction. As mentioned above, the invention of iPSCs made it possible for scientists to create DNA-matched stem cells without cloning and disaggregating human embryos.[152] Then, in 2013, two research teams demonstrated they could edit human cells with CRISPR/Cas9 technology.[153] As a result of these two advances, scientists today can derive iPSCs from the somatic cells of patients and edit them without creating embryos at

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[145] *See* Greely, *Human Reproductive Cloning*, *supra* note 5. This Article does not mean to suggest that iPSC-based therapies are readily available or risk-free. For a discussion of the challenges associated with them, *see* Shinya Yamanaka, *Pluripotent Stem Cell-Based Cell Therapy – Promise and Challenges*, 27 CELL STEM CELL 523 (2020).

[146] *See* National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32170, 32174 (June 30, 2009) [hereinafter NIH Guidelines]. Pro-life forces challenged the guidelines, but the U.S. Court of Appeals for the D.C. Circuit upheld them in 2012 and the U.S. Supreme Court denied certiorari in 2013. *See Sherley v. Sebelius*, 689 F.3d 776 (D.C. Cir. 2012), *cert. denied*, 568 U.S. 1087 (2013).

[147] *See* NIH Guidelines, *supra* note 146, at 32175.

[148] *See, e.g.*, Liang et al., *supra* note 36.

[149] *See* 2017 Report, *supra* note 7, at 57–58.

[150] *See id.* at 58; *see also* 2020 Report, *supra* note 42, at 123–28 (establishing a translational pathway with preclinical testing of human embryos before HGE can be used in clinical trials).

[151] *See, e.g.*, HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 133.

[152] *See supra* text accompanying notes 144–45.

[153] *See* Le Cong et al., *Multiplex Genome Editing Using CRISPR/Cas Systems*, 339 SCIENCE 819 (2013); Prashant Mali et al., *RNA-Guided Human Genome Engineering via Cas9*, 339 SCIENCE 823 (2013).

all.[154] Therefore, in comparison with HRC, HGE has not been as strongly associated with the creation of human embryos solely for the purpose of harvesting stem cells from them. This distinction may help to explain why HGE has not been embroiled in legislative battles to the same extent as HRC.

This line of analysis has the following implications. The pro-life movement will disapprove of any novel reproductive technology in which human embryos are lost or discarded.[155] However, it may not be roused to political action unless that technology is also associated with the manufacture and destruction of human embryos for research on a grand scale, as HRC was. The legal history of HRC predicts that pro-life lobbying may not be enough to produce bans at the federal level, but it may inspire state bans.

VI. IMPLICATIONS FOR FUTURE REGULATION OF NOVEL REPRODUCTIVE TECHNOLOGIES

This Article has identified several factors that may have prompted bans on HRC but not HGE: HRC came first and before Congress hit upon the strategy of preventing the FDA from receiving applications for clinical trials; HRC seemed like a more radical departure from standard human reproduction; HRC's therapeutic value was less obvious to a public that was once dismissive of infertility; and HRC became entangled in a political battle over research cloning. No single factor can explain the outcome; legislators may have had varying reasons for voting for bans. Even so, based on the foregoing analysis, this Article will make some tentative predictions regarding the legal future of novel reproductive technologies, starting with HGE and using mitochondrial replacement therapy and in vitro gametogenesis as further examples.

A. *Heritable genome editing*

Congress currently imposes a *de facto* moratorium on HGE through an appropriations rider that keeps the FDA from acknowledging receipt of applications for clinical trials.[156] This Section discusses two possible changes to the rider. First, Congress could keep

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[154] *See, e.g.*, Giulia Paolini Sguazzi et al., *Induced Pluripotent Stem Cells (iPSCs) and Gene Therapy: A New Era for the Treatment of Neurological Diseases* 22 INT'L J. MOLECULAR SCI. 13674 (2021) (reviewing progress and challenges in editing and using iPSCs to cure disease).

[155] *See* McTavish, *supra* note 98, at 452 (explaining that the Roman Catholic Church considers IVF immoral because human embryos die or are discarded).

[156] *See supra* text accompanying note 8.

the rider but amend it to allow the FDA to receive applications for only some clinical trials—for example, those in which HGE is used to correct genetic mutations that cause serious monogenic diseases.[157] Second, Congress could eliminate the rider altogether, freeing the FDA to receive applications for any type of clinical trial involving HGE.

