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Crafting the Perfect Cure? Embryonic CRISPr Editing and Equality of Access

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Introduction:

"CRISPr" stands for clustered regularly interspaced palindromic repeats.[1] CRISPr based technologies are transforming the state of life sciences around the world.[2] Biotechnology has advanced through the advent of next generation sequencing technologies, allowing for researchers to identify individual genotypes quickly and thoroughly and thus identify the genetic locations of complex diseases.[3] By locating the genetic loci of diseases, physicians can provide more adequate treatment to their patients and recommend lifestyle changes to mitigate disease.[4] Genome-editing tools advance biotechnology a step further by permanently mitigating or eliminating diseases through selective modification of the genome.[5]

CRISPr has emerged as the premier gene editing tool over its predecessors, zinc-finger nucleases "ZFNs" and transcription activator-like effector nucleases "TALENs."[6] ZFN and TALEN are comparatively limited because of the need to engineer a new version of the editing protein for each genetic target.[7] CRISPr only requires a slight alteration to target new sites.[8] CRISPr is currently used to generate and engineer changes in thousands of organisms.[9] CRISPr can cure diseases, increase crop yields, and even increase disease resistance in plants and animals, but much of the spotlight on CRISPr involves controversy.[10] The media presence of

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[1] Matthew P Hirakawa et al., *Gene editing and CRISPR in the clinic: current and future perspectives*, 40 Bioscience REP. 1 (2020).
[2] *Id*.
[3] *Id*.
[4] *Id*.
[5] *Id*.
[6] *Id*.
[7] *Id*.
[8] *Id*. at 2.
[9] Natalie Kofler, *Timely book tells the CRISPR story so far*, Nature, https://www.nature.com/articles/d41586-020-03071-0 (Nov. 3, 2020).
[10] *Id*.

CRISPr has been taken over by talks of the dystopian future of "designer babies," children engineered to have augmented traits.[11] This controversy was stirred when researcher He Jiankui announced he edited the germline genome of two twin girls to make them genetically resistant to HIV.[12] Germline edits are controversial because they create heritable changes.[13] The results of the experiment were met by widespread consternation by scientists, ethicists, and the public.[14] The experiment was not peer reviewed, went against globally shared research norms and ethics, failed to comply with government regulations, and overall was performed by staff that lacked qualifications, training, and experience.[15] Suffice to say, He deviated from research norms.[16]

The resulting public fallout has raised concerns that the future of the field may be in jeopardy.[17] Fred Lanner, a stem-cell scientist at Karolinska University in Stockholm remarked, "the negative focus is, of course, not good," others like Jonathan Kimmelman, a bioethicist specializing in human trials of gene therapies at McGill University in Montreal, Canada, argues swift action after scandal could drive global cooperation and regulation "that would stimulate, not hinder, meaningful advance in this area."[18] Due to the He scandal, there has been a conflation in public sentiment between blatant research infractions and the moral permissibility of heritable gene editing.[19] Studies demonstrate there is no real consensus on the public opinion of the moral permissibility of heritable gene editing.[20] Health care professionals must ensure that public

[11] David Cyranoski, *The CRISPR-baby scandal: what's next for human gene-editing*, Nature, https://www.nature.com/articles/d41586-019-00673-1 (Mar. 11, 2019).
[12] *Id*.
[13] *Id*.
[14] Karen M. Meagher et al., *Reexamining the Ethics of Human Germline Editing in the Wake of Scandal*, 95 Mayo Clinic PROC. 330 (2020).
[15] *Id*.
[16] *Id*.
[17] Cyranoski, *supra* note 11.
[18] *Id*.
[19] Meagher et al., *supra* note 14 at 335.
[20] *Id*.

understanding of emerging gene editing techniques is driven by careful reflection, racially and ethnically informed problem solving, high ethical standards, and not scandal.[21] Discussions about CRISPr germline editing should not strictly devolve into talks of ethics surrounding augmentation and engineering children to embody ideal traits.[22] By only focusing on augmentation and scandal, public discussions on the ethics of the therapeutic applications of CRISPr will be overshadowed.[23] A line should be drawn between CRISPr as a medical treatment, and as a means of human augmentation. In the near future CRISPr could become one of the staple therapies in the assisted reproductive technology "ART" framework.[24]

The rise of IVF and PGT technology has allowed for the reduction of incidences of Tay-Sachs disease in the Ashkenazi Jewish community, rescuing families from the debilitating childhood disease.[25] Other communities that suffer from genetic diseases see reproductive gene editing as an additional tool for carrier screening and assisted fertility to ensure the conception of healthy children.[26] CRISPr germline editing provides a path to eliminate fatal and debilitating monogenetic diseases, and its introduction into the ART framework could compliment preimplantation genetic testing "PGT," diagnoses.[27]

This paper argues that CRISPr germline editing is a novel technology that may be utilized to cure heritable diseases, including diseases that are historically associated with ethnic and racial minority communities. However, out-of-pocket costs for CRISPr germline therapy will likely be prohibitively expensive due to the novel nature of the technology and the historic prices

[21] *Id.* at 336.
[22] *Id.*
[23] *Id.* at 335.
[24] Hirakawa et al., *supra* note 1 at 13-4.
[25] Meagher et al., *supra* note 14 at 332.
[26] *Id.*
[27] Hirakawa et al., *supra* note 1 at 14.

of other gene therapies. Additionally, because CRISPr germline editing necessitates *in vitro* fertilization "IVF," to cure and then implant embryos, the treatment will likely be classified as an infertility benefit for insurance purposes. Under the current state law regime there is likely to be insufficient coverage for CRISPr, thus enhancing inequality to ethnic and racial minorities that disproportionately suffer from genetic diseases. An expansion of state law mandates to require private insurance coverage for infertility benefits including IVF, PGT, and CRISPr germline editing will likely increase coverage for ethnic and racial minorities and thus prevent further exacerbation of historic inequities in access to treatment.

In Part I this paper will address how CRISPr technology and gene editing operate generally, how the CRISPr technique works clinically, describe the specific applications of CRISPr with a focus on CRISPr germline therapies, and discuss the advantages and concerns of CRISPr germline therapies. In Part II this paper will provide the predicted monetary costs of CRISPr germline therapy considering both the historic costs of gene therapies and the costs associated with the ART framework. Part II will also discuss specific insurance provider coverage of existing infertility benefits. Part III analyzes state insurance laws regarding infertility coverage and ART therapy. In Part IV, this paper will address historic racial inequities in access to ART treatments and how an expansion of ART and CRISPr coverage will help address the prevalence of certain genetic diseases in ethnic and racial minorities. Part V concludes with a call for careful reflection and inclusive problem solving to ensure ethical standards in gene editing research are met.

