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Mental Disability Law and CRISPR: Can Current Legal Standards Protect Vulnerable Populations from Overzealous Researchers?

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I. Introduction

In 2012, the imaginings of science fiction came true when scientists revealed that newly-developed technology could enable highly-specified genetic manipulation.[1] This technology, largely known as CRISPR,[2] revolutionized the field of genetics by making gene editing "faster, cheaper, more accurate, and more efficient than other existing genome editing methods."[3] As a result, the medical field is increasingly turning to gene editing as a potential treatment option for innumerable conditions with a genetic basis. Scientists are rapidly pursuing clinical applications, and it is time for leaders, legislators, and regulators to carefully examine the potential impacts of this technology on vulnerable members of society. The law as it currently stands provides insufficient protection from the potential harm posed by unwelcome applications of gene editing technology. This Comment will provide an overview of current laws related to CRISPR technology and suggest possible solutions for the regulation of its more immediate applications.

A. Technology Overview

The field of molecular genetics is a relatively new area of study, as researchers only began to explore genome mechanics within the past century.[4] Beginning in the late 1970's, scientists sought to understand how genes in living cells could be manipulated, leading to the development

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[1] Mussaad M. Al-Razouki, *From Science Fiction to Science Fact: Genetic Engineering*, MEDIUM (May 1, 2018), https://medium.com/@Mussaad/from-science-fiction-to-science-fact-3a38b110f5d0.

[2] CRISPR is an acronym for "clustered regularly interspaced short palindromic repeats". *What are Genome Editing and CRISPR-Cas9?*, NATIONAL INSTITUTES OF HEALTH: GENETICS HOME REFERENCE (Aug. 2017), https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting.

[3] *Id.*

[4] Thomas Wirth, Nigel Parker & Seppo Ylä-Herttuala, *History of Gene Therapy*, 525 GENE 162, 162-63 (2013).

of several techniques to add or remove genetic sequences from strands of DNA.[5] While the field saw massive advances throughout the latter half of the 20th century (due in part to the Human Genome Project),[6] progress stalled in 1999 after clinical trial patient Jesse Gelsinger died from an intense inflammatory reaction to a single gene therapy injection.[7] This tragedy revealed a number of problems with the oversight mechanisms and reporting requirements that regulate the field of genetic human subject research.[8] Since Jesse's death, geneticists and regulators alike have sought to improve the field as a whole, yet biomedical technology continues to far outpace policy and regulation.[9] The discovery of CRISPR once again presents the challenge of tempering scientific promise with an abundance of rightful caution.

CRISPR, an acronym for "clustered regularly interspaced short palindromic repeats" (indicating the DNA sequences that make CRISPR possible), provides scientists with a method to "add[], remove[], or alter[genetic material] at particular locations in the genome".[10] The technology allows for much more targeted gene editing than previous methods because:

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[5] *How Does Genome Editing Work?*, NATIONAL INSTITUTES OF HEALTH: NATIONAL HUMAN GENOME RESEARCH INSTITUTE (Aug. 3, 2017), https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/How-genome-editing-works.

[6] *The Human Genome Project*, NATIONAL INSTITUTES OF HEALTH: NATIONAL HUMAN GENOME RESEARCH INSTITUTE (Oct. 7, 2019), https://www.genome.gov/human-genome-project.

[7] Meir Rinde, *The Death of Jesse Gelsinger, 20 Years Later*, SCIENCE HISTORY INSTITUTE: DISTILLATIONS (June 4, 2019), https://www.sciencehistory.org/distillations/the-death-of-jesse-gelsinger-20-years-later.

[8] *Id.*

[9] *Id.* It is worth noting that CRISPR technology has also created turmoil in the field of patent law, as major institutions on each U.S. coast have fought to control intellectual property rights to the technology. While the patent standing of CRISPR is outside the scope of this article, control of intellectual property rights to the technology may have substantial implications for how CRISPR-related ethical issues evolve. For further discussion, see Megan Molteni, *Crispr's Epic Patent Fight Changed the Course of Biology*, WIRED (Sep. 11, 2018, 3:42 PM), https://www.wired.com/story/crisprs-epic-patent-fight-changed-the-course-of-biology/; Sharon Begley, *Patent Office Reopens Major CRISPR Battle Between Broad Institute and University of California*, STAT (June 25, 2019), https://www.statnews.com/2019/06/25/crispr-patents-interference/; Hannah Mosby, *Biotechnology's Great Divide: Strengthening the Relationship Between Patent Law and Bioethics in the Age of CRISPR-Cas9*, 19 MINN. J.L. SCI. & TECH. 565 (2018).

[10] *What are Genome Editing and CRISPR-Cas9?*, *supra* note 2. For a more basic overview of CRISPR technology, see *What is Gene Editing and How Does It Work?*, The Royal Society (Oct. 4, 2016), https://www.youtube.com/watch?v=XPDb8tqgfjY.