In assessing how legislators might react to these changes, one can set aside factors that inspired HRC bans but are irrelevant here. HGE is a type of sexual reproduction that does not replicate the nuclear DNA of an existing person.[158] HGE is not a treatment for infertility (although it may help carriers of genetic mutations have healthy children).[159] HGE is not closely associated with hESC research.[160] However, HGE does raise other policy concerns, and how legislators react to them may depend on how much leeway Congress grants to the FDA.

Suppose Congress allows the FDA to receive applications for clinical trials in which genetic mutations that cause serious monogenic diseases are corrected. This Article believes that few, if any, state legislatures would be motivated to ban such limited medical uses. In the context of such minute edits, claims that HGE treats children like manufactured products are weak.[161] If the mutations are changed to existing genetic sequences that do not cause disease,[162] arguments against altering the human germline and the genetic inheritance of future generations without their consent lose much of their force.[163]

However, these and other objections may be weightier when HGE is used for enhancement, so let us turn to that topic. Suppose Congress eliminates the rider altogether, so that the FDA is free to receive applications for clinical trials in which scientists edit embryos to bring about the birth of children who are enhanced. Would parents then treat children as manufactured products, as some critics argue?[164] Would enhancing modifications affect future generations that never consented to them?[165] Would society evolve into classes of genetic haves and have nots?[166]

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[157] *See supra* text accompanying notes 45–48.
[158] *See supra* text accompanying notes 68, 81–82.
[159] *See supra* text accompanying notes 45–48.
[160] *See supra* text accompanying notes 151–54.
[161] *See supra* text accompanying notes 102–03.
[162] *See* 2020 Report, *supra* note 42, at 124.
[163] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 76.
[164] *See* REPRODUCTION AND RESPONSIBILITY, *supra* note 101, at 109–10.
[165] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 76.
[166] *See generally* SUSANNAH BARUCH ET AL., HUMAN GERMLINE GENETIC MODIFICATION: ISSUES AND OPTIONS FOR POLICYMAKERS (2005).

A complete analysis of such objections is beyond the scope of this Article,[167] but the short answer is that biological realities stand in the way of such negative outcomes. Desirable traits, such as intelligence, are often polygenic, meaning that multiple genes must work together to create a basis for them.[168] Even if a scientist could identify all the genes associated with a particular trait, she could find it difficult to add them without inadvertently affecting other genes and traits.[169] And even if a child was born with the right genetic profile, environmental factors like upbringing and culture would shape her traits in unpredictable ways.[170] With so many variables in play, and no guarantees, sensible scientists and parents would conclude that HGE for enhancement was not worth the risk.[171]

But what of foolish scientists and parents, who insist on pursuing enhancements?[172] Recall how the FDA stopped HRC: it sent a letter to medical and research institutions informing them that it would not grant permission for clinical trials due to unresolved safety risks.[173] The FDA could shut down enhancing uses of HGE indefinitely by sending a similar letter to medical and research institutions. Such a letter would be justified because editing multiple genes to alter a polygenic trait would pose safety risks to offspring.[174]

If Congress decided that FDA regulation was inadequate to prevent enhancing uses, it might reconsider its position and enact a ban on enhancing uses or HGE in general. Yet, Congress's reliance on the rider thus far indicates that it wants to avoid messy policy debates. Therefore, this Article anticipates that Congress will maintain the rider for the foreseeable future, while possibly carving out exceptions for limited medical uses of HGE.

B. *Mitochondrial replacement therapy*

Mitochondrial replacement therapy (MRT) helps individuals whose eggs have dysfunctional mitochondria (carriers) to have healthy

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[167] For an extensive discussion of these and other objections to HGE, *see generally* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 30–87.

[168] *See id.* at 17–18.

[169] *See id.* at 18–19.

[170] *See id.* at 52.

[171] *See id.*

[172] *See* Andorno et al., *supra* note 41, at 353 (noting that "[s]ome prospective parents are likely to find fertility clinics' marketing appeals compelling even when the genetic modifications offered are dubious").

[173] *See* Nightingale, *supra* note 17.