Part I: Gene Editing, CRISPr Technology, and Applications

A. Gene Editing and CRISPr Generally

"Gene editing" refers to the precise insertion, knockout, and alteration to the genome, genetic code, of an organism.[28] Gene editing tools were once restricted to few select labs, but thanks to CRISPr gene therapy research has bloomed and now even a high school student can perform gene editing experiments.[29] Older gene editing models produced a genetically altered mouse in a year or two, but now with CRISPr complex mouse models can be produced within a couple months.[30] CRISPr is not the first site-specific gene therapy used for gene alteration, but where it revolutionized the field was in its comparative speed and simplicity.[31] CRISPr technology can modify DNA in organisms and cultured cells quickly, precisely, efficiently, and for relatively cheap.[32] CRISPr is thus prime for use in gene function studies, gene therapy studies, drug development, and the production of modified crops and livestock.[33] CRISPr can facilitate the precise editing of genes in both mature and developing organisms.[34] Genome editing with CRISPr seeks to edit genes through "knockout" by inhibiting genes with deleterious function and "knock-in" by restoring function to mutated genes.[35]

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[28] Qi Zhou et al., *Human embryo gene editing: God's scalpel or Pandora's box?*, 19 Briefings in Functional Genomics, 154 (2020).
[29] NCI Staff, *How CRISPR Is Changing Cancer Research and Treatment*, National Cancer Institute, https://www.cancer.gov/news-events/cancer-currents-blog/2020/crispr-cancer-research-treatment (Jul. 27, 2020).
[30] *Id.*
[31] Karim Shalaby et al., *Tissue-Specific Delivery of CRISPR Therapeutics: Strategies and Mechanisms of Non-Viral Vectors*, 21 INT'L J. Molecular SCI. 1, 2 (2020).
[32] Emilia Niemiec & Heidi C. Howard, *Ethical issues related to research on genome editing in human embryos*, 18 Computational & Structural Biotechnology J. 887 (2020).
[33] *Id.* at 887-8.
[34] David M German et al., *Therapeutic Genome Editing in Cardiovascular Diseases*, 4 Basic to Translational SCI. 122 (2019).
[35] *Id.* at 123.

B. The CRISPr Technique

CRISPr is naturally found in bacterial genomes and plays a role in bacterial anti-viral defense, this action is similar to the human immune response.[36] CRISPr repairs the bacterium's DNA after a viral attack.[37] CRISPr is composed of a guide RNA strand "sgRNA", which is used to detect the presence of viral DNA in the bacterium's genetic code, and a specialized enzyme known as "Cas," which carries the RNA around the cell.[38] If the guide RNA detects viral DNA, the Cas enzyme will bind to the viral sequence and cut the DNA at that site.[39] The bacterium's genetic sequence will then be repaired, and the virus will not be able to reproduce.[40] This process of destruction and subsequent repair of a bacterium's genetic sequence proved critical to deriving the genetic tool CRISPr-Cas9.[41] There are many variants of the Cas enzyme, but Cas9 is the variety of Cas enzyme with the most clinical understanding.[42] The CRISPr-Cas9 complex is often referred to simply as CRISPr.[43]

CRISPr-Cas9 is known for its versatility, Cas9 can precisely cut double stranded breaks in DNA that are user directed.[44] To edit a cell of interest, Cas9 and sgRNA need to be introduced, this is normally done through direct injection or a vector.[45] The versatility of CRISPr comes from the customizability of the sequence of the sgRNA strand, which allows researchers to program Cas9 to make double stranded breaks at specific sites.[46] After CRISPr cleaves the

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[36] Asawari Churi and Sarah Taylor, *Continuing CRISPR Patent Disputes May Be Usurped by Its Potential Role in Fighting Global Pandemics*, 39 Biotechnology L. REP. 184 (2020).
[37] *Id.*
[38] *Id.*
[39] *Id.*
[40] *Id.* at 184-5.
[41] *Id.*
[42] *Id.* at 184.
[43] *Id.*
[44] German et al., *supra* note 34 at 123.
[45] *Id.*
[46] *Id.*

desired DNA, repair mechanisms are initiated.[47] There are two mechanisms of repair, non-homologous end-joining "NHEJ" and homology-directed repair "HDR."[48] NHEJ is error prone because reconstruction occurs without a template and is therefore inappropriate if the desired outcome is to make a dysfunctional gene functional, but is excellent if gene inactivation is desired.[49] HDR rebuilds the DNA via a template strand and is therefore more accurate but is less efficient than NHEJ repair.[50] Improving HDR's efficiency is a goal of clinical studies to improve the overall accuracy of CRISPr..[51]

A key distinction made in CRISPr human genome editing is between somatic cell therapies and germline cell therapies.[52] In somatic editing, alterations to the cells are not passed on because changes are limited to body cells.[53] In germline editing, alterations to the cells are heritable because changes are made to cells that pass on genetic information.[54] Germline editing is controversial because of the inherent risks involved with introducing heritable alterations into the genome.[55]

CRISPr germline genome editing "GGE," is used to modify the cells of future organisms through genetic alterations of sperm, eggs, or fertilized zygotes.[56] CRISPr GGE necessitates the use of IVF, all published studies utilizing human CRISPr GGE have utilized IVF zygotes.[57] PGT, previously known as preimplantation genetic diagnosis "PGD," identifies genetically

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[47] *Id*.
[48] *Id*.
[49] *Id*.
[50] *Id*.
[51] *Id*.
[52] Clara C. Hildebrandt & Jonathan M. Marron, *Justice in CRISPR/Cas9 Research and Clinical Applications*, 20 AMA J. Ethics 826, 827 (2018).
[53] *Id*.
[54] *Id*.
[55] *Id*.
[56] Manuel Viotti et al., *Estimating Demand for Germline Genome Editing: An In Vitro Fertilization Clinic Perspective*, 2 CRISPR J. 304 (2019).
[57] *Id*. at 304-5.

healthy zygotes in an IVF cohort that will have the highest chances of implantation and can be used to screen for genetic disease.[58] Patients with a familial history of heritable disease may apply for a PGT-M test to identify and discard embryos in the cohort that carry a disease-causing allele.[59] Implementing CRISPr GGE first requires PGT to test embryos for the disease trait, then CRISPr would be applied to all embryos, and PGT would be applied again to ensure the genetic corrections occurred.[60]

In somatic cell editing, CRISPr edits can occur *ex vivo* where cells are modified outside of the patient and reintroduced, or *in vivo* where CRISPr is directly delivered to the patient's body to edit cells.[61] There are advantages and challenges with both *ex vivo* and *in vivo* methods.[62] The advantage for *ex vivo* procedures are that the procedures are done externally, meaning the patient is not directly exposed to gene alterations and there is greater control of the process.[63] The challenges to *ex vivo* procedures are maintaining the survival and original function of the cells outside the patient long enough for gene alteration to occur, and culturing enough cells for successful reintroduction to the body.[64] For *in vivo* treatments, CRISPr can be delivered intravenously or through local injection to specific tissues.[65] The advantages of *in vivo* procedures are that because they are done intravenously or in site-specific areas, there is no need to create an external cell culture and regraft the cells into the body.[66] However, the challenges of *in vivo* procedures are the degradation of the CRISPr components in the body, the potential for