> [w]ith CRISPR, researchers create a short RNA template that matches a target DNA sequence in the genome. . . Strands of RNA and DNA can bind to each other when they have matching sequences. The RNA portion of the CRISPR, called a guide RNA, directs Cas9 [CRISPR-associated protein 9] enzyme to the targeted DNA sequence. Cas9 cuts the genome at this location to make the edit. CRISPR can make deletions in the genome and/or be engineered to insert new DNA sequences.[11]

This represents a vast improvement in the reliability of gene editing. Where prior methods were resource intensive and technically complex, requiring synthesis of new proteins for each desired change, CRISPR represents a much more simplified (and cheaper) means of achieving a more precise result.[12] Whereas older technologies saw, at best, a ten percent success rate,[13] CRISPR may provide up to six times the efficiency of these methods "at a small fraction of time and price."[14]

As a result of the tremendous promise that CRISPR holds, "CRISPR-Cas genome editing tools have been adopted rapidly in the research community[and] . . . are quickly finding applications in the commercial sector."[15] These potential applications of CRISPR are innumerable and may impact human life positively or negatively, both inside and outside the medical field.[16] While the desire to cure insidious genetic diseases is certainly a noble goal, CRISPR technology also raises a wide variety of ethical issues that scientists must take into account.[17] These concerns go beyond germ-line editing (editing of genes that can be passed on to future generations) and

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[11] *How does Genome Editing Work?*, *supra* note 5.
[12] *Id.*
[13] *Id.*
[14] *Id.*
[15] Dana Carroll, *Genome Editing: Past, Present, and Future*, 90 YALE J. OF BIOL. AND MEDICINE 653 (2017). *See also*, *What are Genome Editing and CRISPR-Cas9?*, *supra* note 2.
[16] *Compare* Victor Tangermann, *A CRISPR Future: Five Ways Gene Editing Will Transform Our World*, FUTURISM (Jan. 30, 2018), https://futurism.com/crispr-genetic-engineering-change-world *with* Heidi Ledford, *CRISPR Concerns*, 538 NATURE 17 (Oct. 6, 2016), https://www.nature.com/news/polopoly_fs/1.20713!/menu/main/topColumns/topLeftColumn/pdf/nature.2016.20713.pdf?origin=ppub.
[17] Arthur L. Caplan, Brendan Parent, Michael Shen & Carolyn Plunkett, *No Time to Waste – The Ethical Challenges Created by CRISPR*, 16 EMBO REPORTS: SCIENCE & SOCIETY 1421, 1425 (Oct. 8, 2015), https://www.embopress.org/doi/pdf/10.15252/embr.201541337.

include applications of gene editing to somatic cells (where edits would not be passed to future generations).[18]

B. The Somatic/Germ-Line Ethical Divide

An additional aspect of the underlying science—whether manipulated genes could be passed on to future generations—complicates the implications of CRISPR technology. This complication arises from the fact that living organisms are composed of two primary cell types. Somatic cells, which make up the vast majority of cells in the human body, do *not* pass their genes on to future generations.[19] "A somatic cell is any cell of the body except sperm and egg cells. Somatic cells are diploid, meaning that they contain two sets of chromosomes, one inherited from each parent. Mutations in somatic cells can affect the individual, but they are not passed on to the offspring."[20] Germ-line cells, on the other hand, develop gametes (or sperm and eggs) and *do* pass genetic information, including CRISPR modifications, to future generations.[21] This ability (or inability) to pass genetic information to future progeny has become the foundation of the present CRISPR bioethics debate.

With the somatic/germ-line distinction forming the dividing line in CRISPR bioethics, many bioethics leaders assert that research on somatic application should forge ahead, while a *voluntary* moratorium should be placed on germline editing.[22] Although nice in theory, the

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[18] *Id.*

[19] *Somatic Versus Germinal Mutation*, An Introduction to Genetic Analysis, 7th ed. (2000), https://www.ncbi.nlm.nih.gov/books/NBK21894/.

[20] "Somatic Cells", National Human Genome Research Institute, https://www.genome.gov/genetics-glossary/Somatic-Cells.

[21] *Somatic Versus Germinal Mutation*, *supra* note 19. *See also* "Germ Line", National Human Genome Research Institute, https://www.genome.gov/genetics-glossary/germ-line.

[22] Giulia Cavaliere, *Background Paper: The Ethics of Human Genome Editing*, WORLD HEALTH ORGANIZATION: Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (2019), at 2, (citing Edward Lanphier, Fyodor Urnov, Sarah Ehlen Haeker, Michael Werner & Joanna Smolenski, *Don't Edit the Human Germ Line*, 519 NATURE 410 (2015)) https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Ethics-paper-March19.pdf.

obvious weaknesses in this approach are readily apparent. Due in part to the non-binding nature of the voluntary moratorium, germ-line use of CRISPR has already been used to manipulate fetal DNA.[23] In 2018, Professor He Jiankui created the first "CRISPR babies" in China,[24] a project he undertook independent of his academic laboratory.[25] Ultimately, there was significant international backlash against Professor He's experiment, and in December 2019, the Chinese government sentenced him to three years in prison.[26] While the Chinese government may be seeking to quell international ethics concerns, criminalization of scientific research will have a dangerous chilling effect on scientists performing necessary and beneficial work.[27] The United States is not immune to germ-line experiments, and it is short-sighted to think that social pressure will control the expansion of ethically challenging applications of CRISPR in American institutions.[28] Researchers in the United States are currently working to apply CRISPR techniques to human sperm[29] and may rely on funding sources that evade typical regulatory schemes.[30] Such

[23] *See* Julia Belluz, *Is the CRISPR Baby Controversy the Start of a Terrifying New Chapter in Gene Editing?*, VOX (January 22, 2019) https://www.vox.com/science-and-health/2018/11/30/18119589/crispr-gene-editing-he-jiankui. *See also*, Pam Belluck, *Gene-Edited Babies: What a Chinese Scientist Told an American Mentor*, N.Y. Times (April 14, 2019) https://www.nytimes.com/2019/04/14/health/gene-editing-babies.html.