[174] *See* 2017 Report, *supra* note 7, at 122 (reasoning that HGE has not been perfected and the risk-benefit calculus for enhancing uses does not meet the standard for clinical trials).

offspring with their partners.[175] Although a detailed account is beyond the scope of this Article, this Part will briefly describe two methods. In maternal spindle transfer, a technician transfers the chromosome-bearing spindle of a carrier's egg into an enucleated donor egg; the reconstructed egg is then fertilized with the sperm of the carrier's partner.[176] In pronuclear transfer, the carrier's egg and a donor egg are both fertilized with the partner's sperm; a technician then removes the pronuclei from the donor's egg and substitutes the pronuclei of the carrier's egg to create a reconstructed embryo.[177] When performed successfully, these methods yield a child who inherits nuclear DNA from the intended parents but healthy mitochondria from the donor egg.[178] Because three individuals contribute, scientists and the media sometimes describe children born through these processes as "three-parent babies."[179]

In the United Kingdom healthy children have been born to carriers via pronuclear transfer.[180] In Greece, a pilot study recently demonstrated that IVF patients with poor egg quality could bear healthy children following maternal spindle transfer.[181] However, in the United States, MRT is not available because the FDA cannot acknowledge receipt of applications for clinical trials thanks to the appropriations rider.[182]

Section II(C) theorized that where the FDA regulates, legislatures may be inactive. If that theory is correct, one would expect to find that Congress and state legislatures have *not* banned MRT. And

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[175] *See* Kerry Lynn Macintosh, *Does Mitochondrial Replacement Therapy Violate Laws Against Human Cloning?*, 43 LOYOLA INT'L & COMPAR. L. REV. 251, 251 (2021) [hereinafter "Macintosh, *Mitochondrial Replacement Therapy*"].

[176] *See id.* at 256.

[177] *See id.* at 257–58.

[178] *See id.* at 256, 258.

[179] *E.g.*, Hana Carolina Moreira Farnezi et al., *Three-parent Babies: Mitochondrial Replacement Therapies*, 24 JGBR ASSISTED REPROD. 189 (2020); Maggie Fox, *Three-Parent Babies Are OK, Experts Say*, NBC NEWS (Feb. 3, 2016), https://www.nbcnews.com/health/health-news/three-parent-babies-are-ok-experts-say-n510626.

[180] *See* Ian Sample, *First UK Baby with DNA from Three People Born after New IVF Procedure*, GUARDIAN (May 9, 2023), https://www.theguardian.com/science/2023/may/09/first-uk-baby-with-dna-from-three-people-born-after-new-ivf-procedure.

[181] *See* Nuno Costa-Borges et al., *First Pilot Study of Maternal Spindle Transfer for the Treatment of Repeated In Vitro Fertilization Failures in Couples with Idiopathic Infertility*, 119 FERT. & STER. 964 (2023).

[182] *See Advisory on Legal Restrictions on the Use of Mitochondrial Replacement Techniques*, *supra* note 62.

indeed, that is the case: appropriations rider aside, Congress has not banned MRT.[183] Nor have state legislatures banned MRT[184] (although some state cloning laws are worded broadly enough to bring MRT within their scope).[185]

Now, suppose Congress amended the rider to free the FDA to receive applications for clinical trials of MRT.[186] Suppose further that the FDA reacted to MRT in the same way it reacted to HRC—that is, by sending letters to medical and research institutions stating that it would not grant permission to conduct clinical trials due to unresolved safety concerns.[187] With clinical trials effectively blocked, few if any

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[183] On November 30, 2023, a Westlaw search for the terms "mitochondrial" and "mitochondrial replacement therapy" in the U.S. Code Annotated database returned no federal statutes.

[184] On November 30, 2023, searches for the term "mitochondrial replacement therapy" returned no state laws in the Genome Statute and Legislative Database of the National Human Genome Research Institute. *See Genome Statute and Legislation Database*, NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/about-genomics/policy-issues/Genome-Statute-Legislation-Database (last visited Nov. 30, 2023). A Westlaw search on the same date for the same term in the "All States" database also returned no state laws.

[185] *See* Macintosh, *Mitochondrial Replacement Therapy*, *supra* note 175, at 265–77.

[186] In 2019, an Appropriations Subcommittee in the House of Representatives removed the rider from the 2020 appropriations bill, but the full Appropriations Committee later restored it. Democrats wanted the rider removed to allow a fuller debate over MRT, but Republicans insisted the rider be maintained. *See* Jocelyn Kaiser, *Update: House Spending Panel Restores U.S. Ban on Gene-Editing Babies*, SCIENCE (June 4, 2019), https://www.science.org/content/article/update-house-spending-panel-restores-us-ban-gene-edited-babies. Although this effort to make a change failed, a future attempt could succeed if MRT continues to yield healthy babies in other countries.