[58] *Id.* at 305.
[59] *Id.* at 306.
[60] *Id.* at 308.
[61] Fathema Uddin et al., *CRISPR Gene Therapy: Applications, Limitations, and Implications for the Future*, 10 Frontiers in Oncology 1, 9 (2020).
[62] *Id.*
[63] *Id.*
[64] *Id.*
[65] *Id.*
[66] *Id.*

uneven distribution of CRISPr components at the site of injection, and less control of the overall procedure.[67]

C. Specific Applications of CRISPr

CRISPr is a rapidly developing technology and has many potential clinical applications.[68] Cancer immunotherapy and the correction of monogenetic disorders seem to be at the forefront of clinical research.[69] This analysis of the applications of CRISPr will focus on CRISPr GGE therapy with brief mention of the applications of somatic CRISPr therapies.

a. CRISPr GGE Applications

The scientific community considers CRISPr GGE clinical applications premature, but future implementation has not been precluded.[70] According to professional recommendations from the medical community, clinical CRISPr GGE acceptance and implementation requires adequate safety measures, improved efficacy of methodology, additional societal consensus approving the technology, and appropriate governance standards to be in place.[71] The most likely application of CRISPr GGE would be its use to prevent the transmission of heritable diseases.[72] In the clinic CRISPr GGE would be paired with IVF to produce a genetically related child that does not possess a genetic trait associated with a given disease.[73] The approach would be available to couples who present a combination of genotypes that would result in some of their children being afflicted by a genetic disease, are aware they are potential carriers, and wish to avoid passing the disease to their children.[74] The primary alternative option for the couple would

[67] *Id*.
[68] Hildebrandt & Marron, *supra* note 52 at 826.
[69] *Id*.
[70] Niemiec & Howard, *supra* note 32 at 888.
[71] *Id*.
[72] Viotti et al., *supra* note 56.
[73] Niemiec & Howard, *supra* note 32 at 888.
[74] *Id*.

be to use IVF coupled with PGT to culture, select, and implant a genetically related and unaffected embryo.[75]

Theoretically, there are scenarios where PGT would be pointless.[76] If both parents are homozygous for a recessive gene disorder all embryos would be homozygous recessive as well.[77] Only CRISPr GGE would prevent the transmission of the disorder.[78] Additionally, if one or both parents are homozygous for an autosomal dominant disorder every embryo will inherit at least one copy of the dominant disease-causing allele.[79] However, both incidences are relatively rare.[80] Homozygosity for severe dominant disorders is often lethal at the embryonic level, meaning the number of sexually mature individuals with homozygous dominant alleles in the general population is relatively low.[81] In the United States, the number of homozygous Huntington's disease cases is in the dozens, meaning the probability of needing CRISPr GGE therapy for this application is minimal.[82] For homozygous recessive diseases like sickle-cell disease "SCD" and Tay-Sachs, the incidence of individuals in the United States that are homozygous recessive are 1 in 3,289 and 1 in 100,000 respectively for the general population.[83] However, the incidence of SCD jumps to 1 in 500 for African Americans and the incidence of Tay-Sachs jumps to 1 in 3600 for those of Ashkenazi Jewish descent because these diseases have a disproportionate impact on those communities.[84] The estimated number of patients that benefit from CRISPr GGE may be considered relatively rare even in these communities when accounting for the incidence

[75] *Id.*
[76] Viotti et al., *supra* note 56 at 308.
[77] *Id.*
[78] *Id.*
[79] *Id.*
[80] *Id.*
[81] *Id.*
[82] *Id.*
[83] *Id.* at 309.
[84] *Id.*

of disease, reproductive age, and fertility rates.[85] However, that does not justify diminishing the significance of the technology and how the option may benefit affected families.[86]

Another potential application of CRISPr GGE would be to perform a procedure known as a "rescue embryo."[87] A rescue embryo describes a scenario where PGT testing could screen for embryos in the cohort with the disease trait, and those embryos would then be isolated and corrected using CRISPr GGE.[88] This method would increase the overall number of viable embryos in the cohort.[89] With current technology CRISPr GGE is most effectively used at the point of fertilization to avoid mosaicism in the embryonic cells as they divide.[90] Mosaicism describes when not all cells in the embryo or organism have the same DNA.[91] So CRISPr needs to be applied to all embryos in the cohort to achieve the desired changes.[92] However, a method could potentially be developed to efficiently edits all cells in a multicellular embryo to reduce mosaicism.[93] Prior genetic testing, isolation, and correction of embryos would then become a possibility.[94] Additionally, CRISPr GGE may be the only strategy for an IVF patient with a genetic condition, that conceived only affected embryos and cannot complete additional cycles of IVF because of advancing age, disease, or prohibitive cost.[95] Genetic enhancement for disease resistance may also be a possibility but is unlikely to have widespread adoption due to ethical

[85] *Id.* at 314.
[86] *Id.*
[87] *Id.* at 308.
[88] *Id.*
[89] *Id.*
[90] *Id.*
[91] *Id.*
[92] *Id.*
[93] *Id.*
[94] *Id.*
[95] *Id.* at 311.

concerns. These ethical concerns are pervasive for the genetic enhancement of complex traits like intelligence.[96]

In one experiment, CRISPr GGE was used to save human induced pluripotent stem cells and mice from the deleterious gene that causes spinal muscular atrophy "SMA."[97] The experiment was a proof of concept to determine if CRISPr could therapeutically intervene in SMA and other RNA-splicing diseases.[98] SMA is a degenerative motor illness that in severe cases leads to muscle weakness, muscle degradation, and eventually death.[99] SMA is the most common inherited cause of infant mortality in the world, and 98 percent of SMA patients are homozygous for the deletion of an SMN1 gene.[100] Results showed CRISPr, "rescued the SMA phenotypes in human induced pluripotent stem cells and in germline-corrected SMA mice."[101] The lifespan of the SMA mice improved from about 400 days to approximately 600 days.[102] The mice saved by CRISPr GGE disruption demonstrated increased lifespans, increased body weight and motor function, and increased motor neurons.[103] The results were inconclusive as to the feasibility of CRISPr having the same effect in humans, but still provide a proof-of-concept for CRISPr's ability to rescue SMA mice from a debilitating disease.[104]

Various animal models have utilized CRISPr GGE including primates.[105] Studies have also utilized GGE to correct mutations with heart disease and beta-thalassemia.[106] However,

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[96] Niemiec & Howard, *supra* note 32 at 888.
[97] Jin-Jing Li et al., *Disruption of splicing-regulatory elements using CRISPR/Cas9 rescues spinal muscular atrophy in human iPSCs and mice*, 7 NAT'L SCI. REV. 92 (2019).
[98] *Id.*
[99] *Id.*
[100] *Id.*
[101] *Id.* at 93.
[102] *Id.*
[103] *Id.* at 97.
[104] *Id.* at 99.
[105] Robert Ranisch, *Germline genome editing versus preimplantation genetic diagnosis: Is there a case in favour of germline interventions?*, 34 Bioethics 2020 60 (2019).
[106] *Id.* at 60-1.