[24] *Id.*

[25] *See China Says Dr. He Jiankui Behind Gene-Edited Babies Acted on His Own*, NBC News: Associated Press (Jan. 21, 2019, 9:51 AM), https://www.nbcnews.com/health/health-news/china-says-dr-he-jiankui-behind-gene-edited-babies-acted-n960926. *But see* Julia Belluz, *CRISPR Babies: The Chinese Government May Have Known More Than It Let On*, Vox (Mar. 4, 2019, 11:00 AM) (suggesting that the project was less "independent" than Chinese officials have publicly stated), https://www.vox.com/2019/3/4/18245864/chinese-scientist-crispr.

[26] David Cyranoski, *What CRISPR-Baby Prison Sentence Means for Research*, NATURE (Jan. 3, 2020), https://www.nature.com/articles/d41586-020-00001-y.

[27] *Id.*

[28] *Cf.* Francoise Baylis, *Before Heritable Genome Editing, We Need Slow Science and Dialogue 'Within and Across Nations'*, STAT: First Opinion (September 23, 2019) https://www.statnews.com/2019/09/23/genome-editing-slow-science-dialogue/.

[29] Rob Stein, *Scientists Attempt Controversial Experiment to Edit DNA in Human Sperm Using CRISPR*, NPR (August 22, 2019) https://www.npr.org/sections/health-shots/2019/08/22/746321083/scientists-attempt-controversial-experiment-to-edit-dna-in-human-sperm-using-cri.

[30] Dr. Gianpiero Palermo, the principal investigator behind CRISPR sperm research in the United States, has created the Palermo Foundation, an organization with the mission of "rais[ing] funds to continue research for both male and female infertility regardless of the underlying cause." Palermo Foundation, *Our Mission* (last visited Feb. 14, 2020), https://www.palermofoundation.org/. "The Foundation plans to establish the premises to nest an advanced reproductive laboratory . . . As the Foundation gains its reputation, fundraising activities will be organized to gain support to build the facility." *Id.*

germ-line edits would inevitably be passed on to future generations,[31] fundamentally altering their development. A middle ground between criminalization and mere social pressure would be helpful in controlling the expansion of these efforts before they go too far.

There is no doubt that the prospect of CRISPR application in a clinical setting has caused significant alarm in both scientific and lay communities; however, this alarm has largely been narrowed to the germline context, leading to a failure to consider negative consequences of somatic application.[32] As a result, somatic research regarding CRISPR applications are more likely to progress without much questioning. Professor He's ability to create CRISPR edited babies reveals just how simple and efficient genetic manipulation has become.[33] In the United States, clinical research on somatic cells currently includes trials for various relapsed cancers, sickle cell anemia, non-Hodgkins lymphoma, and inherited blindness.[34] More fundamental and pre-clinical research is also occurring, and likely to progress quickly.[35] The scientific community is rapidly moving towards application of CRISPR across a variety of biomedical areas.[36] In light of this revolutionary shift, somatic applications cannot be ignored.

The ethical and legal debate cannot stop with germ-line concerns, and it must not be left solely to the scientific community. While germ-line applications are undoubtedly alarming,

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[31] *Is it Ethical to Edit Human Sperm with CRISPR?*, ADVISORY BOARD: The Daily Briefing (August 27, 2019) https://www.advisory.com/daily-briefing/2019/08/27/crispr.

[32] *See, e.g.*, Joel Achenbach, *NIH and Top Scientists Call for a Moratorium on Gene-Edited Babies*, Washington Post (March 13, 2019, 2:00 PM), https://www.washingtonpost.com/science/2019/03/13/nih-top-scientists-call-moratorium-gene-edited-babies/; Amy Maxmen, *Easy DNA Editing Will Remake the World. Buckle Up.*, Wired (2015), https://www.wired.com/2015/07/crispr-dna-editing-2/.

[33] *Id.*

[34] Lila Thulin, *Four U.S. CRISPR Trials Editing Human DNA to Research New Treatments*, Smithsonian Magazine (Sep. 3, 2019) https://www.smithsonianmag.com/science-nature/four-us-crispr-trials-editing-human-dna-for-new-medical-treatments-180973029/.

[35] *See generally This is Broad*, BROAD INSTITUTE, https://www.broadinstitute.org/about-us. *See also* Cui Zhang, Renfu Quan & Jinfu Wang, *Development and Application of CRISPR/Cas9 Technologies in Genomic Editing*, 27 HUMAN MOL. GENETICS R79 (2018).

[36] Patrick D. Hsu, *et al.*, *Development and Applications of CRISPR-Cas9 for Genome Engineering*, 157 CELL 6 (2014) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4343198/.

widespread somatic uses are much closer in time and present their own ethical complexities. Thus, this comment will seek to demonstrate the potential implications of somatic editing by examining its application in the field of psychiatry and assessing the ability of mental disability law to address the negative consequences of such applications. Section II will outline possible somatic applications of CRISPR in psychiatry. Then, Section III will examine the constitutional protections of the bodily autonomy of mentally ill persons and explore the current state of mental disability law regarding bodily autonomy. Finally, Sections IV and V will look to present regulatory structures to determine whether they are capable of addressing somatic CRISPR uses and consider potential solutions for leaders to adopt moving forward.

