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THE IMMEDIACY OF GENOME EDITING AND MITOCHONDRIAL REPLACEMENT

RAYMOND C. O’BRIEN†

ABSTRACT

After human DNA was first defined in 1953, the parallel science of assisted reproductive technology achieved a successful human birth through in vitro fertilization in 1978. Science then went on to facilitate gestational surrogacy, banking human reproductive materials, such as embryos, and greater opportunities for couples and individuals to become parents. Fertility clinics were established throughout the world to help persons and couples achieve parenthood, contributing to a steady increase in babies born through assisted reproductive means. Gradually, both federal and state laws in the United States were enacted to collect data from the fertility clinics, mandate insurance coverage of assisted reproductive procedures, prohibit funding for human embryo research, and either forbid or enable surrogacy contracts. Societal changes occurred, too, including marriage entitlement for same-sex couples, a dramatic rise in the number of nonmarital cohabitants, and the rapid pace of scientific achievements related to human reproduction.

Throughout this evolutionary period there was a concomitant increase in transnational scientific cooperation, illustrated by international committees and treaties. By utilizing medical tourism, individuals who could afford to do so imposed their own medical needs on foreign scientific communities. The global scientific community became increasingly aware that it was now possible to edit both the human genome and a woman’s egg to eliminate mitochondrial disease. Both genome editing and

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mitochondrial replacement have the potential to eliminate serious disease and vastly improve human society. Amidst this scientific optimism, companies that are able to harness the power of new technological achievements have opportunities for monetary gains. However, there are also drawbacks which include the ethical and moral concerns over possible misuse of human materials; the opportunity to create designer babies; the unknown ramifications upon the human germline; the lack of consent of any resulting child; the disparity in the ability to pay for treatment; and the impact on the racial, gender, and the physical plurality existent in human society.

American legislation, illustrated by the federal Dickey-Wicker Amendment and its regulatory system, and as evidenced by the U.S. Department of Agriculture’s Coordinated Framework, is inattentive to the challenges posed by genome editing and mitochondrial replacement. In addition, international treaties and agreements are inapplicable to many countries and ineffective to regulate the research of privately funded scientists. For example, in spite of public condemnation, a baby boy was born in Mexico in 2016 following mitochondrial replacement; in 2018 twin girls were born in China following genome editing. This Article addresses the scientific opportunities and challenges of recent developments precipitated by the immediacy of genome editing and mitochondrial replacement. Although scientific academies in the United States and the United Kingdom suggest caution, transparency, and international scrutiny, science advances at an accelerating pace. This Article suggests immediate congressional involvement, an update to the federal regulatory process, and clear coordination with international scientific communities. Additionally, to safeguard the human values involved, this Article suggests specific goals should apply to the construction of a functional pathway that addresses the human possibility and challenge in genome editing and mitochondrial replacement.
I. INTRODUCTION

Historically, human reproduction has occurred via sexual intercourse.¹ Today, there are expanding options of non-sexual reproductive possibilities and enhancements.² These developments utilize in vitro fertilization ("IVF"), gamete donation, surrogacy, genome editing, mitochondrial replacement, and banks of human gametes for future fertilization or implantation, to list a few.³ One court summarized today's human reproduction options in these terms: "The inescapable reality is that all manner of arrangements involving the donation of sperm or eggs abound in contemporary society, many of them couched in contracts or agreements of varying degrees of formality."⁴ The ascendency of individual human privacy, expressed as reproductive autonomy, is enabled through scientific biological advances. Justice Anthony Kennedy's 2003 conclusion illustrated "that our laws and traditions in the past half century...show an emerging awareness that liberty gives substantial protection to adult persons in deciding how to conduct their private lives in matters pertaining to sex."⁵ This liberty fuels options that science provides with increasing alacrity.

Accelerating scientific advances, both domestically and transnationally, illustrate the options now available to actualize reproductive possibilities. It is now possible for a child to be born with more than two genetic parents;⁶ to avoid threatened disease through editing the gene sequence of a defective embryo;⁷ and, as

¹ Louise Brown, born in 1978, was the first baby born via in vitro fertilization. Jillian Casey et al., Assisted Reproductive Technologies, 17 GEO. J. GENDER & L. 83, 86 (2016). Previously, there were instances of artificial insemination, but they were rare. See Kara W. Swanson, The Birth of the Sperm Bank, 71 ANNALS IOWA 241 (2012). By the mid to late 1980s, gestational surrogates were used in conjunction with IVF procedures. See Remah Moustafa Kamel, Assisted Reproductive Technology After the Birth of Louise Brown, 14 J. REPROD. & INFERTILITY 96, 99 (2013).


³ Casey et al., supra note 1, at 85.

⁴ Ferguson v. McKiernan, 940 A.2d 1236, 1245 (Pa. 2007) (holding that an oral contract between a mother and a sperm donor that relinquished both visitation and child support for resulting child was enforceable).


⁷ See Daryl F. Sas & Hannah Martin Lawrence, CRISPR-Cas9: The Latest Fashion in Designer Babies, 33 ETHICS & MED. 81 (2017); Joshua D. Seitz, Striking a Balance: Policy
a result of gene editing, for a gene to be enhanced to meet a parent's baby specifications, including physical or mental characteristics.\textsuperscript{8} Such a baby may be termed, for better or for worse, a "designer baby."\textsuperscript{9}

Because of the rapidity of medical advances and the complexity of the procedures involved, comprehensive legislative reaction to new science is absent on a national and a transnational level.\textsuperscript{10} However, an absence of legislative pronouncements should not be taken as an expression of public approval or disapproval, but rather as a lack of engagement. The announcement of the birth of genome-edited twins in China on November 29, 2018,\textsuperscript{11} prompted immediate discussion nationally and internationally.\textsuperscript{12} Commentators were concerned that the scientific procedures available may affect human reproduction today and the genetic composition of future human generations tomorrow.\textsuperscript{13} Our ability to edit a human embryo may contribute to social and cultural disparities and less diversity or may foist upon a future human unwanted enhancements. Immediate action is warranted "to move beyond thinking about the immediate consequences of using genome editing [so as to] consider what a society in which such techniques were widely available would be like."\textsuperscript{14} This Article argues that there is such an immediacy today and urges congressional action to create a national pathway for public involvement in the issues raised by genome editing. The pathway

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8. Sas & Lawrence, supra note 7, at 81.


10. See Patton v. Vanterpool, 806 S.E.2d 493, 497 (Ga. 2017) (enforcing a state statute even though it was not intended to apply to current assisted reproductive technology innovations).


12. See id.


suggested in this article, based on specific goals, will permit national involvement and transnational cooperation.

This Article relies on several premises. First, reproductive freedom and individual liberty are within the gamut of the rights affecting genome editing. Human reproductive freedom involves the liberty of the human individual and the liberty interest garnered from legal precedents, mostly occurring in the past one-hundred years but becoming increasingly ascendant. However, the conduct of individual liberty is not unbridled. Certain private, intimate conduct remains subject to public engagement through the legislatures and ultimately the courts. The Constitution of the United States remains the final word, but those interpreting the Constitution must balance legislative priorities and personal privacies to arrive at impartiality. The tension in this balance is emphasized in dicta by the Supreme Court of the United States: "We must . . . 'exercise the utmost care whenever we are asked to break new ground' . . . lest the liberty protected by the Due Process Clause be subtly transformed into the policy preferences of the Members of this Court."17

However, when the Court does break new ground, such as holding that the Constitution guarantees a right to same-sex marriage, some object, arguing that public engagement—not the Court’s judicial opinions—provides the means by which liberty is protected. This opinion is illustrated by Chief Justice Roberts’s dissent in *Obergefell v. Hodges*: "Our cases have consistently refused to allow litigants to convert the shield provided by constitutional liberties into a sword to demand positive entitlements from the State."20 Thus, if the legislative process, as judged by the courts and the Constitution, provides the parameters of individual liberty

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in reproductive freedom, then persons and organizations must prepare to engage with the issues of genome editing and mitochondrial replacement. To create a functional, scientific pathway, all voices must be respected in a context of transparency.

Transparency of discussion is another premise. Undoubtedly, American public engagement on reproductive liberties, embryos, and "playing God" will be factious. The British grasped this fact in a report published in 2018. The British Nuffield Council on Bioethics reported, to its astonishment, that the United States is the most prolific country by far regarding basic genome editing research.\(^1\) This fact seemed incongruous with the deep divisions in America. The report stated:

The fact that this is possible in a country with deep and immobilising moral division between liberalism and Christian fundamentalism, and steeped in permanent conflict over abortion rights that has effectively evacuated any middle ground on which to build a societal consensus, may be attributed to the US constitution and its defence of civil rights and liberties.\(^2\)

Transparency depends on public engagement, media exposure, accurate information, and opportunities for those with a substantial interest in the issues to provide informed opinions. Portions of this Article identify the scientific challenges of newly developed procedures involving genome editing and one of its components, mitochondrial replacement.\(^3\) These research developments occurred neither overnight nor in a vacuum. Rather, there has been and will continue to be a consistent ascendency of assisted reproductive technology ("ART") in the United States—a fact that will only accelerate as medical insurance increasingly covers more procedures.

There is also an ascendant acceptance of assisted reproduction among members of the public\(^4\) which may

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22. Id.
contribute to a more transparent discussion of genome editing. Discussion must contrast risk from benefit and current advantages from long term consequences, all amidst the certainty that no nation lives in isolation but in an international community of discovery. Transparency also includes knowledge of other nation’s experiences. Any policy pertaining to ARTs must incorporate an international perspective, both because of the availability of foreign regulatory safe havens and because of the valuable insights from foreign scientific and regulatory practice. The reality is that both human genome editing and mitochondrial replacement are here, the former in 2018 in China\textsuperscript{25} and the latter in 2016 in Mexico.\textsuperscript{26}

Moreover, genome editing and mitochondrial replacement have the potential to impact future generations. Existing data provide ample evidence that scientific development in human reproduction may affect the human germline in ways that were unanticipated only a few decades ago.\textsuperscript{27} It is the unknown parameters of any modification that provide the current risk:

This means that the modification may be passed on via their gametes (egg or sperm) and is capable of being inherited by descendants, potentially down an indefinite number of future generations, until it is lost through normal mechanisms of recombination and segregation... or it is deliberately reversed through further intervention, perhaps involving genome editing, or simply through not having children.\textsuperscript{28}

Finally, this Article relies on an attitude of scientific positivism, rejecting any fear of the unknown. Change based on

\textsuperscript{25} Statement from the Organizing Committee on Reported Human Embryo Genome Editing, NAT’L ACADS. OF SCI., ENGINEERING, & MED. (Nov. 26, 2018), http://www8.nationalacademies.org/ompinews/newsitem.aspx?RecordID=11262018 ("[o]n the eve of the Second International Summit on Human Genome Editing, [researchers] were informed of the birth of twins in China whose embryonic genomes had been edited.").


\textsuperscript{27} See NAT’L ACADS. OF SCI., ENG’G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 111 (2017) [hereinafter HUMAN GENOME EDITING].

\textsuperscript{28} NUFFIELD COUNCIL ON BIOETHICS, \textit{supra} note 14, at 88.
scientific progress is not odious. Rather, scientific optimism should and does prevail. Scientific achievements and new technological breakthroughs made in the ART field are increasingly viewed with optimism rather than reproach.\textsuperscript{29} The rapidity of scientific possibilities, increased media attention, acceptance of pluralism, and societal attitudes of autonomous decision-making create a milieu of acceptance among an increasing segment of the population.\textsuperscript{30} The number of adults utilizing fertility clinics evinces increasing public acceptance of ART and demonstrates that with public acceptance comes newer technologies and increased use.\textsuperscript{31} This acceptance ascendency is complemented by greater insurance coverage of procedures and greater commercialization opportunities for ART procedures.\textsuperscript{32}

Accepting these premises, this Article is further premised on the idea that the legal process in the United States is not engaged in a material manner with these issues. Thus, this Article proposes Congress initiate an immediate inquiry into how to craft a pathway to best balance the science associated with genome editing and the existing values of the American population, shared with other nations. Established parameters, such as the federal Dickey-Wicker Amendment,\textsuperscript{33} the Coordinated Framework,\textsuperscript{34} and regulatory structures of agencies, such as the Food and Drug Administration ("FDA"),\textsuperscript{35} must be scrutinized for their ability to manage science amidst the current challenges.

Acknowledging these four premises, this Article then suggests that the following actions need to be part of the public engagement. First, both the rapidity and the transnational

\textsuperscript{29}. See, e.g., Julia D. Mahoney & Gil Siegal, Beyond Nature? Genomic Modification and the Future of Humanity, 81 L. & CONTEMP. PROBS. 195, 197 (2018) ("Although human germline editing entails risks, later generations will likely be better served if present day decision makers embrace the Enlightenment principles of daring to know and harnessing knowledge to improve human lives.").

\textsuperscript{30}. See id. at 200, 202-03.

\textsuperscript{31}. See id. at 213.

\textsuperscript{32}. See e.g., Key Findings: Infertility Insurance Mandates and Use of Assisted Reproductive Technology, GTRS. DISEASE CONTROL & PREVENTION (Apr. 1, 2016), https://www.cdc.gov/art/key-findings/insurance.html.


\textsuperscript{35}. U.S. FOOD & DRUG ADMIN., https://www.fda.gov/AboutFDA/WhatWeDo/default.htm#responsibilities (last visited Mar. 9, 2019).
opportunities presented by human genome editing demand an immediacy to alert the public forum of the moral, ethical, and practical issues involved. Second, scientific advancements should be viewed with a sense of optimism, not as a threat, because benefits will outweigh risks if there is sufficient public scrutiny of both risks and benefits. Third, reproduction matters deserve substantial respect because these issues relate to the individual liberty of humans, both those living and those yet to be born. There are justifiable limitations based on values when viewed within a broad pluralistic community. Fourth, human gametes (egg and sperm) are entitled to a "measure of respect"36 because of their involvement in human procreation. So, too, does a blastocyst, which is a preimplantation embryo or a human embryo that is a "developing human individual from the time of implantation to the end of the eighth week after conception, after which stage it becomes known as a fetus."37 Human tissue is entitled to a duty of beneficence in conjunction with respect.38 Thus, any procedure involving human reproduction should, at a minimum, "include concerns about diminishing the dignity of humans and respect for their variety, failing to appreciate the importance of the natural world, and a lack of humility about our wisdom and powers of control when altering that world of the people within it."39 Admittedly, while the world is too pluralistic to allow a single approach, public engagement must respect "a variety of distinct, intersecting, and mutually supporting considerations."40

Words and phrases such as "measure of respect," "dignity," and "beneficence" remain elusive, subject to the cacophony of religious, secular, ethical, and moral expressions throughout the

37. HUMAN GENOME EDITING, supra note 27, at 296.
38. Id. at 31–32 (citing the 1979 Belmont Report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research, which "focused on avoiding infliction of harm, accepting a duty of beneficence, and maintaining a commitment to justice").
40. 1 NAT'L INSTS. OF HEALTH, REPORT OF THE HUMAN EMBRYO RESEARCH PANEL 38 (1994) [hereinafter HUMAN EMBRYO RESEARCH PANEL].
world. 41 Such words can also evoke anger and stifle discussion. Yet, the fact remains that “commentators recognize both the relative respect to which embryonic material is entitled and [at the same time] the value of using that material for scientific and medical research.” 42 If this is true, and concomitantly if it is true that using any one of these diverging perceptions is “not an appropriate or useful grounding for . . . analysis,” 43 then chaos will envelope human assisted reproduction. The solution lies in utilizing the resources of a globally-connected, democratic society to balance the respect owed to human reproductive materials and the benefits to be achieved with each scientific development. Thus, this Article argues that those persons or organizations with opinions regarding human genome editing should formulate their positions, organize, and engage with others in a public forum to influence the progress and process of this advancement.