additional testing needs to be performed before CRISPr GGE gene editing can become part of everyday patient care.[107] Somatic therapies are not always the optimal choice.[108] For example, in cases where early-onset or congenital diseases occur, the symptoms of the disease would already affect the child before somatic therapy could ameliorate the condition.[109] In lysosomal storage disorders the disease manifests virtually no symptoms in infants but within the first days of life the disease proves fatal.[110] Additionally, in the case of Duchenne muscular dystrophy "DMD" symptoms manifest within the first five years of life, but after the symptoms have appeared the condition is virtually irreversible.[111] Huntington's disease also presents an issue for somatic therapy in that the targeted tissue designated for therapy is hard to access in a fully formed child.[112] CRISPr GGE comparatively can easily target a gene within a gamete or zygote in vitro when a parent is a known carrier of the genetic disorder.[113] There is no need to worry about targeting multiple widespread and different types of tissue to accomplish therapy.[114]

Potential targets of CRISPr GGE in cardiovascular medicine include hypertrophic cardiomyopathy "HCM," DMD, and other heritable arrhythmic disorders; all three diseases are heritable and lack effective therapy making them prime for CRISPr GGE therapy.[115] HCM is a cardiac disease that leads to degenerative heart failure.[116] DMD is a disease that leads to progressive muscular weakness and ultimately heart failure.[117] Heritable arrhythmic disorders

[107] *Id.* at 61.
[108] *Id.*
[109] *Id.*
[110] *Id.*
[111] *Id.* at 62-3.
[112] *Id.* at 63.
[113] *Id.*
[114] *Id.*
[115] German et al., *supra* note 34 at 123.
[116] *Id.* at 125.
[117] *Id.* at 126.

cause sudden cardiac death in young children.[118] All these disorders are caused by a single gene mutation.[119] In one United States study, viable human embryos were modified to correct for the genetic traits that cause HCM.[120] HCM is responsible for the most cardiac deaths under the age of thirty.[121] The study proved promising, but additional studies are needed to improve the efficiency of the CRISPr complex before clinical applications may be considered.[122]

b. CRISPr Somatic Therapy Applications

While this paper does not focus on the applications of somatic gene therapies it is noteworthy that these therapies have seen success in clinical cancer immunotherapy and gene disruption therapy.[123] In 2018, the FDA approved a CRISPr clinical trial for cancer immunotherapy, the goal of the clinic was to modify T-cells to target several forms of cancer with relapsed tumors.[124] Another successful clinical trial using CRISPr treatment aimed to provide therapeutic benefits to patients with SCD and later beta-thalassemia by utilizing gene disruption to increase fetal hemoglobin levels.[125] The previous trials both used *ex vivo* modification of cells, which is the most common form of somatic CRISPr therapy.[126] Approaches using *in vivo* techniques have been limited in their clinical applicability because of inadequate access to target tissues. However, some organs, like the eye, are accessible.[127] In one promising treatment, CRISPr components can be delivered directly into the retina to treat patients with Leber congenital amaurosis "LCA," a monogenetic disease that causes childhood

[118] *Id.* at 129.
[119] *Id.* at 123.
[120] Uddin et al., *supra* 61 at 13.
[121] *Id.*
[122] *Id.*
[123] *Id.* at 9.
[124] *Id.*
[125] *Id.*
[126] *Id.* at 12.
[127] *Id.*

blindness.[128] Somatic CRISPr therapies are better suited to treat complex disorders like artery disease and atherosclerosis because of the complicated interplay between genetics and environmental factors that cause these diseases.[129]

D. Limitations and Advantages of CRISPr GGE

a. CRISPr GGE Limitations

CRISPr GGE experiments create hefty public discourse surrounding issues of safety and ethical supervision.[130] Safety issues involve a contradiction between promising technological outcomes and faults caused by the technology's immaturity.[131] Safety concerns of CRISPr GGE include off-target effects, chimeric embryos, and the bad-gene good-gene contradiction.[132] Off-target effects occur when the CRISPr complex mismatches with a non-target DNA sequence and an unintended mutation is introduced.[133] This posits the problem that the unintended mutation is now heritable and passed on to the next generation despite its effects being unknown.[134]. Research is underway to improve the specificity of CRISPr and the method of detection for off-target effects to increase the feasibility of CRISPr GGE therapies.[135] Another concern are chimeric embryos, otherwise known as mosaicism.[136] Mosaicism in GGE is caused by the Cas9 protein not fully degrading before the zygote replicates, which results in a mosaic of cells that have different DNA.[137] The hazard of mosaicism depends on degree of change and the chromosome where the alteration occurred.[138] Using an enzyme that is more precise and

[128] *Id*.
[129] German et al., *supra* note 34 at 124.
[130] Zhou et al., *supra* note 28 at 154.
[131] *Id*. at 155.
[132] *Id*. at 155-6
[133] *Id*. at 156.
[134] *Id*.
[135] *Id*.
[136] *Id*.
[137] *Id*.
[138] *Id*.

controlled in its timing of enzymatic activity may limit the effects of mosaicism.[139] The bad gene good gene contradiction is best described as researchers not fully comprehending all the positive and negative effects of genes, which necessitates a humility when modifying genes to delete a perceived bad gene.[140] For example, the mutation of hemoglobin that causes SCD also prevents a patient from catching malaria.[141] Human CRISPr GGE cannot be approached from the perspective of simply deleting bad traits, rather additional research needs to be done on the cause-and-effect relationships between genes before permanent genomic changes occur.[142]

b. CRISPr GGE Advantages

The clinical value of CRISPr GGE has many applications, CRISPr GGE aims to increase the knowledge and understanding of human development as well as gene functionality, ameliorate genetic defects during development, and treat diseases.[143] CRISPr GGE could potentially cure the 6000 known human genetic diseases that afflict twelve percent of the world's population.[144] CRISPr GGE has an advantage over somatic therapies for treating monogenetic diseases with a wide range of heritability like muscular dystrophy, and genetic diseases that are difficult to treat in fully grown individuals like Huntington's disease.[145] Population control of disease is a broader justification for CRISPr GGE, such that through its use the prevalence of genetic diseases will be diminished.[146] This prognosis requires the delicate balancing of the

[139] *Id*.
[140] *Id*.
[141] *Id*.
[142] *Id*.
[143] *Id*. at 157.
[144] Viotti et al., *supra* note 56 at 304.
[145] Zhou et al. *supra* note 28 at 157.
[146] Niemiec & Howard, *supra* note 32 at 889.

benefits to society, like the economic gains of diminished costs to the healthcare system, against the potential harm to individuals through the introduction of unknown heritable mutations.[147]