II. Potential for Gene Editing to be Exploited in Psychiatry

A. In Pursuit of Neurobiological Clarity

Psychiatry is a particularly pertinent area for CRISPR research for several reasons. First, recent psychiatric research has failed to produce new, effective medications.[37] Drug development has stalled as new medication targets for psychiatric purposes have not been identified in quite some time.[38] The most commonly prescribed psychiatric drugs were approved by the FDA more than 30 years ago,[39] and drugs for diseases such as schizophrenia merely subdue a singular symptom of the disease, rather than treating its underlying cause.[40] As a result of this relative standstill, researchers are seeking out new avenues for potential treatment.[41] CRISPR is not only being explored as a way to cure or eliminate mental illness, but it is also being looked at, more

[37] *Why Study the Genetics of Psychiatric Disorders?*, BROAD INSTITUTE, https://www.broadinstitute.org/files/news/media-kit/WhyStudyGenetics.pdf
[38] *Id.*
[39] Jim Dryden-Wustl, *CRISPR Powers the Hunt for New, Better Antidepressants*, FUTURITY (August 17, 2018), https://www.futurity.org/antidepressants-crispr-1841722/.
[40] *Research Highlight: Schizophrenia*, BROAD INSTITUTE (2016), https://www.broadinstitute.org/research-highlights-schizophrenia.
[41] Dryden-Wustl, *supra* note 39.

immediately, to increase the effectiveness of psychiatric medications.[42] Since this research has, at a minimum, aided scientific understanding of mental illness, it will likely forge ahead in years to come.[43]

In addition to the drug development stalemate, psychiatry is a prime area for somatic applications of CRISPR due to the highly heritable nature of psychiatric disease.[44] Research into the etiology of mental illness shows that genetics, in addition to environmental factors, play a significant role in the development of mental illness.[45] In fact, some of the most debilitating mental illnesses are also thought to have the strongest genetic markers,[46] and research continues to "indicate[] widespread genetic overlap across different types of psychiatric disorders, particularly between attention-deficit/hyperactivity disorder (ADHD), bipolar disorder, major depressive disorder, and schizophrenia."[47] As a result of these strong genetic links, scientists are beginning to explore the possibility of gene editing as a potential treatment avenue for psychiatric illnesses.[48] Ultimately, the impact these diseases have on patients' lives, combined with the fact that they are often difficult to treat, will continue to make them prime targets for CRISPR research and

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[42] *Id. See also Stanley Center Therapeutics Projects*, BROAD INSTITUTE: Stanley Center for Psychiatric Research, https://www.broadinstitute.org/therapeutics/stanley-center-therapeutics-projects.

[43] *See, e.g.*, *Stanley Center Therapeutics Projects*, BROAD INSTITUTE: Stanley Center for Psychiatric Research, https://www.broadinstitute.org/therapeutics/stanley-center-therapeutics-projects.

[44] *Genetic Relationship between Five Psychiatric Disorders Estimated from Genome-Wide SNPs*, NATIONAL INSTITUTE OF HEALTH: Cross-Disorder Group of the Psychiatric Genomics Consortium, 45, NAT. GEN. 984 (2013).

[45] Stephanie P.B. Caligiuri & Paul J. Kenny, *The Promise of Genome Editing for Modeling Psychiatric Disorders*, 43 NEUROPSYCHOPHARMACOLOGY REVIEWS 223 (2018).

[46] These illnesses include major depressive disorder, bipolar disorder, and schizophrenia. Rudolf Uher & Alyson Zwicker, *Etiology in Psychiatry: Embracing the Reality of Poly-Gene-Environmental Causation of Mental Illness*, 16 WORLD PSYCHIATRY 121 (2017).

[47] Karen Zusi, *Psychiatric Disorders Share an Underlying Genetic Basis*, BROAD INSTITUTE: News (June 21, 2018), https://www.broadinstitute.org/news/psychiatric-disorders-share-underlying-genetic-basis.

[48] Angela She, *CRISPR in Neuroscience: How Precision Gene Editing May Unravel How the Brain Works (and Why It Sometimes Doesn't)*, Harvard University Graduate School of Arts and Sciences: Neurotechnology Blog (April 6, 2016), http://sitn.hms.harvard.edu/flash/2016/crispr-in-neuroscience-how-precision-gene-editing-may-unravel-how-the-brain-works-and-why-it-sometimes-doesnt/; *Fighting Depression with CRISPR*, Synthego: The Bench (August 23, 2018), https://www.synthego.com/blog/crispr-depression; S.K. Powell, J. Gregory, S. Akbarian & K.J. Brennand, *Application of CRISPR/Cas9 to the Study of Brain Development and Neuropsychiatric Disease*, 82 MOL. CELL NEUROSCI. 157 (2017).