Human ART remains nascent in spite of startling biologic developments. 44 Therefore, there is little structure surrounding its current use or future direction in the United States or elsewhere; however, there are a few judicial pronouncements, an increasing number of statutes and regulations, and an accelerating debate among commentators and organizations. 45 The common denominator among all is a plea for greater transparency in debate and research; increased public discussion; and meaningful “interplay between government expertise/authority and public consultation.” 46 In this pluralistic age, it is reasonable to conclude

46. HUMAN GENOME EDITING, supra note 27, at 261.
that the only democratic means we have to accord human reproduction the beneficence, dignity, and respect due is to encourage each to influence the pathway of research and practice.

The current moment seems particularly appropriate. Science has progressed beyond IVF and now is able to permit multiple genetic parents, inheritable germline modifications, and enhancements of any fetus.\textsuperscript{47} Viewing science in an optimistic fashion, it is reasonable to expect that those with opinions regarding these matters apprise themselves of the facts and provide an inclusive voice in the debate that is underway. Current procedures are nascent, and therefore, engagement can provide guidance. Nevertheless, immediacy is warranted because "[s]cience and technology are developing rapidly in this field. . . . We should be cautious about predicting the precise form of the technology that we might be trying to govern in 5-15 years' time."\textsuperscript{48} Fashioning a pathway today is our best method of preparing for the future.

We have to consider not only the possibility of technologies emerging in our own jurisdiction, but also the possible transfer of technologies developed elsewhere, which may import ethical problems along with them. There is also the possibility that moral responsibility will be diffused around the system and will not land anywhere: international divisibility and mobility of elements of a technological intervention potentially lead to ‘organized irresponsibility’ in which moral responsibility is distributed across jurisdictions and never run to ground.\textsuperscript{49}

This Article assesses current ART procedures, identifying the creative function of IVF and how this procedure enables surrogacy, genome editing, and mitochondrial replacement. The human impact of these procedures—in such a short period of

\textsuperscript{47} See Nuffield Council on Bioethics, \textit{supra} note 14, at 11 (discussing how germline involves "cells that give rise to sperm and eggs" and hence are heritable through reproduction).

\textsuperscript{48} \textit{Id.} at 31.

\textsuperscript{49} \textit{Id.} at 54–55.
time—is startling and, depending on each person’s point of view, precipitates optimism or alarm. What all agree upon is that because these procedures involve human beings and potentially impact future generations of humans, there is a need to honestly engage interested persons and organizations in civil discourse to address the scientific challenges.

A vibrant and interactive scientific community exists in the United States. As such, this Article references reports from the National Academies of Sciences, Engineering and Medicine. Also, this Article identifies presidential councils, committees, and a host of scientific and public policy journals. In a few instances, state and federal courts have expressed opinions on the procedures and public policy parameters discussed in this Article. The scientific technology, however, moved too quickly to permit sufficient public engagement on issues such as genome editing. Although genome editing may be able to eradicate many diseases, it could also enable enhancement and permanent alteration of the human germline.\(^5^0\) Similarly, mitochondrial replacement has an impact on parenthood and implications for future generations. Engagement will address those who wish to simply say “no” to the science these procedures portend and caution those seeking unbridled discovery to charter a transparent course.

There must be an immediacy to public engagement. The science identified and discussed in this Article will not lie dormant. Immediacy is further justified due in part to the pharmaceutical industry, always alert to the economic profits associated with containment of disease and access to fertility enhancements. While the commercial sector petitions for approval for the most recent scientific innovations, some are mindful of the possibilities inherent in off-label use and the possibility of medical tourism existent in foreign countries. Increasing insurance coverage augments the current private pay option, providing added incentives to create an immediate pathway to public engagement. Interested parties concerned with these issues cannot stand idly by.

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II. CURRENT ART PROCEDURES

A. Beginning with IVF

ART is defined as “[a] fertility treatment or procedure that involves laboratory handling of gametes (eggs and sperm) or embryos [an ovum after fertilization].”\(^{51}\) Its use has provided “alternative methods for people to have children when it is otherwise impossible or infeasible for them to do so naturally.”\(^{52}\) In a significant illustration of assisted reproduction, Louise Brown was born in 1978; this baby girl is often referenced as the first test tube baby.\(^{53}\) Her birth through IVF was accomplished through an assisted reproduction technique in which fertilization is accomplished \textit{outside} the body, as compared to artificial insemination when sperm is injected into a woman and the ovum is fertilized \textit{inside} the woman’s body.\(^{54}\)

Since the birth of Louise Brown, “it is estimated that more than 5 million babies have been born as a result of IVF,”\(^{55}\) and “[a]lthough there are no official numbers, a conservative estimate indicates that more than a million embryos, most of them excess from IVF, remain in storage across the United States.”\(^{56}\) Likewise, there are countless other embryos stored in many foreign countries. Today, ART has come to include not only IVF, but also gamete intrafallopian transfer (eggs and sperm are placed in the fallopian tube and fertilization occurs in the body); zygote intrafallopian transfer (egg is fertilized outside the body and placed in the fallopian tube); and intracytoplasmic sperm

\(^{51}\) Human Genome Editing, supra note 27, at 293; see also Human Embryo Research Panel, supra note 40, at D-1 (“Embryo: in humans, the developing organism from the time of fertilization until the end of the eighth week of gestation, when it becomes known as a fetus.”).


\(^{54}\) IVF is distinguishable from artificial insemination. Artificial insemination involves the introduction of sperm into the uterine cavity to encourage fertilization, whereas the IVF involves the implantation of a fertilized egg that was grown in a petri dish back into a woman’s uterus. See, e.g., Finley v. Astrue, 270 S.W.3d 849, 850 n.2 (2008).

\(^{55}\) Mitochondrial Replacement Techniques, supra note 43, at 60.

\(^{56}\) Id. at 105.
injection ("ICSI") (fertilization occurs outside the woman's body by injecting sperm into an egg). 57

In addition to the expanding number of human embryos cryogenically preserved throughout the world, the number of ART clinics, ART cycles, and infants born as a result of ART continue to rise dramatically.58 The Centers for Disease Control and Prevention ("CDC") collects and publishes data for certain "treatments or procedures which include the handling of human oocytes [developing egg; usually a large and immobile cell][,]59 or embryos."60 In 2017, the CDC reported that in 2015 there were 499 fertility clinics operating in the United States, of which 464 provided data.61 These clinics reported that 231,936 fertility cycles were started in 2015, and the number of infants born as a result was 72,913.62 "An ART cycle is started when a woman begins taking medication to stimulate ovaries to develop eggs" or when there is natural egg production:63 "If eggs are produced, then the cycle progresses to egg retrieval, a surgical procedure in which eggs are collected from a woman's ovaries."64 Once retrieved, the eggs are then fertilized, and, if fertilization is successful, then one or more embryos (fertilized eggs) are transferred back to the woman and


59. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 62. An oocyte is defined as a "[d]eveloping egg; usually a large and immobile cell." HUMAN GENOME EDITING, supra note 27, at 303.

60. 42 U.S.C. § 263a-1 et seq., (2018) (mandating that clinics report data to the CDC or face expulsion from the Society of Assisted Reproductive Technologies ("SART").


62. Id.

63. Id. at 13.

64. Id.
the cycle may then progress to pregnancy and possibly a live birth.\textsuperscript{65}

ART cycles have increased steadily. There were 208,604 ART cycles in 2014\textsuperscript{66} and 231,936 cycles started in 2015. Both years indicate an increase from 2013, when the CDC reported that there were 497 clinics operational.\textsuperscript{67} In 2013 there were 190,773 ART cycles started, and 67,996 infants born as a result.\textsuperscript{68} Similarly, there has been a gradual increase in persons "banking" eggs or embryos for future use.\textsuperscript{69} Banking occurs through cryopreservation, usually done so a woman can avoid undergoing the retrieval process a second time since she has "banked" sufficient eggs.\textsuperscript{70} Banking is popular. In fact, from 2005 through 2014, transfers of more than one banked embryo more than tripled from nine percent to almost twenty-nine percent.\textsuperscript{71} In 2014, twenty-seven percent of all ART cycles used frozen non-donor embryos, and the percentage rose to thirty percent in 2015.\textsuperscript{72}

ART is an expensive procedure, and currently, insurance coverage is spotty.\textsuperscript{73} The cost for an ART cycle leading to a live birth currently ranges from $66,000 to $114,000,\textsuperscript{74} depending upon the location of the procedures. Moreover, a live birth may include many ART cycles.\textsuperscript{75} There are those who argue that competition among clinics and the increased possibility of insurance coverage may contribute to a reduction in price.\textsuperscript{76} Decreasing cost will also increase the number of persons able to

\begin{footnotes}
\begin{itemize}
\item[\textsuperscript{65}] Id.
\item[\textsuperscript{68}] 2015 CDC REPORT, supra note 67, at 7.
\item[\textsuperscript{69}] 2014 CDC REPORT, supra note 66, at 8; 2015 CDC REPORT, supra note 61, at 8.
\item[\textsuperscript{70}] 2015 CDC REPORT, supra note 61, at 63.
\item[\textsuperscript{71}] 2014 CDC REPORT, supra note 66, at 55.
\item[\textsuperscript{72}] 2014 CDC REPORT, supra note 66, at 8; 2015 CDC REPORT, supra note 61, at 8.
\item[\textsuperscript{73}] See Katie Falloon & Philip M. Rosoff, Who Pays? Mandate Insurance Coverage for Assisted Reproductive Technology, 16 AM. MED. ASS'N J. ETHICS 63, 65 (2014).
\item[\textsuperscript{74}] Id.
\item[\textsuperscript{75}] See id.
\item[\textsuperscript{76}] See Zalesne, supra note 52, at 445; see also Casey et al., supra note 1, at 113–15.
\end{itemize}
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utilize the procedures, and insurance may provide greater accountability of services offered. Presently fifteen states have enacted legislation requiring private insurance to cover all or some of the cost of infertility treatments.\textsuperscript{77} Interestingly, the states mandating coverage illustrate the acceptance of ART among all geographical areas of the United States. The states include: Arkansas, California, Connecticut, Hawaii, Illinois, Louisiana, Maryland, Massachusetts, Montana, New Jersey, New York, Ohio, Rhode Island, Texas, and West Virginia.\textsuperscript{78} Even though the laws vary among these states,\textsuperscript{79} it is the acceptance of the procedures which suggests ART will continue to expand among all parts of the population. This acceptance prompts the social acceptance of another form of IVF: surrogacy.

\textbf{B. After IVF: Surrogacy}

Surrogacy has been practiced since biblical times,\textsuperscript{80} through a method which involve what we now term genetic surrogacy. A genetic surrogate is defined as “a woman who is not an intended parent and who agrees to become pregnant through assisted reproduction using her own gamete [eggs], under a genetic surrogacy agreement.”\textsuperscript{81} Compare this woman to a gestational surrogate, defined as “a woman who is not an intended parent and who agrees to become pregnant through assisted reproduction using gametes that are not her own, under a gestational surrogacy agreement.”\textsuperscript{82} Obviously, the distinction involves the fact that a genetic surrogate uses her own ovum, thereby sharing a genetic link with the resulting infant. Very few states permit genetic surrogacy, and those that do mandate a comprehensive statutory scheme, such as allowing the genetic surrogate to withdraw consent to surrender the baby within a


\textsuperscript{78.} Id.


\textsuperscript{80.} See Genesis 16:1-16.

\textsuperscript{81.} UNIF. PARENTAGE ACT § 801(1) (NAT’L CONFERENCE OF COMM’RS ON UNIF. STATE LAWS 2017).

\textsuperscript{82.} Id. § 801(2).
specified time after birth. In the United States today, of the states that permit surrogacy, most permit only gestational surrogacy agreements.

In spite of initial judicial and legislative rejections of surrogacy agreements, the practice of surrogacy has "become increasingly socially accepted, and even welcomed." One commentator writes that "a look at the hundreds of legal and ethical research studies that have been published in recent decades demonstrates the recent shift and accelerated social and legal acceptance of the surrogacy practice." Illustrative of this trend towards acceptance is the 2017 revision to the Uniform Parentage Act. The National Conference of Commissioners on Uniform State Laws, which drafted the revised Uniform Parentage Act, acknowledged that "much has changed in this rapidly developing area of law and practice in the last 15 years." In addition, commentators note that, "[I]liberalization of surrogacy and a wider acceptance of the practice are linked to the expansion of rights for gay couples—the human rights issues that propelled legalization of gay marriage also drove reform in the area of surrogacy." Since adoption and gestational surrogacy are two options by which same-sex couples may become parents, it follows that surrogacy became more acceptable as marriage equality became more acceptable. Concomitantly, IVF has permitted the shift from genetic surrogacy to greater acceptance and utilization

83. See, e.g., D.C. CODE § 16-411(4) (2018); FLA. STAT. ANN. § 63.213 (2018); VA. CODE ANN. § 20-161 (B) (2016); UNIF. PARENTAGE ACT § 814 CMT.
86. Yehenzkel Margalit, In Defense of Surrogacy Agreements: A Modern Contract Law Perspective, 20 WM. & MARY J. WOMEN & L. 423 (2014); see, e.g., P.M. v. T.B., 907 N.W.2d 522, 530–31 (Iowa 2018) (holding that a gestational surrogacy contract was enforceable and did not violate public policy); see also Kamel, supra note 1, at 96–98.
87. Margalit, supra note 86, at 437.
88. UNIF. PARENTAGE ACT art. 8.
89. Id.
90. Zalesne, supra note 52, at 428.
91. Id.
of gestational surrogacy, even while recognizing increasing public acceptance of genetic surrogacy.

Surrogacy still follows a patchwork format among the states. There is no federal legislation; thus, state courts are leading the way in upholding surrogacy agreements, often without the assistance of state statutes. "California is generally considered to be the most favorable for prospective parents." The California Supreme Court stated that it is "not the role of the judiciary to inhibit the use of reproductive technology when the legislature has not seen fit to do so; any such effort would raise serious questions in light of the fundamental nature of the rights of procreation and privacy." California mirrors other more modern state courts that tend to be more permissive, even in jurisdictions otherwise not considered liberal. On the other hand, it appears that the least permissive jurisdictions tend to be ones without binding case law or ambiguous statutory language, but nonetheless have trial courts skewing in favor of enforcing surrogacy contracts. Overall, the trend is towards enforcing surrogacy agreements, which has implications for genome editing, including mitochondrial replacement.

The increasingly permissive stance of state courts towards surrogacy is demonstrated by a decision from the Iowa Supreme Court, which discusses the utilization and acceptance of ART among the general population. The case involved whether to enforce a gestational surrogacy agreement, providing a question of first impression under Iowa law. Plaintiffs were a married couple, unable to conceive their own child, and signed an

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92. Id. at 429–30.
93. See, e.g., In re Paternity of F.T.R., 833 N.W.2d 634 (Wis. 2013) (holding that there was no state public policy objection to enforcing a genetic surrogacy agreement as long as the mother’s parental rights were protected).
95. Casey et al., supra note 1, at 100 (citing Darra L. Hofman, Mama’s Baby, Daddy’s Maybe: A State-by-State Survey of Surrogacy Laws and Their Disparate Gender Impact, 35 WM. MITCHELL L. REV. 449, 460 (2009)).
96. Id. at 100 (quoting Johnson v. Calvert, 851 P.2d 776, 787 (Cal. 1993)).
97. Casey et al., supra note 1, at 103.
98. Id.
99. P.M. v. T.B., 907 N.W.2d 522, 522 (Iowa 2018); see also J.F. v. D.B., 879 N.E.2d 740, 740 (Ohio 2007) (enforcing the agreement because there was no public policy prohibiting this).
100. P.M., 907 N.W.2d at 524.
agreement with defendants, the surrogate and her husband; in exchange for "$13,000 and medical expenses, [the defendants] agreed to have the surrogate mother impregnated with embryos fertilized with the plaintiff-father's sperm and the ova (eggs) of an anonymous donor." After the surrogate became pregnant with twins, she demanded additional monetary payments from the plaintiffs; after the plaintiffs refused, defendants breached the surrogacy agreement. Eventually, the babies were born prematurely and one infant died, but the defendants continued to refuse to surrender the surviving infant to the plaintiffs. Whereupon the intended parents/plaintiffs sued to enforce the agreement and to gain custody of the surviving child. The state district court ordered a genetic test, ruled that the agreement was enforceable, terminated the presumptive parental rights of the surrogate mother and her husband, and established paternity with the biological father, awarding him permanent legal and physical custody of the baby. The defendants appealed.