Part II: Monetary Costs of IVF, PGT, and CRISPr GGE

According to Stanford bioethicist Mildred Cho, PhD, "Gene therapy is not the same as taking a pill from the pharmacy, it's more like getting an organ transplant…Cancer immunotherapy already costs in the hundreds of thousands of dollars per year. There's no way that gene-edited treatments are going to be any less expensive."[148] New biotechnologies used to treat diseases often present a high price tag because gene therapies are difficult to research, are inordinately costly to push through clinical trials, are uncertain in success rate, serve a limited population, and are by their nature permanent.[149] Gene therapies are not like insulin, the aim of gene therapy is to pay for the treatment once and be cured.[150] For example, the Novartis drug Zolgensa is an FDA approved one-time gene therapy treatment of SMA.[151] The drug is priced at $2.125 million and insurers may pay this amount in yearly installments of $425,000 per year.[152] The price of Zolgensa was calculated by Novartis as half the approximate $4 million cost of managing the disease over the course of a decade.[153] Another expensive gene therapy is the Sarepta Therapeutics drug Eteplirsen.[154] Eteplirsen is a novel drug aimed to treat DMD, however the drug was largely denied coverage by insurance companies due to the drug's poor efficacy in

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147 *Id.*
148 Mark Shwartz, *Target, delete, repair CRISPR is a gene-editing tool that's revolutionary, though not without risk*, Stanford Medicine, https://stanmed.stanford.edu/2018winter/CRISPR-for-gene-editing-is-revolutionary-but-it-comes-with-risks.html (last visited December 12, 2020).
149 Jacob S. Sherkow, *CRISPR, Patents, and the Public Health*, 90 Yale J. Biology & MED. 667 (2017).
150 *Id.*
151 Ken Alltucker, *A new drug costs $2.1 million for children with a muscle-wasting disease*, USA Today, https://www.usatoday.com/story/news/health/2019/05/24/zolgensma-2-1-million-drug-nations-most-expensive/ (May 24, 2019).
152 *Id.*
153 *Id.*
154 Sherkow, *supra* note 149 at 669.

clinical trials and its $750,000 annual price tag.[155] There is hope for CRISPr GGE coverage, insurance providers rarely refuse to cover novel therapies and work through prescription benefit managers to reduce pharmaceutical drug prices if the therapy is proven effective.[156]

An important consideration for CRISPr price is patent protection.[157] As CRISPr has progressed toward clinical testing, the dispute over patent ownership has expedited, primarily because the market valuation of the CRISPR technology is in the billions.[158] The dispute for CRISPr ownership is between the University of California, along with the University of Vienna and Umea University, collectively "UC", and the Broad Institute who is partnered with MIT and Harvard, collectively "Broad Institute."[159] Both UC and the Broad Institute have filed for patent ownership to ascertain a monopoly over the CRISPr market in the United States and in Europe.[160] The costs of this heated litigation are likely to be passed on to consumers when the litigation resolves and CRISPr enters clinical trials.[161]

If CRISPr GGE therapy were to underperform in clinical trials and was exorbitantly priced due to patent pressures, it is likely insurance companies would deny coverage.

To approximate the cost of CRISPr GGE therapy it is important to draw comparisons to IVF and PGT because CRISPr GGE treatment requires use of both technologies.[162] ART therapies are most pervasive in affluent countries.[163] IVF and PGT present the necessary

[155] *Id.*
[156] *Id.* at 668.
[157] Churi & Taylor, *supra* note 36 at 184.
[158] *Id.* at 185.
[159] *Id.*
[160] *Id.* at 187.
[161] *Id.* at 185.
[162] Viotti et al, *supra* note 56 at 304-5.
[163] Robert Klitzman, *How Much Is a Child Worth? Providers' and Patients' Views and Responses Concerning Ethical and Policy Challenges in Paying for ART*, 12 PLOS ONE 1, 2 (2017).

framework for couples affected by genetic disorders to conceive a healthy child.[164] The demographic most likely to utilize ART therapies are wealthier patients, which is defined by a household income of greater than $100,000 per year.[165] Under the current insurance regime, patients often must pay first and seek reimbursement later.[166] Insurers frequently do not agree to coverage in advance of treatment and instead make a coverage decision on a case-by-case basis.[167] Given the unpredictability of length and cost of ART treatment, stress and uncertainty are necessarily increased in patients facing the hurdle of relying on coverage for treatment.[168] This stress is exacerbated by couples having to budget both ART treatment and adding a new child to their household.[169] Cost raises the ethical concern of how much couples will value having a child; couples are faced with an ethical dilemma of choosing between solvency and procreation.[170] On average, an IVF cycle can cost from $9,226 to $12,513 per cycle, with PGT adding an additional $2,500 to $6000 per cycle.[171] According to the CDC, successful pregnancy and live birth often requires more than one cycle of ART.[172] Factors that increase the required number of cycles include age, weight, height, previous IVF usage, and prior pregnancies.[173]

Cost remains the most salient factor and barrier to couples deciding to undergo ART treatment.[174] Couples are motivated to geographically shop for states that mandate coverage for

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[164] *Id*.
[165] *Id*.
[166] *Id*. at 6.
[167] *Id*.
[168] *Id*.
[169] *Id*.
[170] *Id*.
[171] Kathryn T Drazba et al., *A qualitative inquiry of the financial concerns of couples opting to use preimplantation genetic diagnosis to prevent the transmission of known genetic disorders*, 23 J. Genetic Counseling 202, 203 (2014).
[172] *Id*.
[173] *Assisted Reproductive Technology (ART) IVF Success Estimator*, CDC, https://www.cdc.gov/art/ivf-success-estimator/index.html (last visited Dec. 12, 2020).
[174] Drazba et al., *supra* note 171 at 208.

IVF if their insurance provider does not provide coverage.[175] Affordable reproductive technologies allow more couples the ability to avoid genetically prone diseases and ensure a higher quality of life for their children.[176] Most U.S. insurers including United Healthcare, Aetna, Cigna, and Anthem cover genetic testing.[177] To qualify, individuals usually need to attend genetic counseling or present a genetic risk based on family history.[178] United Healthcare explicitly carves out screening options for Ashkenazi Jewish carrier screening, whereas other insurers typically enumerate genetic diseases without mention of ethnicity or race.[179] Genetic testing is also available to consumers for a few hundred dollars; this option may be helpful for individuals who lack insurance or want definitive privacy in their genetic results from their insurer.[180]Additionally, some health insurance companies provide coverage for IVF and PGT independent of state mandates.[181] Aetna provides coverage for IVF when the policyholder has ART benefits and the procedure is medically necessary.[182] For Aetna, medically necessary is defined as medical diagnosis of infertility, which in turn means less invasive fertility methods did not result in pregnancy.[183] Aetna will cover PGT if there is a need to diagnose specific,