[187] Although healthy babies have been born through MRT, one baby from the Greek pilot study experienced reversion—that is, when his intended mother's spindle was transferred, a tiny number of her mitochondria hitched a ride into the donor egg and replicated until they accounted for thirty to sixty percent of the mitochondria in his tested tissues. *See* Nuno Costa-Borges et al., *supra* note 181, at 971. The patients in the pilot study were only infertile, but reversion would be a significant concern for carriers of mitochondrial disease, who could give birth to afflicted offspring despite the procedure. *See id.* Some also fear that offspring could suffer from health problems if the intended mother's nuclear DNA and donor's mitochondrial DNA are incompatible. *See* Lucia Gomez-Tatay, Jose M. Hernandez-Andreu & Justo

researchers would bother to submit applications, and state legislatures might leave MRT alone. Yet, the FDA might find it difficult to adopt such a harsh regulatory posture. Healthy babies have already been born abroad through pronuclear transfer and maternal spindle transfer.[188]

Therefore, suppose the FDA began to consider and approve applications to conduct clinical trials. Presumably, if Congress was willing to amend the rider to allow the FDA to receive applications, it would not turn around and ban MRT. However, some states might do so for three reasons. First, as the history of the battle over research cloning indicates, the pro-life movement can be tenacious in defending human embryos, particularly when scientists create human embryos only to destroy them.[189] Pronuclear transfer creates and then destroys two fertilized eggs to reconstruct one fertilized egg with healthy mitochondria.[190] Pro-life individuals have criticized pronuclear transfer on this ground.[191] If the FDA begins to receive applications, legislators in conservative states might bend to pro-life demands for a ban on pronuclear transfer or MRT in general.

Second, the legal history of HRC suggests that people balk at technologies that deviate too much from standard reproduction. Some have already objected to MRT, arguing that a child deserves to have two, and only two, genetic parents.[192] However, the genetic contribution of the person who donates healthy eggs for MRT is tiny compared to that of the carrier and partner, who provide the child with its nuclear DNA.[193] When mitochondrial DNA accounts for less than one percent of the child's genome, it may be unreasonable to consider the egg donor a third parent.[194] Nevertheless, legislators uncomfortable with embryo wastage might seize upon the three-parent aspect of MRT as an additional reason to enact a state ban.

Third, by blending mitochondrial and nuclear DNA from three people, MRT alters the genetic inheritance of future generations that cannot consent.[195] It is difficult to predict how legislators might react to this concern, which did not play a prominent role in HRC debates.

Aznar, *Mitochondrial Modification Techniques and Ethical Issues*, 6 J. CLINICAL MED. 1, 8 (2017).

[188] *See supra* text accompanying notes 180–81.

[189] *See supra* text accompanying notes 134–43.

[190] *See* Macintosh, *supra* note 175, at 259–60.

[191] *See*, *e.g.*, Arina O. Grossu, *Three-Parent Embryo Creation*, 40 ETHICS & MEDICS 1, 2 (2015) (presenting a Roman Catholic moral analysis of MRT).

[192] *See id.*

[193] *See* Macintosh, *Mitochondrial Replacement Therapy*, *supra* note 175, at 256, 258.

[194] *See* Lucia Gomez-Tatay, *supra* note 187, at 10.

[195] *See id.* at 7; *see also* Grossu, *supra* note 191.

However, if legislators object to MRT because it harms some human embryos, they might assert this objection to further justify a ban.

C. *In Vitro Gametogenesis*

In vitro gametogenesis (IVG) is a speculative reproductive technology that could draw legislative attention in the future. Imagine the following scenario: a patient provides a skin or blood sample to a technician.[196] The cells within that sample carry the DNA of that patient.[197] A technician derives iPSCs from those adult cells, and artificial gametes from those iPSCs.[198] If the patient uses the artificial gametes to procreate, he or she will have genetic offspring.[199]

Artificial gametes could have multiple uses, including making IVF easier on patients. Today, a patient must take powerful drugs to stimulate the ovaries and endure surgical retrieval to obtain eggs.[200] In the future, a patient could obtain artificial eggs simply by submitting to a blood draw.[201] Artificial gametes might also benefit men without sperm, older women with nonviable eggs,[202] and cancer patients whose treatments eliminate their ability to produce gametes in vivo.[203] If iPSCs can be prodded into becoming either sperm or eggs, LGBTQIA+ couples might use IVG to have genetic children together.[204] Lastly, IVG could facilitate genetic selection. Couples could create multiple artificial eggs, fertilize them to create panels of embryos, obtain genetic

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[196] *See* Antonio Regalado, *How Silicon Valley Hatched a Plan to Turn Blood into Human Eggs*, TECH. REV. (Oct. 28, 2021), https://www.technologyreview.com/2021/10/28/1038172/conception-eggs-reproduction-vitro-gametogenesis.