The Iowa Supreme Court affirmed the district court's holding that there were neither statutory nor public policy prohibitions and that "this child would not have been born, without [the plaintiffs'] reliance on the surrogate's contractual commitment." Illustrative of the increasing acceptance of ART, reproductive freedom, and genetic parenthood, the court noted that any "contrary holding invalidating surrogacy contracts would deprive infertile couples of the opportunity to raise their own biological children and would limit the personal autonomy of women willing to serve as surrogates to carry and deliver a baby to be raised by other loving parents." Furthermore, the court held that surrogacy cannot be contrary to public policy because "[b]anning gestational surrogacy contracts would deprive infertile couples of perhaps the only way to raise their own biological

101. Id. at 525.
102. Id.
103. Id. at 528.
104. Id.
105. Id.
106. Id. at 525.
107. Id.; see also Iowa Code § 710.11 (2017) (exempting genetic surrogacy arrangements from criminal penalties associated with selling babies but silent as to gestational arrangements).
108. P.M., 907 N.W.2d at 525.
children and would limit the contractual rights of willing surrogates.\footnote{109}

While the facts of the Iowa decision are pertinent to this specific opinion, the decision may have broader applicability. The case also identifies arguments made in other ART procedures, such as genetic editing and mitochondrial replacements. Asserted entitlements to these procedures also are based in claims of individual personal autonomy, reproductive freedom, the value of a genetic relationship, and the right to freedom of contract.\footnote{110} The surrogate had no genetic relationship to the baby; this was a gestational surrogacy, not a genetic surrogacy.\footnote{111} The court wrote: “We agree with other courts that recognize the difference between surrogacy arrangements and giving up one’s own genetic child for adoption.”\footnote{112} Such a distinction exists between genetic and gestational surrogacy, a distinction mandated in some other states.\footnote{113} In addition, this was a surrogacy agreement executed by competent consenting adults.\footnote{114} Relying on precedent from other state courts, the Iowa high court ruled that freedom of contract should be honored, and that absent fraud, duress, or unconscionability, surrogacy agreements do not violate public policy.\footnote{115} Indeed, the court “conclud[ed] that gestational surrogacy agreements promote families by enabling infertile couples to raise their own children and help bring new life into this world through willing surrogate mothers.”\footnote{116}

The 2018 Iowa decision shows a change in public attitude not just towards surrogacy but also towards IVF in general. This

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\footnote{109. \textit{Id.} at 533–34.}
\footnote{110. \textit{Id.} at 525.}
\footnote{111. \textit{Id.}}
\footnote{112. \textit{Id.} at 536.}
\footnote{113. Courtney G. Joslin, \textit{Nurturing Parenthood Through the UPA} (2017), 127 \textit{Yale L.J.F.} 589, 610 (2018) ("[T]he political reality is] that state legislators have been more reluctant to enact legislation expressly permitting [genetic] surrogacy.").}
\footnote{114. \textit{P.M.}, 907 N.W.2d at 533.}
\footnote{115. \textit{Id.} at 540, 544 (noting the agreement the surrogate signed stated: “[S]he has carefully read and understood every word in this agreement and its legal effect, and each party is signing this agreement freely and voluntarily and that neither party has any reason to believe that the other party of parties did not understand fully the terms and effects of this agreement, or that the other party did not freely and voluntarily execute this agreement.").}
\footnote{116. \textit{Id.} at 539; see also \textit{In re} Parentage of F.T.R., 833 N.W.2d 634, 649–50 (Wis. 2013) (holding that a genetic surrogacy agreement should be upheld in part, because it safeguarded family expectations).}
change in perspective—minimal in regard to gestational surrogacy—suggests that first courts, and then legislatures, accept that "technology does not threaten the institution of motherhood." It is a fact of life that scientific and technological advances continue to progress. Scientific developments such as surrogacy may now include: (1) intrauterine or intracervical insemination; (2) donation of gametes; (3) donation of embryos; (4) IVF and transfer of embryos; and (5) intracytoplasmic sperm injection. Traditionally, "marital love making and baby making have gone hand in hand, [whereas] surrogacy and gamete donation involve a medical intervention that necessarily separates procreation from love and sexual intercourse." Can it be that what constitutes parenthood evolves with society? There are those who argue that today's public perception shift is based on an understanding that "parenthood [is] a moral relationship rather than a biological one, and the best interest of the child [is] being determined by social conditions and functional parenthood, not biological relations."

Undoubtedly, greater societal acceptance of surrogacy agreements arose in part because of greater social access to technology generally. Media, smart phone interconnectivity, and the vast array of data portals have made technology accessible and hence friendlier to millions. This immersion in technology has an impact on culture. Also, there is greater acceptance of same-sex couples, who are unable to access parenthood through sexual intercourse. Marriage equality occurred after the Supreme Court declared that both marriage and marriage recognition were mandated by force of the United States Constitution throughout

117. Zalesne, supra note 52, at 432.
118. UNIF. PARENTAGE ACT § 102(4).
119. Zalesne, supra note 52, at 432, 433 ("Reproduction is no longer sacred when a woman carries a child she has no desire to raise, when she gives her eggs to a fertility clinic so she can pay her student loans, or when she harvests her eggs for the future with acknowledgement that she does not want to have children yet.").
120. Id. at 439.
It follows that marriage equality led to increased rates of surrogacy or IVF among same-sex couples who were finally able to access the constellation of benefits attendant upon marriage. An illustration of the modern acceptance of same-sex couples can be found in the newly revised Uniform Parentage Act ("UPA"). The UPA (2017) addresses [any] potential constitutional infirmity by making the marital presumption expressly apply equally to both male and female spouses of the woman who gave birth. With this modification to the UPA, many more of these married same-sex parents will have legally recognized relationships with their children, and these families will have greater certainty and security regarding their familial relationships as they travel about the country.

Wherever surrogacy is not accepted in the United States, persons or couples may use the services of another state or execute a surrogacy contract with a woman in a foreign country. Foreign surrogacy may be termed transnational surrogacy and recognizes the willingness of parties to engage in medical tourism. Thailand and Mexico, among other countries, permit the enforcement of surrogacy contracts between foreigners and local women willing to carry a child to term and subsequently surrender the child after birth. Some countries, such as India, banned foreign surrogacy contracts, a development that signaled greater scrutiny of contractual clauses that possibly involve economic coercion, inadequate consent, sex-based selection of embryos, and improper treatment of the young women who serve

126. Id. at 612.
129. See Allen, supra note 127, at 808 (arguing that foreign surrogacy contracts should be invalid as contrary to public policy). But see Sharmila Rudrappa, Why is India's Ban on Commercial Surrogacy Bad for Women?, 43 N.C. J. INT’L L. 70, 91–92 (2018) (arguing that surrogacy is a valid form of employment for women and should be permitted).
as the surrogates.\textsuperscript{130} Obviously, debate over the enforcement of foreign surrogacy contracts ranges from issues of financial exploitation, adequacy of consent, reproductive freedom, and general public policy.\textsuperscript{131} Although the debate today centers on the validity of the surrogacy agreement, tomorrow international ART will permit more options than whether to enforce a surrogacy contract. Efforts in the United States to address genome editing or mitochondrial replacement must address medical tourism as it relates to foreign availability. People seek out surrogates today, but tomorrow’s “add-on” services may include gender selection, “designer babies,” or the parental rights of a child with a genetic connection to multiple genetic donors.\textsuperscript{132} Transnational surrogacy is the subject of current discussion, but the future will involve more expansive medical procedures and challenges.\textsuperscript{133}

\textbf{C. After IVF: Genome Editing}

In 1953, scientists first achieved the ability to define the structure of DNA.\textsuperscript{134} Fewer than fifty years later, in 1999, the human genome was first fully sequenced.\textsuperscript{135} “The human genome is contained in 23 pairs of chromosomes, 22 autosomes and 1 pair of sex chromosomes, in a sequence of paired chemical bases that are held together in the long molecules of . . . [DNA] that are present in almost all the cells of the body.”\textsuperscript{136} Subsequently, within

\begin{thebibliography}{136}

\bibitem{131} Cherry, supra note 128, at 274–77.

\bibitem{132} See Margalit, supra note 86, at 130.


\bibitem{136} NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 7.
\end{thebibliography}
ten years scientists made specific small changes to the genome.\textsuperscript{137} By the mid-2000s, genome editing became possible, followed by methods based on protein recognition of specific DNA sequences.\textsuperscript{138} The original editing technology was expensive and difficult to work with in laboratories.\textsuperscript{139} but continuing scientific advances made it possible to perform genome editing less expensively and on a broader scale.\textsuperscript{140} Undoubtedly, the future will bring even more efficient methods.

Genome editing involves "making precise additions, deletions, and alterations to the genome—an organism's complete set of genetic materials."\textsuperscript{141} The possibilities resulting from this process are nothing less than extraordinary. The National Academies of Sciences, Engineering and Medicine summarized the potential in its 2017 report:

Genome editing offers great potential to advance both fundamental science and therapeutic applications. Basic laboratory research applying genome-editing methods to human cells, tissues, germline cells, and embryos holds promise for improving understanding of normal human biology, including furthering knowledge of human fertility, reproduction, and development, as well as providing deeper understanding of disease and establishing new approaches to treatment.\textsuperscript{142}

Genome editing involves changing the genome sequence "by adding, replacing, or removing DNA base pairs."\textsuperscript{143} Such editing would permit among, other applications, "restoring normal function in diseased organs by editing somatic cells to prevent[] genetic diseases in future children and their

\begin{itemize}
\item \textsuperscript{137} Jay W. Cormier & Ricardo Carvajal, Ready or Not, CRISPR and Gene Editing Have Arrived and Are Here to Stay, UPDATE (July/Aug. 2016), at 4-5, http://newsite.hpm.com/pdf/CRISPR%20AND%20GENE%20EDITING%20JYC%20RC.PDF.
\item \textsuperscript{138} See id.
\item \textsuperscript{139} Id. at 4.
\item \textsuperscript{140} See id. at 4-5 ("[D]epending on the application, the distinction between gene editing and genetic engineering may really be a distinction without a difference.").
\item \textsuperscript{141} Human Genome Editing, supra note 27, at 1.
\item \textsuperscript{142} Id. at 181.
\item \textsuperscript{143} Id. at 1 n.2.
\end{itemize}
descendants by editing the human germline." In application, "existing and forthcoming genomic sequencing tools have the potential to allow for revolutionary science, including direct sequencing of RNA or proteins, real-time genomic pathogen monitoring or precision medicine based on personal genome sequencing."  

In August 2017, a team from the Oregon Health & Science University corrected a genetic defect in a human zygote that led to the development of viable embryos. "This research shows that correcting a gene mutation in viable human embryos using genome editing methods is feasible." Focusing just on the beneficial aspects of genome editing, the possibilities seems bountiful and endless. Indeed, "[i]n 2017 alone, CRISPR technologies enabled researchers to remove HIV from living animals, edit out Huntington’s disease in mice, slow the growth of cancerous cells, and open the door to the eradication of mosquito-borne diseases." Overall, "[t]he discovery of CRISPR, and its ability to precisely locate and delete genetic mutations, brings the scientific community closer than ever before to the possible eradication of a number of debilitating monogenetic diseases." Among these diseases are cystic fibrosis, sickle-cell disease, and Duchenne muscular dystrophy, all monogenic diseases that result from a single mutation along the human genome.

However, because editing a human genome could have unforeseen consequences for future generations, there is concern despite great promise. For example, international concerns were uniformly expressed at the Second International Summit on Human Genome Editing in November 2018, when it was announced that a rogue scientist in China edited genes in twin

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144. Id. at 1.
147. Id.
149. Id. at 447.
150. Id.
girls who were subsequently born. Likewise, concerns were raised when a boy was born in Mexico after a mitochondrial replacement. There were also many concerns raised over a slippery slope towards designer babies, accentuated class distinctions, and a resurgence of human eugenics.

i. The Science

Currently there are four methods used to edit any gene. These include: Zinc Finger Nucleases, Transcription Activator-Like Effector Nucleases, Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR/Cas9") Nuclease, and the use of Cpf1 as an alternative to Cas 9 nuclease. CRISPR/Cas9 is used most often by scientists, as it "can be engineered more easily and cheaply than these other methods to generate intended edits in the genome." While the scientific technology and uses of genome editing is beyond the scope of this Article, it is pertinent to know that "CRISPR technology is a molecular tool that was created by making adjustments to a bacterial immune system." It can be harnessed because:

The bacterial genome contains a number of repeating DNA sequences that are used by the bacteria to determine whether a virus is infecting the cell, and, if so, to use a specific enzyme that targets the viral DNA to cut the DNA into pieces. . . . [The] repeating pieces of DNA in the bacterial genome [are] to help the bacteria identify the same virus again the next time the virus attempts to infect the bacteria. . . . [The CRISPR/Cas9 system is

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154. Gartland et al., supra note 145, at 5; see also HUMAN GENOME EDITING, supra note 27, at 2.
155. HUMAN GENOME EDITING, supra note 27, at 2; see Cormier & Carvajal, supra note 137, at 9 ("[Y]ou can order your own CRISPR/Cas kit for as little as $150.").
156. Cormier & Carvajal, supra note 137, at 7.
fundamentally the same as traditional rDNA technologies because it uses engineered nucleotide sequences to selectively target sequences in an organism’s genome to make specific intentional changes, whether insertions, deletions, or changes in one base pair or an entire gene.157

Technology will continue to evolve.158 For example, another description of developing CRISPR/Cas 9 technology describes the process as follows:

[Using] two key molecules that introduce a change or mutation into the DNA: first, an enzyme called Cas9 acts as a molecular scissors by cutting the two strands of DNA at a specific location in the genome so that pieces of DNA can then be added or removed and, secondly, a piece of RNA called guide RNA or gRNA. This consists of a small piece of pre-designed RNA sequence (about twenty bases long) located within a longer RNA scaffold. The scaffold part binds to DNA and the pre-designed sequence guides the Cas9 enzyme to the right part of the genome so that it cuts at the intended point in the genome. In theory, the guide RNA will bind only to the target sequence and not to other regions of the DNA. Once the Cas9 enzyme makes a cut across both strands of the DNA, the cell recognizes that its DNA is damaged and tries to repair it. The technology can be used to introduce changes to one or more genes in a cell.159

157. Id. at 5–6.
158. See, e.g., HUMAN GENOME EDITING, supra note 27, at 227–31. ‘‘[O]ther strategies will undoubtedly be forthcoming and should further improve the process, based on knowledge of CRISPR/Cas9 structure.’’ Id. at 228.
While gene editing as applied to animals, specifically pigs, has been studied by Chinese and Korean scientists, an increasing range of genome-edited agricultural products have been considered as not requiring United States Department of Agriculture oversight and are hence able to proceed to market without regulation. Indeed, scientists have already used CRISPR gene editing to create better crops and produce a larger amount of food.