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[175] *Id*.
[176] *Id*.
[177] *See Carrier Testing for Genetic Diseases*, UnitedHealthcare, https://www.uhcprovider.com/content/dam/provider/docs/public/policies/medicaid-comm-plan/carrier-testing-genetic-diseases-cs.pdf (Jul. 1, 2020); *Genetic Testing*, Aetna, http://www.aetna.com/cpb/medical/data/100_199/0140.html (Nov. 5, 2020); *Genetic Testing for Reproductive Carrier Screening and Prenatal Diagnosis*, Cigna, https://static.cigna.com/assets/chcp/pdf/coveragePolicies/medical/mm_0514_coveragepositioncriteria_genetic_testing_repro_carrier_prenatal.pdf (Dec. 15, 2019); *Genetic Testing for Inherited Diseases*, Anthem, https://www.anthem.com/dam/medpolicies/abc/active/guidelines/gl_pw_e000232.html (July 8, 2020).
[178] *Id*.
[179] *Id*.
[180] Madison K Kilbride, *In vitro fertilisation with preimplantation genetic testing: the need for expanded insurance coverage*, J. MED. Ethics 1 (2020).
[181] Michekke Bayefsky & Bruce Jennings, Regulating Preimplantation Genetic Diagnosis in the United States: The Limits of Unlimited Selection, 90 (2015).
[182] Understanding Infertility, Aetna, https://www.aetna.com/individuals-families/womens-health/understanding-infertility.html (Aug. 30, 2018).
[183] *Id*.

detectable single gene mutations.[184] Cigna also offers coverage for the combination of IVF and PGT if there is a medical diagnosis of infertility, of which the definition is similar to Aetna.[185] United Healthcare includes coverage of IVF for reasons of infertility, but causes outside of infertility must be reviewed in accordance with the benefit plan.[186] PGT is offered by United Healthcare for the diagnosis of known genetic disorders, unless there are specific exclusions in a particular plan.[187] It is important to recognize that the costs of CRISPr GGE and IVF are significantly less than the lifelong medical costs accrued because of the genetic disorder.[188] For this reason, insurance providers may be incentivized to cover treatments like CRISPr that reduce healthcare costs over the life of the individual.[189]

Currently, two options exist for prospective parents with a known genetic risk to ensure their biological children do not inherit the genetic condition.[190] These options are prenatal diagnosis "PND," and PGT.[191] PND involves natural conception and a subsequent test for genetic abnormalities.[192] If the condition is found, the pregnancy may be terminated.[193] PGT screens for embryos free of the genetic disease.[194] PND is covered by almost every public and private insurer in the United States.[195] PGT functions in the same diagnostic capacity as PND, just in earlier stages of pregnancy.[196] Therefore, cost is likely the primary reason insurers deny

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[184] Invasive Prenatal Diagnosis of Genetic Diseases, Aetna, http://www.aetna.com/cpb/medical/data/300_399/0358.html (Dec. 8, 2020).
[185] *See* Cigna, *supra* note 176.
[186] *Preimplantation Genetic Testing*, UnitedHealthcare, https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-medical-drug/preimplantation-genetic-testing.pdf (July 1, 2020).
[187] *Id*.
[188] German et al., *supra* note 34 at 130.
[189] *Id*.
[190] Kilbride, *supra* note 180 at 1.
[191] *Id*.
[192] *Id*.
[193] *Id*.
[194] *Id*.
[195] *Id*. at 2.
[196] *Id*.

PGT coverage since PND is a cheaper alternative.[197] The United States Centers for Medicare & Medicaid Services "CMS" present guidelines for what qualifies as medically necessary care.[198] Medically necessary care consists of "health care services or supplies needed to diagnose or treat an illness, injury, condition, disease or its symptoms and that meet accepted standards of medicine."[199] PGT certainly qualifies as a diagnostic procedure, but it may be overshadowed in the insurance framework by the cheaper diagnostic procedure PND.[200] The argument for PGT as a treatment procedure seems attenuated.[201] However, if CRISPr GGE were to meet the accepted standards of medicine threshold through clinical research, it could fulfill the treatment component of the medically necessary definition for ART therapy since CRISPr GGE directly alters the genome to treat disease.[202] Perhaps if the ART framework met both definitions of medically necessary, insurers would be more prone to extend coverage.[203]

Part III: State Law ART Regulations

A comparative analysis of state private insurance coverage laws regulating infertility treatments demonstrates a great disparity between even the states that mandate some form of infertility coverage.[204] Some states may cover fertility testing alone, whereas others cover multiple cycles of IVF.[205] The federal government does not mandate infertility coverage as an essential benefit through the Affordable Care Act "ACA", leaving states to decide whether to

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[197] *Id*.
[198] *Id*.
[199] *Id*.
[200] *Id*.
[201] Zhou et al., *supra* 28 at 157.
[202] *Id*.
[203] Kilbride, *supra* note 180 at 4.
[204] Louise Norris, *Does the ACA require infertility treatment to be covered by health insurance?*, Health Insurance & Health Reform Authority, https://www.healthinsurance.org/faqs/does-the-aca-require-infertility-treatment-to-be-covered-by-health-insurance/ (Oct. 26, 2020).
[205] *Id*.

mandate insurance companies to provide coverage.[206] Currently, nineteen states mandate some form of coverage for infertility treatment, whereas thirty-one states and DC have remained silent on the issue.[207] There does seem to be a trend towards mandating coverage; since 2018, Colorado, Delaware, New Hampshire, and Utah have all passed legislation addressing infertility coverage.[208] Colorado's mandate will take effect in January of 2022, New Hampshire's mandate took effect in January of 2020, and Maryland will expand its coverage as of 2021.[209] Fifteen states have laws requiring health plans to cover at least some infertility treatments.[210] Colorado will join these states in 2022.[211] Two states, Texas and California, require group health plans to offer at least one policy with infertility coverage, but employers can opt for a different plan.[212] One state, Louisiana, prohibits coverage from being excluded based on the diagnosis of a correctable medical condition that results in infertility.[213] This law does not mandate IVF or other fertility drug treatments.[214] Nine states that lack a mandate to cover, as well as DC, have a benchmark plan to provide most individual and small group plans sold in the state with diagnostic and possibly treatment services.[215] Thirteen states have laws that mandate IVF coverage including, Arkansas, Colorado in 2022, Connecticut, Delaware, Hawaii, Illinois, Maryland, Massachusetts, New Hampshire, New Jersey, New York, and Rhode Island.[216] Including Colorado, sixteen states have laws mandating at least genetic testing or other

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[206] *Id*.
[207] *Infertility Coverage By State*, Resolve, https://resolve.org/what-are-my-options/insurance-coverage/infertility-coverage-state/ (Aug. 2020).
[208] *Id*.
[209] *Id*.
[210] Gabriela Weigel et al., Coverage and Use of Fertility Services in the U.S., Kaiser Family Foundation, https://www.kff.org/womens-health-policy/issue-brief/coverage-and-use-of-fertility-services-in-the-u-s/ (Sept. 15, 2020).
[211] *Id*.
[212] *Id*.
[213] Resolve, *supra* note 207.
[214] *Id*.
[215] Weigel et al., *supra* note 210.
[216] Resolve, *supra* note 207.

diagnostic tests.[217] The CDC has deemed Illinois, Massachusetts, New Jersey, and Rhode Island comprehensive coverage states.[218] A comprehensive coverage state is defined as offering at least four egg retrievals within the state mandate.[219] No state mandates PGT.[220] Many mandate to cover states have exemptions for small employers that employ less than fifty people as well as religious exemptions.[221] State laws also do not apply to self-insured plans.[222] A self-insured plan describes when an employer pays for the health services of its workers rather than by purchasing health insurance.[223]