[197] *See id.*

[198] *See* Saskia Hendriks et al., *Artificial Gametes: A Systematic Review of Biological Progress Towards Clinical Application*, 21 HUM. REPROD. UPDATE 285, 285 (2015).

[199] *See id.*

[200] *See* Guido Pennings, *Why We Need Stem-Cell Derived Gametes*, 47(5) RBMO 1, 2 (2023).

[201] *See id.*

[202] *See* Hendriks et al., *supra* note 198, at 286.

[203] *See* Victoria G. Wesevich, Christopher Arkfeld & David B. Seifer, *In Vitro Gametogenesis in Oncofertility: A Review of Its Potential Use and Present-Day Challenges in Moving toward Fertility Preservation and Restoration*, 12 J. CLINICAL MED. 3305 (2023).

[204] *See* Hendriks et al., *supra* note 198, at 286.

profiles for those embryos, and transfer only those likely to produce offspring with desired traits.[205]

Turning to the state of the science, researchers working with murine pluripotent stem cells have created in vitro spermatids[206] and eggs[207] that yielded healthy mouse pups. In one startling experiment, researchers created iPSCs from the tail of a *male* mouse, derived *eggs* from the iPSCs, fertilized the eggs with sperm from another mouse, and produced viable offspring.[208] However, researchers have not yet created human artificial gametes from iPSCs[209] and human births could be many years away.[210]

Nevertheless, in 2023, the National Academies of Sciences, Engineering, and Medicine summoned scientists, physicians, lawyers, and other experts to a workshop "to review the state of the science, understand what is driving progress, what is likely to be achievable versus unrealistic, and recognize the urgent issues that in vitro–derived gametes could raise."[211] When one reads the proceedings, one cannot help but be amazed at the amount of scientific research that has been devoted to developing and perfecting this technology.[212] Participants also reviewed societal and ethical concerns associated with IVG.[213]

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[205] *See generally* Henry T. Greely, THE END OF SEX AND THE FUTURE OF HUMAN REPRODUCTION, CELL HARV. UNIV. PRESS (2016) (predicting this use of IVG).

[206] *See* Yukiko Ishikura et al., *In Vitro Reconstitution of the Whole Male Germ-Cell Development from Mouse Pluripotent Stem Cells*, 28 CELL STEM CELL 2167, 2169 (2021).

[207] *See* Orie Hikabe et al., *Reconstitution In Vitro of the Entire Cycle of the Mouse Female Germ Line*, 539 NATURE 299, 301 (2016).

[208] *See* Kenta Murakami et al., *Generation of Functional Oocytes from Male Mice In Vitro*, 615 NATURE 900, 900 (2023).

[209] *See* EMILY P. DAWSON, CHANEL MATNEY & KATHERINE BOWMAN, IN VITRO DERIVED HUMAN GAMETES: SCIENTIFIC, ETHICAL, AND REGULATORY IMPLICATIONS 3 (2023), https://nap.nationalacademies.org/catalog/27259/in-vitro-derived-human-gametes-scientific-ethical-and-regulatory-implications [hereinafter National Academies Workshop]. However, researchers have created human sperm and egg precursors from iPSCs. *See* Young Sun Hwang et al., *Reconstitution of Prospermatogonial Specification In Vitro from Human Induced Pluripotent Stem Cells*, 11 NATURE COMM. 5656, 5656 (2020); *see also* Chika Yamashiro et al., *Generation of Human Oogonia from Induced Pluripotent Stem Cells In Vitro*, 362 SCIENCE 356, 356 (2018).

[210] *See* Wesevich, Arkfeld & Seifer, *supra* note 203 (acknowledging scientific challenges and suggesting another ten to twenty years might pass before patients can access IVGs).

[211] National Academies Workshop, *supra* note 209, at 3.

[212] *See id.* at 7–30 (discussing the state of the science).

[213] *See id.* at 51–66.