Currently, at least five genome-edited crop plants have been produced, including wheat, mildew-resistant white mushrooms, and herbicide-tolerant canola. More are on the way. The “genetic manipulation of animals has been the basis for much of the research aimed at understanding embryonic development and human diseases.” The Washington Post reports that by 2019 “the first foods from plants or animals that had their DNA ‘edited’ are expected to begin selling.” Specifically, scientists:

[A]re pursuing more ambitious changes: Wheat with triple the usual fiber, or that’s low in gluten. Mushrooms that don’t get brown, and better producing tomatoes. Drought-tolerant corn, and rice that no longer absorbs soil pollution as it grows.


163. Garland et al., supra note 145, at 7. For a summary of FDA and federal regulatory policy for ensuring the safety of biotechnology products, see Cormier & Carvajal, supra note 157, at 7-9.

164. HUMAN GENOME EDITING, supra note 27, at 251.

Dairy cows that don’t need to undergo painful dehorning and pigs immune to a dangerous virus that can sweep through herds.166

The Department of Agriculture reports that new rules are not needed for plants, but the FDA proposed tighter restrictions on gene-edited animals; the agency reported it will provide further guidance in 2019.167

It is one thing to edit animals and agricultural products, however, genome editing is most controversial when the new technology involves human subjects,168 especially when the edits may potentially affect the germline. Nonetheless, in spite of ethical, moral, and legal concerns voiced by domestic and transnational commissions, the pace of human genome editing is escalating rapidly.169 It is this rapid development that prompts a sense of immediacy when discussing genome editing and applications, such as mitochondrial replacement. “Genome projects are taking place on increasingly large scales, such as the Personal Genome Project, in collaboration with Veritas Genetics, and in the United Kingdom, through the 100,000 Genomes Project, led by National Health Service England;” furthermore, the project in the United Kingdom “aims to sequence 100,000 whole patient genomes from sufferers of 100 rare diseases and seven different types of cancer, within three years.”170 By mid-2016, there were more than 2,400 gene-transfer trials, most located in the Americas and Europe, but nonetheless occurring on every populated continent, with the number growing each year.171 At the Second International Summit on Human Genome Editing in 2018, scientists simultaneously denounced gene-edited babies and rejected any moratorium on defined clinical trials.172

166. Id.
167. Id.
168. Skerrett, supra note 39.
169. Gartland et al., supra note 145, at 8.
170. Id. at 5 (“This project involves 13 ‘Genomic Medical Centres’ and 85 NHS Trusts, comprising 1,500 staff and is linked to 2,500 researchers worldwide.”).
171. HUMAN GENOME EDITING, supra note 27, at 264.
Because of the scope of the existing and planned projects and the promise of future innovations, several commercial partners have become increasingly involved. Among these are Illumina for bioinformatics analysis including sequencing, data storage, and interpretation.173 "Twelve commercial pharma, biotech and diagnostics partners have come together through the Genomics Expert Network for Enterprises (GENE) Consortium to be able to use 5,000 whole genome sequences and participant health information on an annual subscription basis, costing in excess of £600,000 per company."174 Not surprisingly, there is increasing interest by commercial enterprise, because "[g]enome editing holds great promise for ... preventing, ameliorating, or eliminating many human diseases and conditions."175 Indeed, the promise of genome editing includes "possibilities rang[ing] from restoring normal function in diseased organs by editing somatic cells to preventing genetic diseases in future children and their descendants by editing the human germline."176 With this promise comes "substantial public support for the use of gene therapy (and by extension, gene therapy that uses genome editing)."177 Undoubtedly, the genome commercial enterprise "will lead to significant job creation opportunities, through drug development, new diagnostic tests, treatments, medical devices and ancillary services, alongside direct patient benefits."178 While the human benefits would be extraordinary, the economic benefits derived from these services would be too.

ii. Public Discussion

Because the technology is currently available, inexpensive, and the benefits both tempting and potentially lucrative, human genome editing is a reality. Concomitantly, issues arise pertaining to the ethical, moral, and policy considerations involved in any procedure that affects living persons and potentially future generations of humans.

173. Gartland et al., supra note 145, at 5.
174. Id.
175. HUMAN GENOME EDITING, supra note 27, at 33.
176. Id. at 1.
177. Id. at 109.
178. Gartland et al., supra note 145, at 5.
The ethical issues regarding the appropriate (and inappropriate) use of CRISPR/Cas technology require such international coordination that the National Academy of Sciences, together with Chinese Academy of Sciences and the Royal Society of the United Kingdom, formed a Human Gene-Editing Initiative and held an International Summit on Gene Editing in Washington D.C. in December 2015.\textsuperscript{179}

This was the first such summit; by the time of the second summit in 2018, twin girls with edited genomes had been born.\textsuperscript{180} In 2017, a report was published by the National Academies of Sciences recognizing that “[g]enome editing holds great promise for preventing, ameliorating, or eliminating many human diseases and conditions.”\textsuperscript{181} However, “[a]long with this promise comes the need for ethically responsible research and clinical use.”\textsuperscript{182} In a concession to the complexity of providing oversight, the Report recommends seven principles to guide governance of human genome editing.\textsuperscript{183} These principles are: (1) promoting well-being; (2) transparency; (3) due care; (4) responsible science; (5) respect for persons; (6) fairness; and (7) transnational cooperation.\textsuperscript{184} These principles are not isolated—they illustrate a theme expressed throughout the Report, “that human genome editing has raised, and will continue to raise, ethical, regulatory, and sociopolitical questions that go well beyond discussions of technical risks and benefits identified by biologists or even philosophical and sociopolitical concerns raised by social scientists and ethicists.”\textsuperscript{185} In matters so important to human life, public discussion and input is an essential parallel to scientific advancements. The Obama administration termed public discussion as “responsible development,” which is defined as

\begin{itemize}
  \item \textsuperscript{179} Cormier & Carvajal, \textit{supra} note 137, at 7.
  \item \textsuperscript{180} \textsc{Nat’l Acads. of Scis., Eng’g, & Med., Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop—In Brief 2 (Jan. 2019)}, \url{https://www.nap.edu/read/25343/chapter/1}.
  \item \textsuperscript{181} \textsc{Human Genome Editing, supra} note 27, at 182.
  \item \textsuperscript{182} \textit{Id}.
  \item \textsuperscript{183} \textit{Id.} at 182–84.
  \item \textsuperscript{184} \textit{Id}.
  \item \textsuperscript{185} \textit{Id.} at 164–65 (internal citations omitted).
\end{itemize}
communication and consultation. \(^{186}\) The rapidity of scientific development, the plurality of opinions available, and the human importance necessitates public discussion. Responsible development suggests the immediacy of developing a pathway forward.

The 2017 Report calls attention to a practical factor in developing a scientific pathway incorporating genome editing. As a practical matter, agency regulation, such as that exercised by the FDA, declines as the application of any scientific breakthrough "holds the potential for great benefit to individuals, and those individuals are willing to accept greater risk." \(^{187}\) Specifically, the Report states that:

As human genome editing improves technologically, there is every reason to believe that the health and safety risks to individuals will diminish. If these risks become de minimis, one might assume that the potential benefits required to justify the risks also will decline. Thus, as the technology improves, its application could extend from serious illnesses, to less serious illnesses, to prevention, and in the long term to enhancement, however defined. \(^{188}\)

The Report omits a specific reference to germline editing, but this is implied. This regulatory evolution, which may be characterized as a slippery slope, is augmented by off-label prescriptions and transnational applications.

Currently there are a few restrictions on what science may do. The Report specifies that "there are some genetic alterations that are insufficiently justified, too risky, or too socially disruptive to be pursued at this time." \(^{189}\) For example, federal funding for research using human embryos is prohibited by the Dickey-Wicker Amendment, although funded research using human embryos

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186. Id. at 168–69.
187. Id. at 151.
188. Id.
189. Id. at 181.
continues in some states and private research centers. This federal amendment enacted each year prohibits the use of federal funds for research involving the creation or destruction of embryos, and for research putting embryos at risk of injury or destruction except when necessary to increase their chance for healthy development. The amendment has been attached to the annual appropriations bills for the Departments of Health and Human Services, Labor, and Education since 1996.

As illustrated by the Dickey-Wicker Amendment, congressional action centers on embryos; there is no mention of genome editing or the potential for germline editing. Prohibiting funding does not curtail research, instead continuing outside of government supervision that always accompanies funding. The amendment lacks applicability in light of current scientific developments. The focus of Congress cannot be solely on the amendment but rather on developing a pathway for the future. This future necessitates a congressional inquiry into how to develop an effective pathway. While important, the human embryo is only the start of the inquiry. Genome editing and germline consequences follow because “[t]he intended genome edits themselves might have unintended consequences which, if inherited, would also affect descendants.” “[T]he efficiency of CRISPR/Cas in targeting nuclease-enhanced editing to specific sites in the genome has raised new vistas including possible human germline editing.” There is also concern over eugenics, the general respect traditionally afforded human reproductive

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190. Id. at 80; see, e.g., 410 ILL. COMP. STAT. ANN. 110/1-50 (West 2019); MONT. CODE ANN. § 50-11-103 (2017); NEB. REV. STAT. § 28-346, (2016); NEB. REV. STAT. § 71-7606(3) (2016).

191. HUMAN GENOME EDITING, supra note 27, at 33.

192. Kearl, supra note 33.


195. See infra Part III.

196. HUMAN GENOME EDITING, supra note 27, at 188.

197. Id. at 240–41 (detailing that there are alternatives to editing an embryo, such as editing the eggs or sperm before fertilization, but the issue of the effect upon germline descendants remains).
material, and suspicion that human embryo enhancement will become the overall goal.\textsuperscript{198}

Caution and deliberation permeate both the Report and resulting recommendations.\textsuperscript{199} In addition, "recent history and current events both undercut this conception of how things do and should work."\textsuperscript{200} Science is both independent and precedent of substantive deliberation. Scientific independence was illustrated in July 2017, when it was announced that the first human embryos were edited in the United States,\textsuperscript{201} an announcement that was made prior to gene-edited twin girls born in 2018. Both of these gene-editing procedures, the latter more aggressive than the former, occurred independently of governmental regulations or recommendations. In late 2017, scientists at the Salk Institute developed a technique to alter the activity, as distinct from the underlying sequence, of genes associated with disease.\textsuperscript{202} Admittedly, there is a distinction between genome editing on nonreproductive human cells, called somatic cells,\textsuperscript{203} and editing of germline cells. Germline cells are cells that at any point in the lineage of cells that could give rise to sperm or eggs, which could fuse during sexual intercourse to create an embryo and thus continue into the next generation.\textsuperscript{204} This latter procedure is contentious "because the resulting genetic changes could be inherited by the next generation, and the technology therefore would cross a line many have viewed as ethically inviolable."\textsuperscript{205} There are other examples, too. Obviously, government recommendations or funding restrictions are not barriers to experimentation. Science continues to progress independent from public discussion and policy formation. Nonetheless, it seems preferable to make the government more than an observer.

\textsuperscript{198} Id. at 42, 153, 159.
\textsuperscript{199} See id.
\textsuperscript{200} Mahoney & Siegal, supra note 29, at 201.
\textsuperscript{202} Mahoney & Siegal, supra note 29, at 202 (citing Hsin-Kai Liao et al., In Vivo Target Gene Activation via CRISPR/Cas9-Mediated Trans-Epigenetic Modulation, 171 CELL 1495 (2017)).
\textsuperscript{203} HUMAN GENOME EDITING, supra note 27, at 306 (discussing how a somatic cell is any "cell of a plant or animal other than a reproductive cell or reproductive cell precursor").
\textsuperscript{204} Id. at 299.
\textsuperscript{205} Id. at 6–7.
Congress, working with public consensus, needs to establish a pathway forward.

iii. Regulation

a. Funding versus Sanction

Currently, modification of the human germline is not prohibited in the United States, however federal funding for this form of research is forbidden by Congress through the Dickey-Wicker Amendment. The Congressional prohibition specifies that none of the funds made available by Congress under the appropriations act "may be used to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product . . . in research in which a human embryo is intentionally created or modified to include a heritable genetic modification." Note that prohibiting the procedure and prohibiting funding of the procedure are distinctive, the Amendment doing the latter. Thus, researchers able to garner private funding may proceed, but private research may eliminate the public scrutiny which permits evaluation of risk, morality, and process. This is a loss for the public.

The National Institutes of Health ("NIH") approved a proposal for the clinical use of human T-cell editing as a part of a cancer immunotherapy program. Although this proposal is barred by restrictions on live human embryo research prohibited by the Dickey-Wicker Amendment, funding resulted from guidelines prompted by an executive order issued by President


207. 129 Stat. at 2283.


209. *See*, e.g., Zhao, *supra* note 23, at 127–28. For criminal sanctions imposed on genetic editing, see for example P.R. Laws Laws Ann. tit. 33, § 4743 (2005) ("Any person who uses technology to alter the human genome for purposes other than diagnosis, treatment or scientific research in the field of human biology, particularly genetics or medicine shall incur a second degree felony.").

Obama.\textsuperscript{211} These orders resulted in new NIH guidelines that were established in 2009.\textsuperscript{212} These revised guidelines permit researchers to obtain federal funding for human embryo research if: the embryos were created using IVF for reproductive purposes; the embryos were voluntarily given by individuals who no longer needed them; and the embryos were used for research purposes.\textsuperscript{213} It appears that these guidelines apply to CRISPR/Cas research,\textsuperscript{214} but the incremental exceptions permitted by the revised guidelines illustrate the hurdles researchers face when seeking government funding for newer technologies. Despite the government hurdles, newer applications of human genome editing continue. However, Francis Collins, Director of the NIH in 2016, issued a statement affirming that the NIH would not fund any use of gene-editing technologies in human embryos.\textsuperscript{215} Subsequently, in 2017, the National Academy of Sciences and the National Academy of Medicine both recommended the use of the existing regulatory infrastructure to evaluate aspects of genome editing, including possible germline applications, when compelling reasons presented, based on risk versus benefit parameters.\textsuperscript{216}

A robust public discussion about the values to be placed on the benefits and risks of heritable genome editing is needed now so that these values can be incorporated as appropriate into the risk/benefit assessments that will precede any decision about whether to authorize clinical trials [of human genome editing].\textsuperscript{217}

\begin{itemize}
\item \textsuperscript{211} See Removing Barriers to Responsible Scientific Research Involving Human Stem Cells, Executive Order 13505, 74 Fed. Reg. 10,667 (Mar. 9, 2009).
\item \textsuperscript{212} See National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009).
\item \textsuperscript{213} Tomlinson, supra note 148, at 457 (citing National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170, 32,175 (July 7, 2009)).
\item \textsuperscript{215} See id.
\item \textsuperscript{216} HUMAN GENOME EDITING, supra note 27, at 133–34.
\item \textsuperscript{217} Id. at 134.
\end{itemize}
Of course, private research continues and often includes risk/benefit analysis. In 2017, scientists at the Oregon Health and Science University utilized CRISPR/Cas9 to correct mutations in the MYBPC3 human gene which leads to sudden death in young athletes.\(^{218}\) Human gene "editing was successful in 42 out of 58 human embryos, with 41 of these embryos containing two healthy, wild-type copies of the MYBPC3 gene."\(^{219}\) Based in part on recent successes, some predict that the actual editing of humans is only about ten to twenty years away,\(^{220}\) but public funding for germline editing, the most significant hurdle, was placed on hold by the NIH pending further developments, including more information about the risks associated with the practice.\(^{221}\) Pendency deprives the government of an active role in planning a value-oriented pathway.

Private laboratories and scientists may be leery of a government pathway. Interaction between public versus private funding pertaining to biotechnology has a history peppered with federal and state statutes, federal agency regulations, and private laboratories addressing serious human diseases and thereby marketing products from which they will derive commercial benefit.\(^{222}\) Congressional prohibitions, such as the Dickey-Wicker Amendment, are most often noted as illustrative of the barriers researchers confront because they are singular prohibitions, but illustrative of systematic restraint.\(^{223}\) In addition to Congressional appropriations amendments, there is a history of regulatory barriers that have effectively prevented funding of biotechnology in various settings.\(^{224}\) These barriers are illustrated in the regulatory pathway.