application in the clinical setting. At present, at least two major U.S. institutions have dedicated substantial projects to exploring genetically-based treatments of mental illness.[49] The Stanley Center for Psychiatric Research of the Broad Center of MIT and Harvard, based in Cambridge, Massachusetts, is focused on exploring the etiology of schizophrenia and other mental illnesses, identifying biomarkers of psychiatric disease, and "above all, [developing] new treatments."[50] Meanwhile, the University of California at Los Angeles has launched a "Grand Challenge" focused on Depression, and the Center for Neurobehavioral Genetics will focus its efforts on developing new genetically-based treatments for the illness.[51] Ironically referring to the Grand Challenge as the "Manhattan Project for depression," UCLA researchers intend to make a tremendous impact,[52] and there is no doubt that the development of CRISPR technology will help them, and others[53], move quickly towards their goals.[54]

B. Pumping the Brakes on Psychiatric Genetics

i. Substantive Concerns

While it clearly makes sense to explore the genetic underpinnings of mental illness, there are also a number of reasons why advancement in this area via the application of CRISPR

[49] *See, e.g.*, *Stanley Center*, BROAD INSTITUTE, *infra* note 50, and UCLA Grand Challenges, *infra* note 51.
[50] *Stanley Center*, BROAD INSTITUTE: Stanley Center for Psychiatric Research, https://www.broadinstitute.org/stanley.
[51] *See Depression*, UCLA GRAND CHALLENGES, https://grandchallenges.ucla.edu/depression/.
[52] Linda Marsa, *Can We Eliminate Depression? A Massive New Project Aims to Do Just That*, DISCOVER (Oct. 9, 2019), https://www.discovermagazine.com/mind/can-we-eliminate-depression-a-massive-new-project-aims-to-do-just-that.
[53] The Virginia Institute for Psychiatruc and Behavioral Genetics at the Virginia Commonwealth University seeks to study the genetic etiology of psychiatric illness as well; however, the VCU Institute is pursuing more general understandings through foundational research, as opposed to the solution-driven focus of the Broad Institute and UCLA's Grand Challenge. *See* Virginia Institute for Psychiatric and Behavioral Genetics, *Mission Statement* (last visited Feb. 14, 2020), https://vipbg.vcu.edu/about/mission-statement/.
[54] Interestingly, two of the leaders of the UCLA project identified the first genetic markers of depression by studying Chinese women. *See id*.; Roseann E. Peterson, *et al*, *The Genetic Architecture of Major Depression in Han Chinese Women*, 74 J. AM. MED. ASS'N PSYCHIATRY 162 (2017). China's protection of its citizen's genetic information and privacy is questionable at best. *See, e.g.*, Emma Yasinski, *China Clamps Down on Foreign Use of Chinese Genetic Material and Data*, THE SCIENTIST (June 17, 2019), https://www.the-scientist.com/news-opinion/china-clamps-down-on-foreign-use-of-chinese-genetic-material-and-data-66016; Sui-Lee Wee, *China Uses DNA to Track Its People, With the Help of American Expertise*, NY TIMES (Feb. 21, 2019), https://www.nytimes.com/2019/02/21/business/china-xinjiang-uighur-dna-thermo-fisher.html.

technology must be approached with extreme caution. Although mental illness is highly heritable, scientists suspect that these illnesses are also *polygenic*, meaning that multiple genes contribute to their pathogenicity. In addition, the role of epigenetics (changes to the DNA that do not affect the sequences themselves but can influence gene expression nonetheless) in the development of psychiatric illnesses is not fully understood.[55] Both of these aspects of the underlying science can apply to diseases that are non-psychiatric in nature, and somatic editing for those illnesses my present similar challenges. These challenges are not only technological, but also presents ethical in nature. For example, primary candidates for initial, experimental uses of psychiatric (and non-psychiatric) somatic gene-editing will be those patients afflicted with the most serious conditions, experiencing the most severe symptoms and facing the greatest amount of treatment resistance via conventional treatment methods.[56] As these patients are likely *desperate* for new treatments for their illnesses, researchers must have an awareness of the impact such desperation can have on patients' decision-making.[57]

In addition to the technological issues presented, polygenicity may pose other concerns as well. The impact that changing only one or two genes contributing to an illness, as opposed to all of the genes known to be associated, could have unimaginable and unpredictable consequences.[58] Furthermore, the very nature of what CRISPR technology would seek to do, i.e., "erase" or "replace" characteristics at the very core of a person, warrants serious concern and questioning about its role in psychiatric treatment and medical care more generally. This concern about

[55] *What is epigenetics?*, National Institutes of Health: Genetics Home Reference, https://ghr.nlm.nih.gov/primer/howgeneswork/epigenome.
[56] Alexandra L. Foulkes, Takahiro Soda, Martilias Farrell, Paola Giusti-Rodriguez & Gabriel Lazaro-Munoz, *Legal and Ethical Implications of CRISPR Applications in Psychiatry*, 97 N.C.L. REV. 1359, 1383-86 (2019), https://docs.wixstatic.com/ugd/ba77b5_5d2805bbecea47dbb70ec3eda4fdc199.pdf.
[57] *Id.*
[58] Carolyn Brokowski & Mazhar Adli, *CRISPR Ethics: Moral Considerations for Applications of a Powerful Tool*, 431 J. MOL. BIOL. 88, 90 (2019).