In California, group insurers must offer coverage for infertility treatments and diagnosis, but they are not required to provide the coverage, nor do employers need to include it in their insurance plans.[224] The state mandate notably excepts IVF from coverage.[225] Infertility is defined by the law as a demonstrated condition, recognized by a licensed physician and surgeon as a cause of infertility; or the inability to conceive pregnancy or fully carry a live birth to term after a year or more of sexual relations absent contraception.[226] The law further carves out an exception for religious employers stating they do not offer coverage that is inconsistent with the organization's religious or ethical principles.[227] There was a notable amendment that specified treatment, "shall be offered and, if purchased, provided without discrimination on the basis of age, ancestry, color, disability, domestic partner status, gender, gender expression, gender identity, genetic information, marital status, national origin, race, religion, sex, or sexual

[217] *Id*.
[218] Weigel et al. *supra* note 210.
[219] *Id*.
[220] Resolve, *supra* note 207.
[221] Weigel et al. *supra* note 210.
[222] *Id*.
[223] *Id*.
[224] *See* Cal. Health & Safety Code § 1374.55; Cal. Insurance Code § 10119.6
[225] *Id*.
[226] *Id*.
[227] *Id*.

orientation."[228] As evidenced by the law, California's state mandate of infertility coverage is extremely conservative in its application.

New Jersey law requires health insurers with 50 or more employees that provide pregnancy related coverage of medically necessary expenses incurred in diagnosis and treatment of infertility, including IVF, artificial insemination, diagnosis and testing, embryo transfer, surgery, medications, gamete intrafallopian transfer, zygote intrafallopian transfer, intracytoplasmic sperm injection, and four completed egg retrievals per lifetime of the covered person.[229] IVF is further expanded, coverage includes both using donor eggs and when an embryo is transferred to a surrogate.[230] Notably infertility treatments that are experimental or investigational are not covered as well as cryopreservation of gametes.[231] Coverage of IVF, zygote intrafallopian transfer, and gamete intrafallopian transfer are only required if the patient has used all reasonable less expensive options covered by insurance and still has not become pregnant, the maximum number of egg retrievals has not been used, the person is under 46 years old, and the procedures are performed at facilities conforming to the American Society for Reproductive Medicine "ASRM" or the American College of Obstetricians and Gynecologists "ACOG."[232] New Jersey defines infertility broadly in accordance with the ASRM and ACOG to include a disease or condition that results in abnormal function of the reproductive system including where a couple cannot get pregnant after two years of unprotected sex, where the female partner is under the age of 35; or one year of unprotected sex where the female partner is over the age of 35; or when a couple is unable to carry a pregnancy to term.[233] New Jersey also

[228] *See* 2013 Cal. Stats., Chap. 644 (AB 460)
[229] *See* N.J. Stat. Ann. § 17:48-6x; § 17:48A-7w; § 17:48E-35.22; § 17B:27-46.1x (2001)
[230] *Id*.
[231] *Id*.
[232] *Id*.
[233] *Id*.

has a similar religious organization exemption to California where coverage can be excluded if it is contrary to a religious employer's bona fide religious tenets.[234] New Jersey's laws are comprehensive in their mandate to cover, especially when compared to California.

Illinois law also requires insurers to provide coverage for infertility treatment, but is even more liberal in that employers with fewer than 25 employees do not need to provide coverage.[235] Infertility is defined in Illinois as the inability to conceive after one year of unprotected sexual intercourse or the inability to sustain a pregnancy.[236] Otherwise, Illinois coverage provides for the diagnosis and treatment of infertility, IVF, uterine embryo lavage, embryo transfer, artificial insemination, gamete intrafallopian transfer, zygote intrafallopian transfer and low tubal ovum transfer.[237] To utilize IVF, zygote intrafallopian transfer, and gamete intrafallopian transfer the patient must not have been able to sustain a successful pregnancy through less costly infertility treatment covered by insurance.[238] A religious exemption is also carved out.[239] Additionally, the patient is covered by four egg retrievals unless a live birth occurs, then only two more retrievals are covered.[240] Compared to New Jersey and California, Illinois law places the least amount of restrictions on ART treatment. Although both New Jersey and Illinois are comprehensive in their mandates, fundamental differences can still be observed in how that coverage is attained, most notably the lack of an age barrier to attain treatment in Illinois law.

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[234] *Id*.
[235] Ill. Rev. Stat. ch. 215, § 5/356m (1991, 1996)
[236] *Id*.
[237] *Id*.
[238] *Id*.
[239] *Id*.
[240] 1996 Ill. Laws, P.A. 89-669

Part IV: CRISPr GGE and Benefits to Ethnic and Racial Minorities

A. Inequity of Access to ART therapy

Under the current insurance regime there is concern that if CRISPr GGE were clinically available it would be prohibitively expensive, not covered by private insurance, and thus limited to socio-economic classes that can afford out-of-pocket treatment. Lack of access to treatment would exacerbate already existing health inequities in ethnic and racial minorities. An expansion of state law mandates to require private insurance coverage for infertility benefits including IVF, PGT, and CRISPr GGE will likely increase coverage for ethnic and racial minorities and thus address disparate ethnic and racial outcomes in health.

In the United States race and ethnicity are often linked to a disproportionate access to healthcare affecting primarily Hispanic and Black patients.[241] In states that mandate insurance coverage of IVF, the utilization of ART therapy by Hispanic and Black Non-Hispanic women, aged fifteen to forty-four, nearly doubled when compared to states without an insurance mandate for IVF treatment.[242] The main factor contributing to ART use is affordability, when ART therapy is not covered by insurance it can impose great financial hardship on couples.[243] Socio-economic factors can indicate ART use; women with higher income and higher levels of educational attainment are more likely to utilize ART.[244] Residential segregation of certain minority groups into areas with lesser economic opportunities can present an economic barrier to access fertility options.[245] Even when coverage is mandated, rates of ART use among Hispanic

[241] Ada C. Dieke et al. *Disparities in Assisted Reproductive Technology Utilization by Race and Ethnicity, United States, 2014: A Commentary*, 26 J. Women's Health 605 (2017).
[242] *Id*.
[243] *Id*.
[244] *Id*.
[245] *Id*.

and Black women are still less than White and Asian/Pacific Islander women.[246] However, this disparity is thought to be caused by out-of-pocket expenses like deductibles and copays, as well as non-economic factors such as the negative communal stigma on infertility.[247] To reduce this disparity, health care providers could provide incentives for infertility clinics to operate in lower income areas.[248] Increasing awareness, affordability, and expanding access to low-income areas may be enough to defeat communal stigmas and increase equitable access to ART therapy.[249]