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\(^{218}\) See Hong Ma et al., Correction of a Pathogenic Gene Mutation in Human Embryos, 548 NATURE 413, 418 (2017); Kristina M. Smith, Note, Germline Editing: Two Steps Forward, One Step Back?, 21 SMU SCI. & TECH. L. REV. 101, 103 (2018) (noting that the first human germline editing in the world occurred in China in 2015, but it was not considered a success).

\(^{219}\) Seitz, supra note 7, at 71.


\(^{221}\) Britt E. Erickson, Editing of Human Embryo Genes Raises Ethics Questions, 93 CHEMISTRY & ENGINEERING NEWS 20, 20–21 (2015).

\(^{222}\) MITCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 62.

\(^{223}\) Id.

\(^{224}\) Id. The statutes and regulations prohibit the Department of Health and Human Services funding for research, but they do not prohibit the research itself. Id. at 64.
b. Regulatory Pathway

In 1973, the U.S. Department of Health, Education and Welfare prohibited research on live human embryos. Then, in 1974, Congress included within the ban all embryos created through IVF. Eventually, as science sufficiently progressed so as to enable genome editing, the NIH created a Recombinant DNA Advisory Committee to oversee proposals for research funding at NIH. In 1985, that committee recommended against funding proposals that would involve germline alterations. Rather than focus on embryos and the potential issues relating to human life, the NIH committee was concerned about germline editing and the possibility of eugenics, which could propel research into creating a mythically superior human being. Admittedly, the heightened concern over eugenics has a storied background compiled from a:

[L]ong and troubling history of eugenics . . . replete with dogma that creates hierarchies of human quality based on race, religion, national origin, and economic status, and it demonstrates how scientific concepts, such as natural selection, and public welfare measures, such as public hygiene, can be subverted for purposes of cruel and destructive social policies.

Historically, eugenics was associated with breeding of human beings possessing desired qualities and characteristics with

226. Id.
228. Id. at 50.
229. Id. at 2.
230. HUMAN GENOME EDITING, supra note 27, at 153; see Immigration Act of 1924, H.R. 7995, 68th Cong. (1924); Buck v. Bell, 274 U.S. 200, 207 (1927) (holding that sterilization of young women was warranted to prevent degenerate offspring); see also DANIEL J. KELVES, IN THE NAME OF EUGENICS: GENETICS AND THE USES OF HUMAN HEREDITY 117-21 (1985).
the aim to produce a master race. The NIH Committee took note of this.

Although eugenics has a long history, genetically engineered eugenics, a much newer science, has a short history. In the 1950s, the structural basis of how DNA duplicates itself was discovered and people realized that individuals “could be chemically modified to have ‘more’ of the ‘good’ genes.” Since the early 1950s, scientific advances have fueled the debate over issues such as permitting enhanced embryos and the possibility that adults could create “designer babies” that possess what some think are desired characteristics or qualities. Thus, even though science may intend to curtail disease, eventually the technology can address more cosmetic characteristics.

Concern arises over permitting parents to “bioengineer children” through “genetic enhancement, which might ultimately allow parents to produce physically and intellectually superior children.” Not just beautiful children, but children that are stronger in mind and body. Some argue that because this technology is only available to the wealthy, unequal access to embryo enhancement would widen societal divisions. In 2017, the American Society of Human Genetics (ASHG) published a statement on germline editing to address these concerns. Overall, the ASHG’s statement supports public funding for research on possible future clinical applications of gene editing, but suggests that such research must be based on a compelling medical rationale, evidence that supports its clinical use, an ethical justification, and a transparent public process to solicit and

231. Eugenics, HISTORY (Aug. 21, 2018), https://www.history.com/topics/germany/eugenics. Recall the fanatical racial goals of Adolf Hitler for one example of the dangers of eugenics. Id.

232. See id.


234. See, e.g., Sas & Lawrenz, supra note 7.

235. Zalesne, supra note 52, at 455.

236. See id.

237. Id.

incorporate public input.\textsuperscript{239} It is easy to notice the variety of interested parties, each having an opinion on the matter, which suggests the need for public input and engagement.

But while some see risk in genetic editing, others dismiss the “designer baby” concern and focus solely on the possibility to eliminate heritable human disease.\textsuperscript{240} Others argue that eugenics and freedom from disease are irrelevant. The single focus should be upon an adult’s individual reproductive liberty and concomitant privacy entitlement. Proponents of this argument assert that the starting point on any discussion of genome editing should be an adult’s reproductive freedom.\textsuperscript{241} The people voicing the call for reproductive freedom argue “that the burden is on the state to articulate an identifiable harm to identifiable persons in its justification for prohibiting the conduct of private parties, not on the private parties to articulate why their conduct is morally permissible.”\textsuperscript{242}

Since 1974 seven national commissions have been formed to discuss bioethical issues.\textsuperscript{243} One of these, a 1982 presidential commission, wrote in its conclusions that it found no ground for concluding that any current or planned form of genetic engineering was intrinsically wrong or irreligious per se.\textsuperscript{244} Then, in 2001, a federal bioethics commission was created to focus not on costs or benefits associated with bioethics, but rather on parents’ ultimate control over their children.\textsuperscript{245} The commission’s concern was “that germline enhancement might encourage people to view children as something to be designed and

\textsuperscript{239} Id. at 173.
\textsuperscript{240} Zalesne, supra note 52, at 459.
\textsuperscript{241} Id. at 460.
\textsuperscript{242} Id.
\textsuperscript{244} PRESIDENT’S COMM’N FOR THE STUDY OF ETHICAL PROBLEMS IN MED. & BIOMEDICAL & BEHAVIORAL RESEARCH, SPlicing LIFE: A REPORT ON THE SOCIAL AND ETHICAL ISSUES OF GENETIC ENGINEERING WITH HUMAN BEINGS 77 (1982).
\textsuperscript{245} HUMAN GENOME EDITING, supra note 27, at 157.
manipulated." The commission’s discussion of the best interest of the child, rather than the reproductive rights of the adult, provide a different approach to individual liberty interests.

There is an important development that has repercussions today. In 1986 the White House Office of Science and Technology Policy ("OSTP") gave regulatory authority over biotechnology to a troika of three federal agencies. The action created what is called the Coordinated Framework, an important factor in regulating bioethics today. The three federal agencies comprising the Coordinated Framework are the FDA, the Environmental Protection Agency ("EPA"), and the U.S. Department of Agriculture ("USDA"). Few commentators on bioethics gave serious thought to the Coordinated Framework until Americans became concerned about genome editing and food production, a regulatory process entrusted to the USDA. Likewise, the EPA became the subject of public attention when James Clapper, former United States Director of National Intelligence, identified genome editing as a weapon of mass destruction and proliferation. In tandem with concerns raised by James Clapper, the 2017 Departments of Health and Human Services, Labor, and Education Appropriations Bill included an amendment that required the Office of the Director of National Intelligence to

246. Id. But see Zalesne, supra note 52, at 455 (noting that parents have always sought to improve their children).

247. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 138 ("Consent by intended parent(s) to a process that would result in the birth of a child through MRT could not fully protect the interests and welfare of future children.").


formulate a plan to "monitor advances in life sciences and biotechnology that addresses... [United States] competitiveness in the global bio-economy and the risks and threats in genetic editing technologies," such as CRISPR."

Today, as human genome editing becomes increasingly possible, the FDA has become the focus of scrutiny because it has regulatory responsibility for, among other procedures, genome editing. "The FDA, as the sole federal regulatory agency for biomedical products in the United States, focuses on safety and efficacy when evaluating gene-transfer products, from the first time they are used in humans through their commercial distribution and over the lifetime of their use." Indeed, clinical testing of somatic cell genome editing could not begin in the United States without the FDA's first approving an Investigational New Drug ("IND") application, and the clinical protocol would require institutional review board ("IRB") approval and ongoing review. The IND applications for gene therapy are regulated by the Office of Tissues and Advanced Therapies (Previously the Office of Cellular, Tissue and Gene Therapies) within the Center for Biologics Evaluation and Research ("CBER"). Any Human Genome editing products may benefit from accelerated review by the FDA under the 21st Century Cures Act, signed into law in December 2016.

The Obama administration was concerned that the Coordinated Framework, which was established in 1986, was not evolving sufficiently to address current technological advances, thus creating regulatory confusion and lost opportunities. Hence, in 2015, the White House directed the Office of Science and Technology "to update the Coordinated Framework to ensure that the Framework was modernized and prepared for future

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254. HUMAN GENOME EDITING, supra note 27, at 56.
255. Id. (citation omitted). For a summary of the regulatory pathway for a medical product created using genome editing, see id. at 36-37.
256. Smith, supra note 218, at 105.
257. HUMAN GENOME EDITING, supra note 27, at 51.
biotechnological advancements." Specifically, the OSTP wanted to modernize the Coordinated Framework to clarify "the mechanism and timeline for regularly reviewing, and updating as appropriate, the [Coordinated Framework] to minimize delays, support innovation, protect health and the environment, and promote the public trust in the regulatory systems for biotechnology products." The update is still underway and the outcome far from conclusive. Meanwhile, there are those who contend that "the irony of subjecting groundbreaking scientific discoveries to an archaic regulatory scheme is causing many researchers to lose faith in the system." The only solution for some is for Congress to enact legislation authorizing the creation of a new regulatory agency focused specifically on the oversight of reproductive and genetic biotechnologies. There is a sense of urgency too. "The dearth of IVF and biotech competent countries with adequate legislation for genetic modification of humans is troubling. Countries need to modernize their legislative and regulatory systems to ensure that premature use of [technology] in the human germline is prevented, saving the collective human genome from future cataclysm." As stated, each federal agency within the Coordinated Framework has individual responsibilities. The FDA has regulatory authority over cell and gene therapy products marketed to the public. "Human embryo research clearly falls outside the purview of [agriculture] and [the environment], and the FDA is currently blocked from even considering proposals that involve human embryo research at this point." This prohibition results from the wording of the Dickey-Wicker Amendment. However,

260. Cormier & Carvajal, supra note 137, at 9; see also Borel, supra note 251.
263. See Zhao, supra note 209, at 137.
266. Id. at 475. See also HUMAN GENOME EDITING, supra note 27, at 43 ("A single-cell fertilized egg is treated as if it were an embryo for most relevant state and federal laws, and restrictions on the work or on the funding would apply.").
government-regulated in vitro research is currently underway in China, using nonviable embryos, and research has been approved using viable embryos in Sweden and the United Kingdom. Of course, there are parallel privately funded research projects.

In the United States, "[w]here a company to seek approval of use of CRISPR/Cas directly administered to a patient, [the] FDA would likely conclude that the targeting sequence/nuclease complex is a biological product subject to regulation in FDA’s Center for Biologics Evaluation and Research (CBER)." Then, "[m]arketing authorization would depend on the company demonstrating that the specific CRISPR/Cas complex can be reliably and consistently manufactured, is safe to use, and has its intended effect on the human patient." The 1994 NIH Human Embryo Research Panel concluded that research creating embryos for research is justified if there is no alternative and the research is "potentially of outstanding scientific and therapeutic value." If these guidelines are applicable, it would appear that "the genome-editing research necessary to test edited gametes would seem to fall within this exception." However, the NIH is not the FDA, and this research responsibility lies with the FDA under the Coordinated Framework.

c. Food and Drug Administration

To date, the FDA and its CBER “has never approved a proposal to modify the germline," or approved any gene editing product, although it has authorized a number of gene therapy trials. But the FDA has not yet approved a gene therapy for market. When the FDA scientific advisory committee reviews a

268. HUMAN GENOME EDITING, supra note 27, at 41–42.
270. Cormier & Carvajal, supra note 137, at 7.
271. HUMAN GENOME EDITING, supra note 27, at 44.
272. Id.
274. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 62.
277. HUMAN GENOME EDITING, supra note 27, at 35.
gene therapy or genome-editing protocol, the committee meeting is open to the public, and a public representative must be included among the advisory members.278 Were a company to seek approval of CRISPR/Cas directly administered to a patient, FDA would likely treat this as a biological product subject to regulation in the FDA’s Center for Biologics Evaluation and Research.279 Upon review, CBER would want to know if CRISPR/Cas were targeted sufficiently so that no “untoward off-target effects would be observed.”280 But if the CRISPR/Cas complex is used to edit genomes, then regulation would depend upon whether the cells are within the human body or have been removed.281 The latter process would have an easier and a shortened review compared to the former.282 Furthermore, any laboratory seeking approval from the FDA “will have an added burden of educating the FDA, and of wading against the natural precautionary tendencies of an agency faced with a high-profile and unproven technology.”283

Today the focus of regulatory bodies, such as the FDA, is upon the distinction between prevention of disease and personal physical enhancement, the former receiving attention and funding if the primary goal is to lessen the impact of any disease.284 However, the latter, involving cosmetic or performance-enhancement, will be denied funding unless approved by the Recombinant DNA Advisory Committee (“RA”), the institutional biosafety committees (“IBC”s), and the IRBs.285 One commentator

278. Federal regulations require that an Institutional Review Board include experts with appropriate technical training, and “at least one member whose primary concern is in a nonscientific area and one lay member who is not otherwise affiliated with the institution.” See id. at 46.
280. Id. at 8.
281. Id.
282. Id. Removed or stored human specimens are protected under the Common Rule that governs federal agencies and departments, effective January 2018. See, e.g., Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7,149, 7,150 (Jan. 19, 2017) (noting that “exempt research would be required to undergo limited [Institutional Review Board] review to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens”).
284. See Seitz, supra note 7, at 84; The FDA Supports Research to Reduce Health Disparities, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm404387.htm (last updated Apr. 19, 2017) (explaining that FDA uses data from clinical trials to determine whether medical products are safe and effective for disease treatment).
285. HUMAN GENOME EDITING, supra note 27, at 169.
suggests that it is permissible to retain the Coordinated Framework and the Congressional Dickey-Wicker Amendment forbidding funding to pay for research in which a human embryo is intentionally created or modified to include a heritable genetic modification.\textsuperscript{286} What is needed, the commentator argues, is "a specific exception or exceptions, such as those that would allow the FDA to receive and review [IND] applications for the use of [human germline modification] to treat specific monogenic diseases."\textsuperscript{287} Specifically, the commentator argues, the Congressional rider on the Consolidated Appropriations Act would permit an exception for:

\begin{quote}
[A] submission pertaining to the treatment of embryos where there is a substantial risk that the child will be born with a severe or life-threatening genetic disease, where the disease has a well-established and specific genetic cause, where the modification results in wild-type gene, and where the patients could not obtain equally effective treatment using other means.\textsuperscript{288}
\end{quote}

Perhaps what is needed is a more comprehensive scientific pathway to accommodate the increasing scientific developments, particularly a pathway that results from greater access to public opinion.