"erasing " characteristics also applies to non-psychiatric diseases, as the manipulation of "bad genes" to "good genes" will undoubtedly reduce diversity, neural and otherwise.[59, 60] Clinicians must engage with patients in a careful risk-benefit analysis that takes into account the individual needs of the patient and seeks to ensure that "the risks and burdens that accompany the intervention [are not] greater than the baseline state of the individual."[61] They must also carefully consider the biological and sociological implications that an inevitable reduction in diversity might have.[62]

ii. Procedural Concerns

Psychiatric research on human patients also involves substantial concerns regarding informed consent and voluntary participation.[63] Care must be used in the informed consent protocol of any experimental application of new technology; however, the nature of mental illness is such that eligible patients are at a heightened risk of being taken advantage of and manipulated during the medical decision-making process.[64] Even the Supreme Court, in *Zinermon v. Burch*, has recognized the inherent concerns regarding the ability of mentally ill patients to provide legitimate informed consent regarding their medical treatment:

> The risk is that some persons who come into [the state's] mental health facilities will apparently be willing to sign forms authorizing admission and treatment, but will be incompetent to give the "express and informed consent" required for voluntary placement under [the statute]. Indeed, the very nature of mental illness makes it foreseeable that a person needing mental health care will be unable to understand any proffered "explanation and disclosure of the subject matter" of the forms that person is asked to sign, and will be unable "to make a knowing and willful decision" whether to consent to admission. A person who is willing to sign forms but is incapable of making an informed decision is, by the same token,

[59] FRANCOISE BAYLIS, ALTERED INHERITANCE: CRISPR AND THE ETHICS OF HUMAN GENOME EDITING 19-35 (2019).
[60] For a discussions of neurodiversity, see John Elder Robison, *What is Neurodiversity?*, PSYCHOLOGY TODAY (Oct. 7, 2013), https://www.psychologytoday.com/us/blog/my-life-aspergers/201310/what-is-neurodiversity, and Robert D. Austin & Gary P. Pisano, *Neurodiversity as a Competitive Advantage*, HARVARD BUSINESS REVIEW (June 2017, 99-103), https://hbr.org/2017/05/neurodiversity-as-a-competitive-advantage.
[61] Laura Weiss Roberts & Shaili Jain, *Ethical Issues in Pharmacology*, 28 PSYCHIATRIC TIMES (May 7, 2011), https://www.psychiatrictimes.com/bipolar-disorder/ethical-issues-psychopharmacology.
[62] BAYLIS, ALTERED INHERITANCE, *supra* note 59.
[63] John S. Carroll, *Consent to Mental Health Treatment: A Theoretical Analysis of Coercion, Freedom, and Control*, 9 BEHAVIORAL SCI. & L. 129 (1991).
[64] *Id.*

> unlikely to benefit from the voluntary patient's statutory right to request discharge. . . . Such a person thus is in danger of being confined indefinitely without benefit of the procedural safeguards of the involuntary placement process, a process specifically designed to protect persons incapable of looking after their own interests."[65]

Thus, the increased vulnerability of the mentally ill can make it difficult to determine whether consent *without coercion* has truly been given.[66] These concerns are likely present with other vulnerable populations as well, such as minors or developmentally delayed individuals. Furthermore, the stigma surrounding mental illness is of particular concern for psychiatric patients, as this stigma has the potential to lead to force, manipulation, or inappropriate persuasion from medical professionals and family members, whether these individuals are aware of their impact or not.[67] Shame and emotional pain associated with psychiatric disease may encourage an individual's loved ones to assert significant pressure to accept treatment, leading to consent that is not truly voluntary and autonomous.[68]

In addition to the concerns surrounding informed consent, use of CRISPR in the psychiatric context also warrants serious consideration regarding patient privacy. Whether CRISPR is used to directly modify a patient's DNA or derivatives of the technology are used to identify better pharmacological treatment options, application of CRISPR in the clinical psychiatric context will "likely require collecting participant's genetic information."[69] Genetic privacy is not the only concern here—privacy of mental health records is also of extreme importance, especially due to the widespread stigma about psychiatric diagnoses that persists in society.[70] Since genetic information will be directly tied to data about a patient's mental health status, "clinicians and

[65] Zinermon v. Burch, 494 U.S. 113, 133 (1990).
[66] John S. Carroll, *supra* note 63.
[67] *Id.* at 130.
[68] *Id.* at 131.
[69] Foulkes, *et al.*, *supra* note 56, at 1388–89.
[70] *Id.*

researchers should take particular care to protect this population from improper disclosure and misuse of medical information."[71]

III. Constitutional Authority on the Bodily Autonomy of the Mentally Ill

Most Americans would recognize that bodily autonomy is a fundamental right possessed by *all* persons and that this right is treated with such high regard in our legal system that little can overcome it. These ideas are supported by the longstanding "recogni[tion] of the common law right against bodily intrusions,"[72] evidenced "in the torts of battery and trespass."[73] Despite the fact that bodily autonomy "is considered among the most cherished of rights,"[74] the Supreme Court's treatment of the bodily autonomy of vulnerable groups, such as the mentally ill, complicates this view[75]—"[f]ailure to appreciate the true invasiveness of many bodily intrusions has made the Court exceedingly deferential to state authority and 'professional judgment' in deciding when intrusions are necessary."[76] Ultimately, the jurisprudence of our nation's highest Court reveals that respect for individual bodily autonomy is substantially undermined by the Court's treatment of persons traditionally seen as "biologically inferior". This Section will examine jurisprudence regarding the mentally ill; however, the notion of "biological inferiority" extends beyond this context and has been evidenced in both our nation's and the world's history.[77]