Minority communities are aware of disparities in the distribution of cutting-edge medical technology, and that potential genetic enhancements from CRISPr may exacerbate health disparities in these communities.[250] American socioeconomic status has a strong association with race and ethnicity, which raises concerns that if CRISPr treatments were limited to out-of-pocket payments, racial and ethnic minorities would not equally share in the fruits of gene therapy.[251] Gene therapy may pose a risk of widening health disparities, but if scientists, physicians, and healthcare policymakers pledge to ensure justice in gene therapy, the technology may be used as a tool to eventually reduce health inequities.[252]

B. Prevalence of Certain Genetic Conditions

Fairness and equitable access must be at the forefront in developing GGE CRISPr policy. Underserved patients must share in equal access to ground-breaking biotechnologies through a collaborative dialogue and policy decisions informed by the needs of underserved populations. The *National Academics of Science Engineering and Medicine* has delineated seven principals

[246] *Id*.
[247] *Id*.
[248] *Id*.
[249] *Id*.
[250] Hildebrant & Jonathen, *supra* note 52 at 827.
[251] *Id.* at 828.
[252] *Id*.

for the governance of human genome editing: the science should promote wellbeing, increase transparency to the community, take due care in research studies, follow the standards of responsible science, respect persons right to autonomy and integrity, be fair in the distribution of risks and burdens, and support transnational cooperation and collaboration.[253]

Clinical applications of CRISPr GGE for ethnic and racial minorities will be to correct mutations in zygotes that cause fatal or debilitating monogenetic diseases.[254] Certain monogenetic diseases have a higher incidence rate in ethnic and racial minority communities.[255] Such diseases include SCD, Ty-Sachs, and beta-thalassemia.[256] The corrected gene would then be heritable and passed on to the next generation.[257] The prevalence of genetic diseases in these communities would thus be reduced.[258] Reducing incidence of disease would diminish economic strains and increase the number of healthy children born.[259] Economic strains include the cost of lifetime management of disease for the individual and their family.[260] Economic strains on the healthcare system would also be reduced.[261]

The most common monogenetic disorder caused by a single point mutation is SCD, making the disease a prime target for CRISPr GGE therapy.[262] SCD also has a disproportionate impact on those of African descent.[263] Currently, more than 100,000 people in United States live

[253] NAT'L ACADS. OF SCIS., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 12 (2017).
[254] Hirakawa et al., *supra* note 1 at 13.
[255] *Genetic Screening: Ethnic based*, Boston Medical Center, https://www.bmc.org/genetic-services/ethnic-based (last visited Dec. 13, 2020).
[256] *Id*.
[257] Hirakawa et al., *supra* note 1 at 13.
[258] Niemiec & Howard, *supra* note 32 at 889.
[259] German et al., *supra* note 34 at 130.
[260] *Id*.
[261] *Id*.
[262] Frédéric B. Piel et al., *Sickle Cell Disease*, 376 NEW ENG. J. MED. 1561 (2017).
[263] *Sickle Cell Disease*, CDC, https://www.cdc.gov/ncbddd/sicklecell/data.html (last visited Dec. 13, 2020)

with SCD, the incidence of which is disproportionately Black.[264] SCD occurs in one in every 365 Black births, with sickle cell trait "SCT" occurring one in every thirteen Black births.[265] Sickle cell trait describes a condition where the child has one abnormal allele but does not show the severity of SCD symptoms.[266] The first signs of SCD appear during the first year of life, usually around five months.[267] The symptoms can range from mild to severe, and the disease worsens over time.[268] The characteristic symptoms include acute pain crises, swelling in the hands and feet known as hand-foot syndrome, acute chest pain similar in feeling to pneumonia, as well as anemia and the associated symptoms of dizziness, tiredness, irritability, and difficulty breathing.[269] SCD requires a lifetime of management of lifestyle and potentially necessitates a lifetime of medications.[270] The SCD community has been historically disenfranchised and there has been little advancement on the ease of access of SCD treatments.[271]

Tay-Sachs disease is a fatal genetic disorder that causes the progressive degeneration of the central nervous system.[272] Children born with Tay-Sachs appear unaffected at birth and symptoms do not appear until about four or six months of age.[273] The child will begin to lose motor skills and gradually lose the ability to see, hear, and swallow.[274] By two years old, most children diminish in mental function.[275] The child eventually becomes completely cognitively

[264] *Id*.
[265] *Id*.
[266] *Id*.
[267] *Id*.
[268] *Id*.
[269] *Id*.
[270] *Id*.
[271] Keith Wailoo, *Sickle Cell Disease - A History of Progress and Peril*, 376 NEW ENG. J. MED. 805 (2017).
[272] BMC, *supra* note 255.
[273] *Id*.
[274] *Id*.
[275] *Id*.

impaired, paralyzed, and unable to respond.[276] Death usually occurs by age four.[277] Tay-Sachs disease has no cure.[278] The incidence of Tay-Sachs is much higher in individuals of Ashkenazi Jewish descent, with an estimated one in twenty-five individuals being a carrier for the disease.[279] Since Tay-Sachs does not have an effective cure, possesses no genetic benefits to the individual, and has a disparate impact on an ethnic minority, CRISPr GGE therapy will be an optimal treatment to reduce the incidence of Tay-Sachs in the Ashkenazi Jewish community.[280]

Beta-thalassemia is a blood condition that impacts the production of hemoglobin.[281] The disease has two forms, thalassemia intermedia and thalassemia major.[282] Thalassemia intermedia appears in early childhood and is characterized by symptoms of weakness and anemia.[283] Thalassemia major can become life-threatening, children with major develop progressively worse anemia and have reduced immunity.[284] Thalassemia major may require regular blood transfusions.[285] Beta-thalassemia has a high incidence amongst the Hispanic community, with between one in thirty and one in fifty individuals being a carrier for the disease.[286]

Part V: Conclusion

All people should share in the breakthroughs of scientific discovery, classes of people should not be denied access to technology that can ensure a healthier life for their progeny based solely on personal wealth and the availability of coverage. If CRISPr is left to only those who

[276] *Id*.
[277] *Id*.
[278] *Id*.
[279] *Id*.
[280] *Id*.
[281] *Id*.
[282] *Id*.
[283] *Id*.
[284] *Id*.
[285] *Id*.
[286] *Id*.

can afford out-of-pocket costs, future generations of already marginalized communities will be further disenfranchised through the denial of access to therapy that seeks to diminish genetically prone diseases. In equity and in fairness, state infertility mandates should be expanded to afford ethnic and racial minorities a greater opportunity to share in the fruits of emerging biotechnologies. Minimum standards that need to be established before CRISPr GGE can be adopted include, the development of acceptable methodologies for measuring off-target effects, establishing an acceptable threshold of allowable off-target mutations, and setting precedent for when CRISPr GGE may be utilized.[287] Ethical considerations must be undertaken in human GGE research to set a boundary between therapeutic treatment and genetic enhancement of individuals. Human GGE research must ensure the principles of beneficence and justice are respected through research and innovation. Healthcare professionals can ensure justice and ethical regulation by defining the relevant stakeholders of GGE research, establishing ethics committees to review and supervise research, and by maintaining public contact to stay informed on the needs of society.

[287] Niemiec & Howard, *supra* note 32 at 890.