Eventually "progress will be necessary before any genome-editing intervention for indications other than the treatment or prevention of disease or disability can satisfy the risk/benefit standards for initiating a clinical trial [involving gene editing]."\textsuperscript{289} Federal regulators take a cautionary approach. An illustration is the approval of the human growth hormone ("hGH"), which became the focus of discussion in 1985.\textsuperscript{290} The issue revolved

\begin{itemize}
\item \textsuperscript{286} See Seitz, supra note 7, at 75–76.
\item \textsuperscript{287} Id. at 80.
\item \textsuperscript{288} Id. at 91. For a definition of what constitutes a serious disease, see 21 C.F.R. § 312.300(b)(1)(2018).
\item \textsuperscript{289} Human Genome Editing, supra note 27, at 159 (noting that this is true for both somatic and heritable germline editing). One author argues that Congress should permit funding for human genome editing if it will address severe genetic diseases that have no better alternative. See Seitz, supra note 7, at 61.
\item \textsuperscript{290} See Human Genome Editing, supra note 27, at 160.
\end{itemize}
around whether giving the hormone to children or adults constituted treatment, prevention, or enhancement, and which of these uses might be appropriate.291 Eventually, the FDA approved hGH for use in children and adults, but only for a narrowly defined list of diseases involving stature.292 Caution was illustrated in the FDA's restricted use of the growth hormone hGH.293 Initially, the FDA did not prevent "off-label" use of the drug for enhancement purposes, but increasingly the drug was used for unintended purposes such as antiaging or enhancement of athletic performance.294 As a result, Congress enacted the Crime Control Act of 1990,295 which prohibits any person from knowingly distributing or possessing human grown hormone intending to use it for any purpose not unauthorized by the Secretary of Health and Human Services.296 Conviction for a violation is considered a felony, punishable by fines and up to ten years in prison.297

Currently, legislative and public policy forums relating to human embryonic research are characterized by cautious dialogue, scientific reports, and rejections of government funded research.298 However, there are those who argue that "hitting the pause button on human germline editing may not be as viable an option as its proponents assume. . . . [B]roken momentum means lost opportunities."299 During this status quo, research continues unabated in the private community, bolstered by the independence of the independently funded laboratories arguing

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291. Id.; see also David B. Allen & Leona Cuttler, Treatment of Short Stature, 368 NEW ENG. J. MED. 1220 (2013).
293. See HUMAN GENOME EDITING, supra note 27, at 160.
297. Id.
299. Mahoney & Siegal, supra note 29, at 206.
both freedom from "devastating genetic diseases,"\textsuperscript{300} and the advantageous financial incentives that would result were these breakthroughs to be realized. The ability to argue for betterment of the human race trumps any cautionary tales of eugenics or inadequacy of consent.

We live in an age of medical tourism, which means that researchers are able to utilize foreign locations "for faster and cheaper therapeutic options, as well as newer or less regulated interventions, [which] will be impossible to control completely if the technical capabilities exist in more permissive jurisdictions."\textsuperscript{301} The financial benefits will be extraordinary if successfully harnessed by a global pharmaceutical company. Indeed, studies suggest that in our interconnected world the medical tourism market is currently worth more than $61 million, with every expectation this market will continue to expand.\textsuperscript{302} Also, the rise in the number of assisted reproductive procedures, IVF, and professional clinics throughout the world suggests both a need and a market for the types of services offered pertaining to genome editing.

Transnational regulation is public, but ineffective. For example, in 2015 the Council of Europe's Convention on Human Rights and Biomedicine and UNESCO's Universal Declaration on the Human Genome and Human Rights wrote that germline modification would jeopardize the inherent and therefore equal dignity of all human beings and renew eugenics.\textsuperscript{303} The Council of Europe's Oviedo Convention "specifically calls for a prohibition on the use of genetic engineering of the germline or changing the makeup of the following generations."\textsuperscript{304} Also, every nation in the European Union has adopted the EU Directive on Clinical Trials, which "requires member states to adopt a system for the review of clinical research consistent with internationally recognized

\textsuperscript{300.} Id.; see also Donald B. Kohn et al., Ethical and Regulatory Aspects of Genome Editing, 127 BLOOD 2553, 2554 (2016); Philip Kitcher, The Lives to Come: The Genetic Revolution and Human Possibilities 65 (1996).

\textsuperscript{301.} Human Genome Editing, supra note 27, at 190.


\textsuperscript{304.} Human Genome Editing, supra note 27, at 263.
standards for good clinical practice for the ethical and scientifically valid design, conduct, and report of trials.” Chinese agencies have published regulatory guidelines for human embryo research and IVF practices. Finally, some countries and locales, such as Mexico City, Panama, and Columbia, provide criminal penalties for those using genetic manipulation for any reason other than for the elimination or treatment of a serious defect or disease. But attempts at uniformity of regulation only illustrates the complexity of control and the shortcomings of government regulation. And successful human gene editing procedures in each of these nations belittles any claim to effectiveness of control.

Because nations have different historical, economic, social, and cultural systems and values, “reaching consensus among 100 or more nations on regulatory requirements for any technology is a laborious and resource-intensive undertaking that in the end may not be successful.” Instead, the Human Genome Editing Report published by the American National Academies of Science suggests that a better goal is to foster international cooperation and coordination so as to develop common ground that permits a balance between innovation and precaution. Such language, as found in the Human Genome Editing Report, suggests developing a pathway based in transparency and consultation, rather than fixed approval or disapproval.

International cooperation was evident in 2016, when the International Society for Stem Cell Research (“ISSCR”) published


308. HUMAN GENOME EDITING, supra note 27, at 268.

a statement: “Until further clarity emerges on both scientific and ethical fronts, the ISSCR holds that any attempt to modify the nuclear genome of human embryos for the purpose of human reproduction is premature and should be prohibited at this time.”

Similarly, an international group of experts suggested that heritable genome editing “might be acceptable,” but suggested that a number of safety, efficacy and cultural attitudes should be explored prior to approval. Illustrative of this cautionary approach is the British Nuffield Council on Bioethics; it concluded in its 2018 report that in reference to genome editing technologies, categorical limits should not be imposed “if such experiments would not be biologically reckless and they would be consistent with the welfare of future people, not socially divisive and not initiated without prior societal debate, they would not unnecessarily undermine the concept of human rights or the rights of the future individual concerned.”

Amidst competing arguments over all elements of genome editing, the reality of the immense monetary gains that may be made from the procedure is likely to moot any obstacles. To illustrate, “[i]n May 2017, MarketsandMarkets published a report predicting that the genome editing market will be worth $3.5 billion in just four years.” As further illustration of the promise of commercialization, in Boston, three start-up companies partnered with pharmaceutical companies such as Bayer and Novartis and raised an aggregate $1 billion to address the possibilities inherent in genome editing. The prediction is that genome editing may be “sold as an ‘add-on’ at fertility clinics,” where couples or individuals could purchase genome editing options, establishing a system of consumer-based eugenics for those able to afford it. As summarized in a 2018 report by the

312. NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 97.
314. Id.
Nuffield Council on Bioethics, "[m]any interest groups sustained either by patients themselves or by pharmaceutical companies offer strong advocacy for the funding and development of new treatments for genetic diseases, including the extension of reproductive options."\textsuperscript{316}

\textbf{D. After IVF: Mitochondrial Replacement Transfer}

i. The Science

Mitochondrial replacement transfer ("MRT") is a new technique, evolving from IVF and the expansion of ART.\textsuperscript{317} It is a form of editing that carries with it significant ethical, moral, technological, and legal issues because it could introduce permanent and heritable changes to the human gene pool.\textsuperscript{318} By editing a defective oocyte (egg) or a zygote (fertilized oocyte) in females, the modification in the DNA could result in heritable change; the effects of this are unknown and therefore a cause for concern.\textsuperscript{319} In its 2016 Report, the National Academies of Sciences concluded that there are several inherent complexities associated with mitochondrial genetics.\textsuperscript{320} "Overall, these complexities underscore the relatively unpredictable nature of mitochondrial genetics, which could complicate the ability of preclinical studies to predict with certainty the safety and efficacy of MRT in humans."\textsuperscript{321}

As with genome editing, MRT makes possible eradicating a disease for which there is no known cure, but the effects of which

\textsuperscript{316} NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 18.
\textsuperscript{317} Cussins & Lowthrop, supra note 302, at 74.
\textsuperscript{318} See id. MRT and genome editing are considerably different in technical terms. The first recombines intact sequences of mitochondrial DNA and nuclear DNA in novel biological constructs, while the second makes changes to nuclear DNA sequences themselves. \textit{Id.} at 76.
\textsuperscript{320} MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 6–7.
\textsuperscript{321} Id. at 54. Specifically, uncertainties of MRT research involve: (1) limitations of current animal and in vitro models, as well as available data for purposes of predicting safety and efficacy; (2) uncertainty of techniques involved for validating efficacy of MRT—namely for quantifying pathogenic mtDNA carryover and heteroplasmy load; and (3) the potential for yet unknown adverse effects of reagents and manipulations employed in MRT on the resulting embryo, fetus, or future child. \textit{Id.} at 57.
may affect a human brain, muscles, heart, gastrointestinal tract, and liver. As a result of recent scientific discoveries, specifically the gene editing tool, CRISPR, it is possible to “remov[e] the nuclear DNA from the target egg’s defective mtDNA and [place] it within a donated egg with healthy mtDNA. The nuclear DNA of the donated egg is similarly removed so that the healthy mtDNA is the only contribution by the donor.” The procedure will not help those already born and suffering from mitochondrial disease, but it does prevent a second-generation transmission of mtDNA-based diseases. These significant diseases may be circumvented while at the same time permitting an affected mother to have genetically related children.

The procedure was used successfully with the birth of a baby boy in 2016. Dr. John Zhang, of the New York New Hope Fertility Center, worked with a couple from Jordan and then traveled to Mexico, performing a “maternal spindle transfer.” Eventually, on April 6, 2016, a healthy baby boy was born to the Jordanian couple in Mexico City. There have been other reports of MRT being used by a physician in Kiev, Ukraine, to correct “the problem” and allow a patient to give birth to a healthy baby genetically her own. After the birth in Mexico, the British Parliament voted to permit a MRT exception to a policy in the United Kingdom prohibiting human germline editing, a policy shared with an additional thirty-eight countries that have such a ban. There is no such exception in the United States, which prohibits funding for “research in which a human embryo is intentionally created or modified to include a heritable genetic modification.”

322. Id. at 37.
324. Id.
327. Drabiak, supra note 325, at 1–2.
The National Academies of Sciences, Engineering and Medicine wrote in 2016 that four scientific events occur as a result of MRT. First, embryos may be created that, if taken to term, would result in offspring with genetic material from three different persons, including two women of different maternal lineage. Second, a mitochondrial transfer would constitute a genetic modification that could be passed down through future generations if the offspring were female. Third, any genetic modification made today could have future unknown effects, which would not be reversible. And fourth, any genetic modification would affect every cell type of the resulting individual, thus affecting the total organism rather than being confined to a specific organ system. Like human genome editing, MRT could enable heritable genetic modification, a historic development. It also “irrevocably alters the face of assisted reproduction from a discipline focused on infertility to one with a far broader portfolio.” This fact is significant as MRT may be another element in the list of options available at current and future fertility clinics throughout the United States and the other advanced nations of the world.

To date, no federal or state regulatory authority of the United States has received an application to pursue a cytoplasm transfer technique such as MRT; thus, no approval has been given for “a cell-based product that involves genetic material from two women of different maternal lineages.” However, in spite of the lack of explicit approval, the National Academies of Sciences Report, after extensive investigation and public involvement, “concludes that it is ethically permissible to conduct clinical investigations of MRT, subject to certain conditions and principles

331. Id.
332. Id. at xiv.
333. Id.
334. Id.
336. Id. (citing Adashi, supra note 335, at 1332).
337. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at xii–xiv, n.2.
laid out in [its] report." Specifically, the report states that the primary focus should be the best interest of any child born as a result of MRT: "Clinical investigation should collect long-term information regarding psychological and social effects on children born as a result of MRT, including their perceptions about their identity, ancestry, and kinship."  

In addition, clinical investigations should be limited to women who may potentially transmit serious mtDNA disease, and also to transfer only male embryos for gestation so as to avoid introducing heritable genetic modification during initial clinical investigations. Using male embryos rather than female embryos would prevent introducing heritable genetic modifications, but the FDA’s Cellular, Tissue and Gene Therapies Advisory Committee recommends using female embryos when three conditions have been met. First, there is compelling evidence of safety and efficacy in use of the procedure in male embryos; second, there is preclinical animal research showing evidence of intergenerational safety and efficacy; and third, an existing shared framework, including international research, concerning the acceptability of, and moral limits on, heritable modification. Interestingly, the United Kingdom Human Fertilisation and Embryology Authority ("HFEA") takes a position against any male-embryos-only policy, thereby countenancing heritable modification. The British Authority’s rationale is that using sex selection after MRT would expose the embryos to gender selection, an additional intervention that might generate extra risk.  

Even though the National Academies of Sciences recommends clinical investigations, there is an absence of governmental approval. Indeed, similar to genome editing, there

338. Id. at xv. ("The committee concludes that the most germane ethical, social, and policy considerations associated with MRT could be avoided through limitations on the use of MRT or are blunted by meaningful differences between the heritable genetic modification of nDNA and that introduced by MRT.").  
339. Id. at 12. "In assessing the ethics of the balance of benefits and risks in MRT clinical investigations, minimizing the risk of harm to the child born as a result of MRT is the primary value to be considered." Id. at 116.  
340. Id. at xv.  
341. Id. at 131.  
343. Id.
is sufficient government policy in place that would hinder, if not prohibit MRT.\textsuperscript{344} And yet, like genome editing, MRT is a reality.\textsuperscript{345} Both procedures complement the greater availability of assisted reproduction and both are likely to garner increasing public support. This, together with the encouragement of pharmaceutical companies, suggest that the issue of how government should respond is imminent.

ii. Public Discussion

Public support for human genome editing and for MRT is derived from the possibility that each may be an effective means to prevent the transmission of heritable disease. mtDNA diseases, correctable through MRT, "vary in presentation and severity, but common symptoms include developmental delays, seizures, weakness and fatigue, muscle weakness, vision loss, and heart problems."\textsuperscript{346} Any of these diseases, alone or in tandem, may lead to morbidity and in some cases premature death.\textsuperscript{347} However, through MRT a woman may have a healthy, genetically related child, and may never see her child suffer.\textsuperscript{348}

Not all commentators find that the promise of eliminating serious disease warrants the resources necessary for MRT. Some argue that mitochondrial disease incidence is too rare to warrant either the investment or the resources: "The bottom line is that the number of candidates for [nuclear genome transfer] treatment is quite small, with estimates for the number in the [United Kingdom] ranging from several dozen to several score."\textsuperscript{349} Similarly, "[i]t is estimated that one out of 4,000 births in the United States results in a child with mitochondrial disease, although the true prevalence is unknown."\textsuperscript{350} Based on these levels of incidence, some commentators argue that investment in MRT "comes at the opportunity cost of researching treatment for mitochondrial disease that would benefit actual, living disease

\textsuperscript{344} Mitochondrial Replacement Techniques, supra note 43, at 1–2.
\textsuperscript{345} Id. at 2.
\textsuperscript{346} Id. at 1.
\textsuperscript{347} Id.
\textsuperscript{348} Id.
\textsuperscript{349} Cussins & Lowthrop, supra note 302, at 79.
sufferers." The argument follows that, rather than use assets on cycles of IVF, "[t]he National Institutes of Health could take a strong and important stance in developing its funding agenda by asserting that our medical dollars could be better spent elsewhere." Similarly, there are those who argue that MRT only benefits those with money, those able to afford the time commitment necessary, and those with expensive insurance coverage. Classes are distinguishable because of what can be afforded by the privileged few. As a result, because we rely on technology to correct human imperfections, we create "a society that becomes more technified and where what we consider makes us human is lost."

However, other commentators emphasize an individual person’s right to a genetically connected child, and that class has nothing to do with it. The argument is that any prohibition or restriction placed upon MRT "would unduly infringe on [an individual’s] reproductive freedoms," including the right to a genetically connected child free from disease. Reproductive freedom "recognises the interests of individuals in deciding for themselves what happens to their bodies," including genetic affinity. It is irrelevant whether an individual may afford it or not. An element within reproductive freedom is the individual’s right to a genetically connected child who is also free from serious disease: "Generally, social trends in the use of assisted reproductive technology (ART) support the argument that many prospective parents see value in having genetically related children, although many who pursue ART place greater importance on having children regardless of their genetic relation." Overall, individuals pursuing greater availability of

351. Id.; see also Ezekiel J. Emanuel et al., What Makes Clinical Research Ethical?, 283 JAMA 2701, 2705 (2000).
354. Id. at 93.
355. Schaefer & Labude, supra note 6, at 1579; see also MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 86 (discussing the positive right of adults to avail themselves of new reproductive technologies). But see Rulli, supra note 350, at 46.
356. See Schaefer & Labude, supra note 6, at 1578.
357. Id. at 1579.
358. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 82 ("Having a child genetically related to both prospective parents may be part of one’s conception of traditional family formation.").
MRT today—and added genome editing tomorrow—argue that they are entitled to current and expanding reproductive freedoms, that science can and should create a society with significantly greater freedom from disease, and that they are entitled as a matter of individual reproductive liberty, in reference to MRT, to genetically related procreations.