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[71] *Id.*
[72] Caitlin E. Borgmann, *The Constitutionality of Government-Imposed Bodily Intrusions*, 2014 U. ILL. L. REV. 1059, 1060 (2014).
[73] *Id.* at 1064.
[74] *Id.* at 1060.
[75] *See infra* Sections III(A)–(C).
[76] Borgmann, *supra* note 72, at 1062.
[77] Such beliefs became popular during the 1800s after Charles Darwin published his "survival of the fittest" theory, which sparked the rise of Social Darwinism. *Social Darwinism*, HISTORY (Aug. 21, 2018), https://www.history.com/topics/early-20th-century-us/social-darwinism. These ideas have been applied to various categories of persons, for example certain racial groups or socioeconomic classes. *See, e.g.*, Michael B. Katz, *The Biological Inferiority of the Undeserving Poor*, 11 SOCIAL WORK & SOCIETY INT'L ONLINE J. 1 (2013), https://www.socwork.net/sws/article/view/359/709. Moreover, the concept of scientific racism, and other forms of "biological inferiority", persists in the modern era. *See* W. Carson Byrd & Matthew W. Huey, *Born That Way? 'Scientific' Racism is Creeping Back into Our Thinking. Here's What to Watch Out For.*, WASH. POST (Sept. 28,

A. Forced Sterilization

The starkest example of disrespect for the bodily autonomy of "biologically inferior" mentally ill persons can be seen in the Court's infamous opinion in *Buck v. Bell*. In *Buck*, the Court upheld the constitutionality of forced sterilization for "feeble-minded imbeciles" that were being held in state-run institutions.[78] Carrie Buck, a supposedly mentally ill woman,[79] had been committed to the state mental institution "in due form,"[80] language intended to suggest that her due process rights had not been violated. Buck's mother was also mentally ill, and Buck, herself, was the mother of a mentally ill child.[81] As a result of her "feeble-minded" lineage, Ms. Buck was subjected to a surgical sterilization procedure at the discretion of the institution's superintendent.[82] She was just eighteen years old at the time.[83] In upholding the constitutionality of the procedure against a Fourteenth Amendment challenge, Justice Holmes stated: "[i]t is better for all the world, if . . . society can prevent those who are manifestly unfit from continuing their kind."[84]

Though *Buck v. Bell* is an old case, it has never been directly overturned by the Court[85], and the Court has explicitly declined the opportunity to do so.[86] The case has been dismissed as a product of its time, with modern courts admitting that its language is incendiary[87]; however, the

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2015), https://www.washingtonpost.com/news/monkey-cage/wp/2015/09/28/born-that-way-scientific-racism-is-creeping-back-into-our-thinking-heres-what-to-watch-out-for/?arc404=true.

[78] Buck v. Bell, 274 U.S. 200 (1927).

[79] *See, e.g.*, Paul A. Lombardo, *Three Generations, No Imbeciles: New Light on Buck v. Bell*, 60 N.Y.U.L. REV. 30, 52 (1985) (evidence not presented at trial could have refuted the assertion that Carrie Buck was, in fact, mentally deficient).

[80] Buck, 274 U.S. at 205.

[81] *Id.* For a debate regarding whether Carrie Buck's mother and daughter actually did suffer from mental illness, see generally Lombardo, *supra* note 79.

[82] Buck, 274 U.S. at 205–06.

[83] *Id.* at 205.

[84] *Id.* at 207.

[85] *See, e.g.*, David Bianculli, *The Supreme Court Ruling that Lead to 70,000 Forced Sterilizations*, NATIONAL PUBLIC RADIO: FRESH AIR (March 24, 2017, 3:46 PM), https://www.npr.org/2017/03/24/521360544/the-supreme-court-ruling-that-led-to-70-000-forced-sterilizations.

[86] *See* Skinner v. Oklahoma, 316 U.S. 535 (1942) (holding that the Oklahoma Habitual Criminal Sterilization Act unconstitutional because the law was applied differently to habitual criminals based on the types of crimes they committed but refusing to apply this reasoning to mentally ill persons).

[87] *See, e.g.*, Chamul v. Amerisure Mut. Ins. Co., 486 S.W.3d 116, 117 (TX Ct. App., 1st District, 2016).

validity of this idea is, at best, questionable, since forced sterilization was a contentious issue even in 1927 when the case was decided.[88] Despite the repudiation that has occurred, its continuance as a case that has merely been questioned, rather than overturned, leaves the door open for highly invasive, government-imposed procedures to be held constitutional. Ultimately, "*Buck* [continues to] represent[] a milestone in the affirmation of governmental power over individual rights, but more specifically, *Buck* is a landmark in the endorsement of intrusive medical procedures as tools to be used for state ends."[89] Its continued presence in the Supreme Court's jurisprudence poses a dangerous precedential threat in our present genetic age.