Concerns vary with the uses proposed for artificial gametes[214] and a full analysis of them is beyond the scope of this Article.

In another session, participants discussed the regulatory environment for IVG.[215] Peter Marks, the Director of the CBER, explained that the FDA had authority over clinical trials of artificial gametes.[216] The participants were divided on whether the appropriations rider applied to IVG. Some argued that the rider should not apply because artificial gametes made from a person's own somatic cells would not include intentional heritable genetic modifications.[217] However, Marks predicted the FDA would interpret the rider to include IVG because the technology could cause unintentional heritable genetic modifications; he warned that if the FDA received applications for clinical trials, Congress might amend the rider to cover IVG.[218]

This Article believes that attempts to sidestep the rider could backfire in another way. Reasoning by analogy to the legal history of HRC,[219] if legislators feared that FDA regulation was an inadequate barrier, they might ban IVG altogether. For example, Congress could make it a crime to conceive a child with artificial gametes. Once such a law was in place, researchers and doctors might lack the legislative clout to repeal it. To be sure, Congress might not have enough votes to outlaw IVG altogether; but one or more state legislatures might enact bans, if they thought they had good reasons to do so. The history of HRC suggests three such reasons.

First, as Part V explained, HRC became entangled in a debate over research cloning and the destruction of human embryos.[220] IVG could meet a similar fate depending on how artificial gametes were used. Infertile or LGBTQIA+ couples might make only enough embryos to ensure a healthy birth; but couples screening for desired traits might make hundreds or even thousands of embryos and discard the spares.[221] If IVG became associated with mass slaughter of embryos, state legislatures might limit the number of embryos created, prohibit the destruction of surplus embryos,[222] or ban IVG altogether.

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[214] *See* Sonia M. Suter, *In Vitro Gametogenesis: Just Another Way to Have a Baby?*, 3 J.L. & BIOSCIENCES 87, 88 (2016).

[215] *See* National Academies Workshop, *supra* note 209, at 79–98.

[216] *See id.* at 87–88.

[217] *See id.* at 84, 87, 90.

[218] *See id.* at 88.

[219] *See supra* text accompanying notes 22–23.

[220] *See supra* text accompanying notes 134–43.

[221] *See* National Academies Workshop, *supra* note 209, at 56, 65; Suter, *supra* note 214, at 116.

[222] *See id.* at 59–60.

Second, as Section III(A) discussed, because HRC is asexual reproduction, some found it unnatural.[223] IVG differs because it is sexual reproduction: it creates artificial sperm or eggs that must be combined with other gametes to conceive embryos.[224] However, some legislators in conservative states might still oppose IVG on the ground that it is unnatural for same-sex or transgender individuals to procreate together using artificial gametes.[225]

Lastly, HRC faced charges that it treated cloned children as manufactured products.[226] IVG could face similar complaints if couples used artificial gametes to create scores of embryos, screened them for desired traits, and discarded the spares.[227] The more embryos created and discarded, the stronger the argument, giving legislators an additional reason to oppose IVG.

VII. CONCLUSION

Congress has enacted an appropriations rider that prevents the FDA from acknowledging receipt of applications for clinical trials of HGE,[228] MRT,[229] and possibly IVG.[230] In the future, Congress could eliminate the rider or amend it to allow the FDA to receive and approve applications for such trials. However, once the prospect of FDA approval looms on the horizon, Congress (in a different session) or state legislatures could be motivated to ban one or more of these

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[223] *See, e.g.*, CALIFORNIA REPORT, *supra* note 25, at 31.

[224] *See* Seppe Segers et al., *In Vitro Gametogenesis and Reproductive Cloning: Can We Allow One While Banning the Other?*, 33 BIOETHICS 68, 74 (2019) (acknowledging this distinction between HRC and IVG but questioning whether it carries any moral weight).

[225] *See* National Academies Workshop, *supra* note 209, at 45 (predicting that some societies may deny access to IVG to single people, same-sex couples, or couples that include a transgender person); *see also id.* at 36 (forecasting that people who object to noncoital reproduction will oppose IVG).

[226] *See* HUMAN CLONING AND HUMAN DIGNITY, *supra* note 67, at 104–07; *see also* CALIFORNIA REPORT, *supra* note 25, at 25; NBAC REPORT, *supra* note 96, at 71–73.

[227] *See* Eli Y. Adashi et al., *Stem Cell-Derived Human Gametes: The Public Engagement Imperative*, 25 TRENDS IN MOL. MED. 165, 165–66 (2019); *see also* Suter, *supra* note 214, at 114–15.