Because a human embryo is involved, there are legislative considerations at both the federal and state levels. Any emphasis on transparency and engagement among different societal points of view begins with an acknowledgement that the human genome possesses an "inherent dignity" because of its human potential, a dignity warranting protection at the state, national, and international level. However, there are different views as to the level of dignity warranted. There are those who argue that humans should not "play God" by altering human genomes, especially when initiating germline modification. Not all share this point.


360. Human Genome Editing, supra note 27, at 181 ("Basic laboratory research applying genome-editing methods to human cells, tissues, germline cells, and embryos holds promise for improving understanding of normal human biology, including furthering knowledge of human fertility, reproduction, and development, as well as providing deeper understanding of disease and establishing new approaches to treatment.").


364. See, e.g., Human Genome Editing, supra note 27, at 112 ("failing to appreciate the importance of the natural world, and a lack of humility about our wisdom and powers of control when altering that world or the people within it"); id. at 124 ("humans lack a god-like omniscience"); id. at 155 ("lead to a new theology of science"); Mitochondrial Replacement Techniques, supra note 43, at 91 ("Overall, the metaphor 'playing God' itself is too vague and indeterminate to guide...without additional premises and arguments."); Human Embryo Research Panel, supra note 40, at xv ("To many, such research appears to represent a tampering with the natural order in unacceptable ways.").
of view. Although it is important to recognize the depth and diversity of views among many in American society regarding religion and ethics, "the metaphor 'playing God' itself is too vague and indeterminate to guide such judgements without additional premises and arguments." Still others argue, on a more secular level, that a child born as a result of MRT or genome editing has not consented to the scientific procedure, which burdens any child—or future generations of children—with decisions made by parents. There are those who argue that this is contrary to doing what is in the best interest of the child. However, any assertion that all actions must conform to the best interest of the child, at least in the context of federal and state law, fails to take into consideration that a parent is always presumed to act in the best interest of his or her child. Only actual clear and convincing evidence to the contrary may rebut this presumption.

In addition to the potential risk associated with the best interest of a child is the arguable promotion of the dignity of each human genome. Not all agree on the existence of a duty towards the human genome, but it reasonable to include this consideration in the balancing of risk and benefits framed by the Belmont Report. The 1979 Belmont Report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research was the first public national body to shape bioethics policy in the United States. It was formed in the

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366. Mitochondrial Replacement Techniques, supra note 43, at 138–39. But see Human Genome Editing, supra note 27, at 111–13 (discussing that failure to obtain consent from a minor is not an obstacle to the use of MRT).
367. Mitochondrial Replacement Techniques, supra note 43, at 116, 126. But see Human Embryo Research Panel, supra note 40, at xii (“Given the conclusions the Panel reached about the moral status of the preimplantation embryo, it concludes that the health needs of women, children, and men must be given priority.”).
368. See, e.g., Troxel v. Granville, 530 U.S. 57 (2000) (holding that a child’s parent has a fundamental right to act on behalf of a child under the Fourteenth Amendment of the U.S. Constitution).
371. Id.
aftermath of the Tuskegee Experiment, a racial scandal, and the
Commission was a part of the United States Department of Health,
Education, and Welfare until 1978. The Report concludes that
scientific research involving human subjects should focus on three
principals: first, avoid the infliction of harm; second, accept a duty
of beneficence; and third, maintain a commitment to justice.
These three principals serve as the basis of judgement for
evaluators seeking to “ensur[e] a reasonable balance between risk
and hoped-for benefits, to the individual and to society, and on
ensuring that both risks and benefits are equally shared.” The
real test of these three principles occurs when they can
accommodate the rapidly expanding array of scientific
opportunities, the realities of off-label use, international
involvement, and the lure of profits and acclaim. These factors
contribute to the risk to human genomes and to society at large.

Another element in balancing risk against benefit is what
has come to be termed “scientific optimism.” It is arguable that
optimism, rather than fear, of scientific progress developed as a
result of the European Enlightenment, emphasizing reason and
individuality rather than corporate tradition. One author
classifies its impact thusly: “Today, knowledge and technology
are breaking up the natural forms ... And whereas [previously]
man considered himself a part or a ‘member’ of nature, the
feeling today is that he can ‘handle’ it in unlimited freedom,
bending it to his will for prosperity or destruction.” The 1994
Report of the Human Embryo Research Panel captures the
optimism of what is scientifically possible: “The promise of human
benefit from research is significant, carrying great potential
benefit to infertile couples, families with genetic conditions, and
individuals and families in need of effective therapies for a variety
of diseases.” Buttressed by global media, incessant scientific
changes, secularization, and greater individuality, larger segments
of the global population are willing to accept what seems new and
better with a sense of optimism.

373. See Nat’l Comm’n for the Prot. of Human Subjects, supra note 370.
374. Id.
375. Human Genome Editing, supra note 27, at 32.
376. Romano Guardini, The End of the Modern World 188 (Joseph Theman &
377. Id.
Nonetheless, not all share in the benefits of scientific optimism equally. It is arguable that scientific advances accentuate economic social inequality; the wealthier can afford to have healthier babies, smarter babies, even designer babies.\textsuperscript{379} An optimistic perception may provide the milieu for allowing human germline editing, yet efforts to eradicate disease may propel scientist down “a slippery slope” sending us “toward less compelling or even antisocial uses,”\textsuperscript{380} even a form of eugenics. Current restrictions on germline modification illustrate the belief that science is suspicious that “there are some genetic alterations that are insufficiently justified, too risky, or too socially disruptive to be pursued at this time.”\textsuperscript{381} In spite of these concerns and competing views regarding their potential dangers, the fact remains that there is evidence that germline modification already exists.\textsuperscript{382} Any suspicions are balanced against current scientific optimism, which provides assurance that “[g]enome editing holds great promise for preventing, ameliorating, or eliminating many human diseases and conditions.”\textsuperscript{383}

Finally, another policy consideration is the transnational aspect of modern science. The experiences of international human genome research make irrelevant any restrictions imposed by the United States. These would be inapplicable in foreign countries. Furthermore, for those able to afford any desired medical procedure available in a foreign country, “medical tourism” or safe-haven options permit newer, faster, and more accommodating options in permissive jurisdictions.\textsuperscript{384} The most notable illustration of this occurred in Mexico when the first MRT baby was born there April 6, 2016, resulting from the genetic

\begin{footnotesize}
\textsuperscript{379} See id. at 56; see also Criteria for IRB Approval of Research, 45 C.F.R. § 46.111(a)(2) (2018); HUMAN GENOME EDITING, supra note 27, at 127–28; MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 95–97.


\textsuperscript{381} HUMAN GENOME EDITING, supra note 27, at 181.


\textsuperscript{383} HUMAN GENOME EDITING, supra note 27, at 99.

\end{footnotesize}
material of three different people. However, the birth is illustrative of the international application of ARTs. Furthermore, "some reports suggest that there has been successful use of three-parent IVF in Ukraine and that efforts are now underway to commercialise the procedure in Mexico." So too, the British Parliament legalized MRT, however, it currently remains banned in much of the world, evidencing both geographic disparity and opportunity among scientific discoveries.

International organizations seek to monitor developments in different countries, but their efforts are largely ineffective. For example, at a 2015 International Summit convened by the science and medicine academies of the United States, the United Kingdom, and China, the assembled scientists called for a pause of some undefined duration in any attempt at heritable genome editing. Rather than banning the science of human genome editing, the focus at the international level appears to be on understanding the evolving views of international counterparts, illustrated by such groups as the International Pharmaceutical Regulators' Forum. The emphasis is on bringing on board the widest possible diversity of actors that would not normally interact with each other, on matters of science and technology. But admittedly, at play during discussion are unique historical, economic, and cultural factors.

386. Id.
387. Schaefer & Labude, supra note 6, at 1577; see also Marni J. Falk et al., Mitochondrial Replacement Techniques—Implications for the Clinical Community, 374 NEW ENG. J. MED. 1103 (2016).
cultural, and economic factors involved with only the hope for identifying common ground on specific substantive or technical aspects upon which to produce learning benefits. In the meantime, funded by independent private resources, research continues, subject only to the possibility of international opprobrium upon any scientific announcement.

The United States offers its own public policy guidelines pertaining to MRT. In its 2016 report, the National Academies of Sciences utilized a consensus derived from a diverse group of experts on the ethical, social, and policy issues at the core of MRT and concluded that:

The desire of prospective parents to have children who are at significantly reduced risk of manifesting serious mtDNA disease and with whom they have an nDNA connection is justifiable, and clinical research on the use of MRT could be permitted within limits. These limits would be focused on protecting the health and well-being of the children who would be born as a result of MRT.

This conclusion was in response to a request made by the FDA and the Institute of Medicine of the National Academies of Sciences, Engineering, and Medicine. A committee was formed to consider MRT and particularly, whether the ethical, social, and policy issues involved preclude the FDA from moving forward with consideration of MRT and clinical investigation. The committee emphasized the need for transparency, public and patient engagement, transnational partnership, data quality, limitations to women with a compelling medical need, and long-term follow-up. Interestingly, the public policy espoused forms the basis for the regulations that follow.

392. See Xiaomei Zhai et al., No Ethical Divide Between China and the West in Human Embryo Research, 16 DEVELOPING WORLD BIOETHICS 116, 120 (2016).
393. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 7.
394. Id. at 87.
395. Id. at 149.
396. Id. at 142-44.
iii. Regulation

a. FDA Process

If clinical research on MRT were to proceed in the United States it would be subject to “a complex landscape of state and federal laws and regulations,” with another level of regulation awaiting at the transnational level.\textsuperscript{397} For background, currently “[t]wenty-nine countries prohibit germline modification; the salient laws or regulations of 10 more countries, including the United States, are either ambiguous or would restrict but not fully prohibit it.”\textsuperscript{398} In the United Kingdom, reproductive biomedicine is controlled pursuant to the Human Fertilisation and Embryology Act of 1990.\textsuperscript{399} The British legislation controls research at three levels: first, through statutory provisions that distinguish those things that are prohibited absolutely (and subject to criminal penalties); second, those things that are permissible under licenses issued by the licensing regime that permits the Human Fertilisation and Embryology Authority to determine what licensable activities may be carried out, by whom, and in what circumstances; and third, through the HFEA’s oversight of fertility clinics, which ensures that the licensable activities are carried out in accordance with license conditions and in conformity with the HFEA’s statutory Code of Practice.\textsuperscript{400} Interestingly, and in sharp contrast to gender equality and individual liberties within American jurisprudence, is HFEA’s stipulation for women not to “be provided with treatment services unless account has been taken of the welfare of any child who may be born as a result of the [fertilization] treatment (including the need of that child for supportive parenting), and of any other child who may be affected by the birth.”\textsuperscript{401}

However, the legal regulatory process in the United States is more fragmented. At the federal level, similar to human genome editing, the FDA would regulate MRT under its authority to regulate any “human cells or tissues that are intended for

\textsuperscript{397} Id. at 59.
\textsuperscript{398} Id. at 63.
\textsuperscript{399} NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 101-02.
\textsuperscript{400} Id. at 105.
\textsuperscript{401} Id. at 106 (citing Human Fertilisation and Embryology Act 1990 c. 37 § 13(5) (UK) (as amended)).
implantation . . . into a human.”

“FDa does not regulate MRT as a technique per se, but rather the ‘product’ that is considered a drug and/or biologic—in this case, the manipulated oocytes or zygotes.” Regulating “MRT would likely involve the same statutes and regulations that apply to IVF, PGD, preimplantation genetic screening (PGS), and cloning.” Any approval of an Investigational New Drug Application by the FDA would require first, respect for the moral status of a human embryo. Second, clinics need to employ skilled technicians with expertise in micromanipulations of human gametes and/or embryos.

Currently, federal funding for MRT research in the United States would be prohibited because of Congressional legislative restrictions against funding research on human embryos. However, there are those who argue that an exemption is warranted in the treatment of selected, well-studied monogenic diseases. If there were an exemption to allow for federal funding of MRT clinical trials, the process would commence with an IND application and, if approved by the FDA, clinical trials in humans.


403. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 65.

404. Id. at 60.


407. See 114 CONG. REC. H9434, 9445 (daily ed. Dec. 17, 2015) (“None of the funds made available . . . may be used . . . in research in which a human embryo is intentionally created or modified to include a heritable genetic modification.”) But even though funding for the research is prohibited, there is no such prohibition on the research itself. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 64.

408. See, e.g., Seitz, supra note 7, at 89-90 (“It is estimated that monogenic diseases affect up to 13 million people in the U.S., causing nearly one-fifth of infant mortality. Many of the thousands of monogenic diseases lead to severe physiological impairment or early death.”).
would begin. If the application is authorized, clinical investigations may commence and, if successful, a Biologic License Application or a New Drug Application may be submitted. Then, if the FDA considers that the product is safe and effective—and benefits outweigh the risks—the application is approved and the product may be marketed in the United States.

Approval by the FDA would employ an oversight and IRB risks and benefits review. "Any institution that receives federal funds for research involving human subjects must establish an IRB, and all such research performed at the institution must be reviewed by the IRB, regardless of its source of funding." IRB review would involve balancing the risks and benefits for five potential parties affected by MRT. They are: (1) individuals who provide gametes (oocytes or sperm) that are then used to construct embryos; (2) any intended parent or parents; (3) gestational carriers if one is needed; (4) any child born as a result of MRT; and (5) any potential future offspring of female children born as a result of MRT. Each applicable party would need to provide informed and voluntary consent to participating in the process. When intended parents provide consent to any MRT procedure, they would, in essence, be consenting on behalf of any future children. Also, there would have to be post-approval oversight to ensure that the National Academies of Sciences primary consideration is protected, that being assessing risk and benefit to the health and well-being of future children.

b. Post-Approval Oversight

In its 2016 report on MRT, the National Academies of Sciences, Engineering, and Medicine made several recommendations for oversight of the procedure through emphasis on transparency, public and private engagement, sharing of information with domestic and foreign researchers and regulatory agencies, evaluation of high-quality data, and an

409. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 68.
410. Id. at 115, 131–32.
411. LINDA ALDOORY ET AL., BEST PRACTICES AND NEW MODELS OF HEALTH LITERACY FOR INFORMED CONSENT REGULATIONS ON HEALTH LITERATE COMMUNICATIONS 26 (2014).
412. MITOCHONDRIAL REPLACEMENT TECHNIQUES, supra note 43, at 138.
incremental approach to monitor effects and commitment to long-term follow-up.\textsuperscript{414} As part of this follow-up the FDA has a Risk Evaluation and Mitigation Strategy program to monitor postapproval developments.\textsuperscript{415} The Food and Drug Administration Amendments Act of 2007 provides the FDA with the authority to ensure that a product approved by the FDA is then used in a postapproval manner such that its benefits outweigh its risks.\textsuperscript{416} The postapproval review applies to on or off-label use.\textsuperscript{417}

There are a few examples where government regulation bans certain scientific research. To date, states and the federal government have banned cloning of human beings,\textsuperscript{418} and human eugenics has been widely condemned.\textsuperscript{419} Off-label use of the human growth hormone has been made a criminal offense, but “[p]ostmarket use may also encompass uses that go beyond the indications for which a therapy was approved.”\textsuperscript{420} Thus, with few exceptions, off-label use in clinical care is entirely legal and has become a common practice among physicians, which could apply to gene editing once it is approved. Physicians “are regulated at the state level by their licensing and disciplinary bodies, [and] may be limited by availability of patients’ insurance coverage for novel interventions.”\textsuperscript{421} Physicians are also constrained by the prospect of tort liability for malpractice, should they be deemed reckless of negligent.\textsuperscript{422}

Regulation at the state level varies:

\begin{itemize}
\item \textsuperscript{416} Id.
\item \textsuperscript{418} CAL. HEALTH & SAFETY CODE §§ 24185–87 (1998); Memorandum from the Office of the Press Secretary for the Heads of Executive Departments and Agencies (Mar. 4, 1997) (on file with the White House); Cloning Californians? Report of the California Advisory Committee on Human Cloning, 55 HASTINGS L.J. 1143 (2002).
\item \textsuperscript{420} \textit{HUMAN GENOME EDITING}, supra note 27, at 36.
\item \textsuperscript{421} Id.
\item \textsuperscript{422} See, e.g., Bos. Coll. Law Review Staff, \textit{supra} note 313.
\end{itemize}
California, for example, has been funding embryo research and embryonic stem cell research for a decade using funds from a state bond issued during the years when federal funding was limited to a small number of older embryonic stem cell lines. Connecticut, Maryland, New Jersey, and New York also created funds for research that could not be federally funded.423

Additionally, state licensing boards, which monitor physicians, vary widely in their stringency. Any practitioner, however, could be disciplined for use of MRT—on label or off-label—that was inappropriate for the patient or that was provided prior to properly obtaining voluntary consent.424 Interestingly, in its 2018 report on genome editing and human reproduction, the British Nuffield Council on Bioethics reported that a policy of good practice is “very well embedded” in the field of human reproduction due in part to high professional standards and among scientists and practitioners.425 The Council also suggests that good practices result from public engagement and “the hawk-like media attention given to issues in reproductive biomedicine.”426 Likewise, insurance coverage and its threat of denial of coverage, is often a stringent restraint on off-label use by physicians.427 That, and the prospect of tort liability.428

Amid these competing arguments, review panels, agencies, and legislatures must make decisions pertaining to funding of laboratory research, preclinical trials, clinical trials, and potential medical uses. And federal and state laws haltingly address accelerating, even revolutionary, advances in medical technology.429 These groups and regulatory pronouncements also


425. NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 106.

426. Id.

427. Id. at 13 n.32, 15.

428. See Bos. Coll. Law Revew Staff, supra note 313, at 332–33, 335.

are interactive with the regulatory infrastructures of other countries. Their task is made more difficult because of three identifiable undercurrents existing in the United States today: scientific optimism, off-label development, and international opportunities.

c. International Oversight

As has been discussed above, genome editing exists within a transnational community; modern technology does not permit scientific development to be contained to a single nation. "The globalisation of neoliberal capitalism has created the conditions not only for greater possibilities of diffusion and movement of knowledge, technology, skills, patients, tissues, data, etc., but also their independence of movement." Hence, while the United States may prohibit funding for embryonic research and impose a lengthy regulatory procedure prior to approval of any products or procedures, other developed countries may permit genome editing or mitochondrial replacement resulting in "designer babies" or heritable modifications. For example, MRT is now legal in Great Britain. In China, which is more prolific in research on human embryos and genome editing, biomedical research is governed by the National Health and Family Planning Commission. Although Chinese law bans gene manipulation on human gametes, zygotes, and embryos for the purpose of reproduction, "reproductive services such as sex selection and surrogacy, which are technically illegal in China, are nevertheless available in practice." The fact that a Chinese scientist, working at the Southern University of Science and Technology in Shenzhen, China, was able to announce the birth of two genome-edited babies at the start of the 2018 Second International Summit

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430. HUMAN GENOME EDITING, supra note 27, at 57.
431. Id.
432. NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 113.
434. NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 110–11.
435. Id. at 111.
436. Id.

Many factors contribute to a nation’s explicit or tacit acquiescence in human genome editing procedures: first, there are large profits to be made from a growing demand for assisted reproductive services, hence unauthorized private clinics can establish a clientele and practice absent government scrutiny; second, if government oversight lacks focus and explicit direction the cumbersome nature of regulatory bureaucracy allows for only piecemeal enforcement of any regulations; and third, public awareness and resulting public debate prompt more efficient regulatory review of practices and products, but their absence permits tacit permissiveness.\footnote{See Donna Rosato, How High-Tech Baby Making Fuels the Infertility Market Boom, MONEY (July 9, 2014), http://money.com/money/2955345/high-tech-baby-making-is-fueling-a-market-boom; Nick Malyshev, The Evolution of Regulatory Policy in OECD Countries 17–19, OECD, https://www.oecd.org/gov/regulatory-policy/41882845.pdf (last visited on Mar. 22, 2019) (explaining the importance of regulatory oversight that is well-organized and monitored and the necessity of an open process to the public as a way to improve regulatory review).}

As was summarize by the Nuffield Council on Bioethics, “[u]nlike the US, where debate is open and fierce, if lacking in focus, or like the UK, where debate tends to be more coherently oriented towards regulatory or parliamentary activities,” there exists “little public and media debate in China that allows space for diverse stakeholders and points of view, and no evidence of public engagement initiatives, either on the part of government-related bodies or civil societal organisations.”\footnote{NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 112.}

Fourth, the rapidity of human scientific biomedical developments, coupled with increasing scientific optimism resulting in part from this rapidity, blunts the immediacy of addressing societal concerns over human genome editing.\footnote{See Genome Editing: What Are the Ethical Concerns About Genome Editing?, NAT’L HUM. GENOME INST. (Aug. 3, 2017), https://www.genome.gov/27569225/what-are-the-ethical-concerns-about-genome-editing.} Fifth, the complexity of the
scientific terminology and procedures blunt public participation and obfuscate transparency. 441

Only one international document explicitly addresses heritable genetic modification, the 1997 Oviedo Convention. 442 Not all member states of the Council of Europe have ratified the Oviedo Convention, including the United Kingdom, but the principles espoused in the Convention find resonance in foreign research reports on the subject of genome editing. 443 The Convention and corresponding reports suggest, first, that any human genome editing should serve human health, not physical appearance or gender selection, and second, modification may not introduce changes that can be passed on to future generations. 444

Frustration with current international regulatory and governance protocols concerning clinical use of heritable germline editing was illustrated at the Second International Summit on Human Genome Editing convened in Hong Kong, China in November 2018. Confronted with the announcement of "an unexpected and deeply disturbing claim that human embryos had been edited and implanted, resulting in a pregnancy and the birth of twins," 445 the Organizing Committee "suggest[ed] that it [was] time to define a rigorous, responsible transnational pathway toward such [clinical] trials [of germline editing]." 446 This announcement was both an admission that genome editing was a reality and that it was time to establish a clear pathway to address it or it "could produce unintended harmful effects for not just an individual but also for that individual’s descendants." 447


442. NUFFFFFFF COUNCIL ON BIOETHICS, supra note 14, at 115.


445. On Human Genome Editing II, supra note 151.

446. Id.

447. Id.
Specifically, the Committee proposes an ongoing International Forum that will foster broad public dialogue, develop strategies for increasing equitable access by members of the underserved populations, speed the development of regulatory science, provide a clearinghouse for information on regulatory options, develop common regulatory standards, and enhance coordination of research and clinical applications through an international registry of planned and ongoing experiments. This is quite an agenda, but it illustrates that the longer a pathway is delayed, the more it will take to define its parameters.

The alarm over the reality of human genome editing, including its effects upon the human germline, is significant. Yet because of the individuality of nations and the plethora of private and semi-private elements within each nation, any international forum will serve an advisory role and nothing more. The inability of the international community to curtail nuclear arms or international terrorism is illustrative of this. Today, the best that can be achieved is for each nation to take responsibility to recognize the immediacy of human genome editing and, as the Summit suggests, establish a pathway towards a consensus of agreement rather than default.

III. CONCLUSION

Plotting a pathway for the future begins with knowing the past, but the past does not extend far. It was in 1953 that James Watson and Francis Crick discovered the double helix, the twisted-ladder structure of deoxyribonucleic acid, better known as DNA. This was the beginning. The paired structure of DNA, which encodes the genome, enables the copying mechanism that allows...
the genome to be transmitted from generation to generation.450 The genome of each individual is composed of approximately one-half provided by the biological mother and the other half provided by the biological father.451 Genetic materials from each of the parents is transmitted during reproduction, resulting in the unique genome of the offspring of the two parents. Once formed, the genome contains the full sequence of genetic material (DNA in humans) in an organism or species.452

Today, as a result of recent scientific research and developments it is possible to edit a genome, that is, to “modify[] an embryo or the cells from which it is formed by techniques of genome editing, in order to ensure that a future child has the selected genetic variants.”453 When we speak of genome editing we mean the process by which the genome sequence is changed through intervention of a DNA break or other DNA modification.454 Because of modern scientific ability to edit the genome, science began the study and diagram of the human genome variants, by which it could decipher the array of human characteristics, the propensities for disease in any given embryo, and how an individual may live in an environment that may precipitate reactions to various environmental factors.455

Genome editing would not be possible without parallel developments in the science IVF.456 Slightly more than two decades after the discovery of DNA in 1953, a physician in Oldham, England, performed an IVF procedure that resulted in

451. NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 6.
452. Id. at 174.
453. Id. at 6.
454. HUMAN GENOME EDITING, supra note 27, at 299.
455. Id. at xi.
456. In vitro fertilization is “[a]n assisted reproduction technique in which fertilization is accomplished outside the body.” Id. at 301. “Clinically, IVF refers to a procedure in assisted reproduction wherein eggs are removed from the body (often flowing artificial stimulation of the ovaries) and mixed with sperm in a dish, or injected with sperm in ICSI. A resulting embryo may then be transferred to a woman’s uterus with the intention of establishing a pregnancy.” NUFFIELD COUNCIL ON BIOETHICS, supra note 14, at 175.
the birth of Louise Brown in 1978.\textsuperscript{457} She is heralded as the first child conceived in a laboratory dish rather than in a living woman.\textsuperscript{458} Since the birth of this first “test tube baby,” ART has developed rapidly, permitting both gestational and genetic surrogacy arrangements, genetically connected births to heretofore infertile couples, posthumous conception and resulting births, and the banking of eggs, sperm, and embryos in fertility clinics throughout the world.\textsuperscript{459} The number of IVF procedures, and the children resulting from these procedures, increase each year in the United States and transnationally.\textsuperscript{460} It is the combination of the discovery of DNA, IVF, and genome editing that we arrive at this point.

By 2012, scientists developed a cheaper and efficient method to edit genomes.\textsuperscript{461} Currently, the best method is called CRISPR-Cas9, and it provides scientists with the ability to cheaply and precisely target and alter DNA in living cells.\textsuperscript{462} Because of this revolutionary technology—and the more efficient ones that follow—it is now possible to “edit” genomes comprising DNA sequences that encode a functional product such as a protein or RNA molecule.\textsuperscript{463} Because of this editing process, scientists may prevent severe debilitating disease from ever developing in babies. This can be done through a MRT that will prevent mitochondrial disease.\textsuperscript{464} However, in addition to eliminating disease, it is also possible to edit other genes, thereby affecting personal appearance, gender, and other distinguishing characteristics that precipitate the diversity heretofore characteristic of human society.\textsuperscript{465} Of greater concern, editing a gene in an embryo today may have unknown repercussions, good and bad, in generations to follow as a result of germline editing. The scientific ability to edit genes and precipitate germline modifications prompts concerns

\begin{itemize}
  \item 458. \textit{Id.}
  \item 460. \textit{Id.}
  \item 462. \textit{Id.}
  \item 463. \textit{Id.} at 174–75. The RNA transfers information from genomic DNA to the protein-synthesis machinery of cells.
  \item 464. \textit{Id.} at 75 n.248.
  \item 465. \textit{Id.} at 53 n.172.
\end{itemize}
about public policy, public interest, and public morality. This concern is illustrated in the reports from scientific groups in the United States and international organizations and is reflected in a statement by a group from the United Kingdom, the Nuffield Council on Bioethics:

[We] conclude that what is important is not the conservation or alteration of a particular range of characteristics at the level of the genome, but rather the potential consequences of genomic interventions for people and the social relations in which they stand to one another. These are expressed not in pursuit of uncertain outcomes, but in the orientation towards those futures.

Continuing scientific achievements, the multi-billion-dollar pharmaceutical industry, and what has come to be termed "medical tourism" accelerate the immediacy of the concern over genome editing and mitochondrial replacement. This immediacy is illustrated by the announcement on November 28, 2018, that a scientist in China seemingly succeeded in genetically editing the genes of twin girls when they were embryos, but were later born apparently healthy. This is the first reported instance of human genome editing, but it signals that the issue is no longer academic, but real. The condemnation of the scientist's action by the scientific community was immediate, challenging the scientist's "rogue" action as lacking in transparency and conformity with international norms. Various scientific organizations throughout the world recognized that this day was coming, hoping that calls for transparency, international responsibility, and a coordinated approach would delay its arrival. Now it is here. What is to happen? First, the consensus is that science is unstoppable. This is a given. Moreover, scientific achievements are welcomed with a sense of optimism. However, this recognition does not alleviate responsible application of all

466. Id. at 51–53.
467. Id. at 95.
468. See, e.g., Cohen, supra note 413.
469. Stein, supra note 172.
470. On Human Genome Editing II, supra note 151.
scientific advancements. What then should be our application within the United States?

First, responsible public policy, based in positive law and regulatory function, should manifest a pathway towards an acceptable ethical and moral approach towards genome editing and, as an element thereof, mitochondrial replacement, formulated with contributions from all those interested in its impact on society.

Second, the forum for developing this pathway begins with the United States Congress. The specific goal for Congress to consider is whether the current Dickey-Wicker Amendment is responsive to the impact of genome editing and mitochondrial replacement. Inasmuch as the Amendment prohibits, without exception, it is not a responsible approach towards protecting American current and future populations.

Third, as a regulatory approach to approval of genome editing, an appraisal must be made of the Consolidated Framework as to whether it adequately addresses not only current challenges, but ones that lie on the horizon.

Fourth, it must be determined whether the regulatory process by which the FDA regulates products that will be marketed within the United States is sufficiently responsive to both the benefits and risks of genome editing and mitochondrial replacement.

Fifth, any biologic pathway established must include a process for interaction with the transnational community of scientists and national policy-makers.

Sixth, any pathway must include the following specific goals:

(1) Precise risk versus benefit guidelines must be developed with a focus on the best interest of any child born in association with genome editing;

(2) Peer responsibility must be fostered among national and transnational scientists to establish proper guidelines to manage germline editing, and also to regulate international applications of newer means to edit human germlines;

(3) Means must be established to interact with persons with different societal backgrounds envisioning inclusion of all, social justice, plurality, and moral persuasion;

(4) A responsible pathway must be drafted through transparency, an engaged media, sufficient opportunity for all
significantly interested parties to be heard, and adequate information concerning the procedures involved; and

(5) The dignity of all human voices must be respected to include religious, ethical, and proponents of reproductive liberties and gender equality.

The advent of genome editing, including mitochondrial replacement, involves several aspects never previously encountered by human beings. This is a transnational issue that portends significant profits for pharmaceutical companies and miraculous treatments of serious hereditary diseases that have perpetually plagued humanity. The scientific community’s interconnectedness provides sufficient commentary to formulate the challenges presented with abundant clarity.

However, of particular difficulty is the fact that genome editing challenges societies to reexamine their social structure and plurality, including its shameful historical episodes of eugenics. Finally, the opportunity of genome editing and mitochondrial replacement prompts an immediacy of action on the part of governments, not to ban, condemn, or to castigate, but rather to chart a scientific pathway by which the national and transnational communities can balance scientific optimism with the values that make us all human together.