[228] *See, e.g.*, Consolidated Appropriations Act, 2023, 117 Pub. L. No. 328, tit. VII, § 737, 136 Stat. 4459, 4504 (2022).

[229] *See Advisory on Legal Restrictions on the Use of Mitochondrial Replacement Techniques*, *supra* note 62.

[230] *See supra* text accompanying notes 216–18.

technologies. To discern whether they would be likely to do so, this Article has drawn lessons from the legal histories of HRC and HGE.

HRC teetered on the edge of prohibition in Congress for years, and seventeen states have banned it.[231] Yet, neither Congress nor the states have banned HGE.[232] This Article analyzed this disparity and found several factors that may have motivated HRC bans. As a form of asexual reproduction, HRC was unfairly associated with copying and human manufacture.[233] HRC had potential as a treatment for individuals without viable gametes, but dismissive attitudes towards infertility may have caused that potential to be discounted.[234] Finally, HRC became entangled in the politics of research cloning, a controversial technology that creates and then destroys human embryos for their stem cells.[235]

Some factors that hurt HRC are not as relevant to other novel reproductive technologies. For example, HGE, MRT, and IVG combine gametes to facilitate sexual rather than asexual reproduction.[236] Sexual reproduction produces novel blends of chromosomes and genes[237] rather than the replicated nuclear DNA that made HRC so controversial. Moreover, the dismissiveness that once undermined HRC has been replaced by growing sympathy for the infertile.[238] That sympathy now also extends to people who need reproductive technologies to have normal, healthy children.[239]

However, when evaluating the legislative prospects of novel reproductive technologies, one must also consider the impact of the pro-life movement. IVF remains legal in the United States, even though couples may freeze or discard some embryos.[240] Yet, the legal history of HRC predicts that reproductive technologies will face stiff opposition when they are linked to deliberate or excessive destruction

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[231] *See* MACINTOSH, HUMAN CLONING, *supra* note 3, at 180–86.
[232] *See* MACINTOSH, ENHANCED BEINGS, *supra* note 8, at 123, 32.
[233] *See supra* Part III.
[234] *See supra* Section IV.
[235] *See supra* Part V.
[236] *See supra* text accompanying notes 68, 176–78, 224.
[237] *See supra* text accompanying notes 64–65.
[238] *See supra* text accompanying note 126.
[239] *See supra* text accompanying note 121.
[240] *See* I. Glenn Cohen, Judith Daar & Eli Y. Adashi, *What Overturning Roe v Wade May Mean for Assisted Reproductive Technologies in the US*, 328 JAMA 15, 16 (2022) (reasoning that states have banned abortion but not IVF because the politics are different); *see also* Henry T. Greely, *The Death of Roe and the Future of Ex Vivo Embryos*, 9:2 J.L. & BIOSCIENCES 1, 13–15 (2022) (arguing that IVF is unlikely to be banned because the pro-life movement likes babies).

of human embryos.[241] For example, a conservative state legislature might ban pronuclear transfer because that technology destroys two fertilized eggs to make one.[242] Similarly, if couples begin to use IVG to create hundreds or thousands of embryos for genetic screening, and discard the vast majority, Congress might react by banning IVG altogether.[243] And once legislatures realize that technologies entail embryo destruction, they may find additional reasons to outlaw them. The three-parent aspect of MRT and procreation by same sex or transgender couples through IVG come to mind.[244]

Finally, the fate of HGE may depend on how it is used. This Article expects that Congress and state legislatures will tolerate minor edits that have a medical purpose, such as correcting genetic mutations that cause serious monogenic diseases.[245] However, if the field moves in the direction of enhancing traits, the FDA would probably refuse permission for clinical trials due to serious safety concerns.[246] Meanwhile, Congress and state legislatures would be confronted with policy issues they have not debated before, including the potential impacts of genetic enhancements on current society and future generations. To avoid entanglement with these controversial issues, Congress might choose to maintain the appropriations rider indefinitely while carving out exceptions for limited medical uses of HGE.

[241] *See supra* text accompanying notes 134–43.
[242] *See supra* text accompanying notes 190–91.
[243] *See supra* text accompanying notes 221–22.
[244] *See supra* text accompanying notes 192–94, 225.
[245] *See supra* text accompanying notes 45–48.
[246] *See supra* text accompanying notes 172–74.