B. Forced Medication

While *Mills v. Rogers* is less obviously problematic than *Buck v. Bell*, the case still serves to undermine the rights of mentally ill persons within the American justice system. *Mills v. Rogers* involved coerced administration of medication to a mentally ill patient, and the parties involved decided to stipulate at trial that a liberty interest in avoiding such administration of psychoactive drugs exists.[90] This stipulation ultimately enabled the Supreme Court to avoid determining whether such an interest is protected by the Constitution.[91] In *assuming* the stipulation, the Court leaves room for an argument against a Constitutional right against this sort of bodily intrusion, weakening the protection the Constitution provides to psychiatric patients. Furthermore, the Court uses a circular argument to avoid saying anything substantive on the matter. Relying on the stipulated assumption that a liberty interest in avoiding forced medication exists, the Court asserts

[88] Alex Wellersterin, *States of Eugenics: Institutions and Practices of Compulsory Sterilization in California*, REFRAMING RIGHTS: BIOCONSTITUTIONALISM IN THE GENETIC AGE (Sheila Jasanoff ed., 2011) at 32.
[89] Lombardo, *supra* note 79, at 33.
[90] *Mills v. Rogers*, 457 U.S. 291, 299 (1982).
[91] *Id.* at 299 n.16.

that state law could only increase any interest that *may* exist, yet still fails to provide any guidance regarding how these interests are to be assessed or balanced against state interests.[92]

By essentially punting on whether individuals actually do have a liberty interest in avoiding forced medication, the Supreme Court left the question open for lower courts to decide in a scattered and hesitant manner.[93] In asserting that federal constitutional requirements for due process do not control and leaving such process concerns to states to decide, the Court underlined its refusal to apply strict scrutiny in cases concerning government intrusions of bodily autonomy,[94] and left open a black hole in which the Eleventh Amendment could be asserted by states against the rights of the individual.[95] After a slew of litigation between state and federal courts, the *Rogers* litigation ultimately ended with the First Circuit deciding that state level protections were sufficient.[96]

C. Involuntary Commitment

The Supreme Court's lack of respect for the bodily autonomy of the mentally ill can even be seen in its jurisprudence around involuntary civil commitment. In *Addington v. Texas*, the constitutionality of indefinite civil commitment to a mental hospital was challenged.[97] Frank Addington was sentenced to involuntary commitment for an indefinite period of time following a conviction of "assault by threat" on the basis of a "clear and convincing evidence" standard.[98] Addington appealed, arguing that the jury should have been instructed on the basis of a "beyond a reasonable doubt" standard.[99] Ultimately, despite the fact that such involuntary commitment

[92] *Id.* at 299–300.
[93] Ellen Wright Clayton, *From Rogers to Rivers: The Rights of the Mentally Ill to Refuse Medication*, 13 AM. J.L. & MED. 7, 39–40 (1987).
[94] Caitlin E. Borgmann, *supra* note 72, at 1059.
[95] Ellen Wright Clayton, *supra* note 93, at 41–43.
[96] *Id.* at 43.
[97] Addington v. Texas, 441 U.S. 418 (1979).
[98] *Id.* at 421.
[99] *Id.* at 421–22.

would have the same impact on Addington's bodily autonomy as a prison sentence, the Supreme Court upheld the use of the lesser evidentiary standard, stating that it did not violate due process when used for civil confinement purposes.[100]

The *Addington* opinion also suggests that substantial deference should be given to psychiatric professionals for purposes of the balancing test required in the civil commitment context.[101] Since the courts must balance both the interests of the individual (in not being confined) and the interests of the state (under its *parens patriae* powers),[102] the "beyond a reasonable doubt" standard is too high a burden for a juror to assess on the basis of a psychiatrist's evaluation of "whether the individual is mentally ill and . . . is in need of confined therapy."[103] Thus, the Court is essentially applying "therapeutic jurisprudence" to "permit[] the state, in the name of therapy, to deprive people of their liberty without the 'great safeguards' of the criminal law," and relegating mentally ill persons to a lesser personhood status in the legal system.[104]

D. Current Status of Mental Disability Law

i. The Impact and Legacy of Sell

Coinciding with the rise in gene editing technology, has been relative silence on the part of the Supreme Court to rule on issues that protect the bodily autonomy of the mentally ill. The Court's most recent case, *Sell v. United States*, was decided over 15 years ago, when CRISPR was still in the earliest stages of its development as a gene editing tool.[105] In *Sell*, the Court determined that the constitutionality of involuntary administration of antipsychotics to render an individual

[100] *Id.* at 428–29.
[101] *Id.* at 429–30.
[102] *Id.* at 425–26.
[103] *Addington*, 411 U.S. at 418, 429–30.
[104] Eric S. Janus, *Preventing Sexual Violence: Setting Principled Constitutional Boundaries on Sex Offender Commitments*, 72 IND. L.J. 157, 159–160 (1996).
[105] Sell v. United States, 539 U.S. 166 (2003).

competent to stand trial is based on a balancing test.[106] This test considers (1) whether the treatment is medically appropriate, (2) whether the treatment is substantially unlikely to have side-effects that may undermine the trial's fairness, and (3) whether, in the absence of less intrusive alternatives, the treatment is necessary significantly to further important governmental, trial-related interests.[107] Though the Court attempted to narrow its holding only to the criminal "competency to stand trial" context, the *Sell* test ultimately implies that a "dangerousness" determination is not required to coerce an uncooperative mental patient to undergo treatment with antipsychotic medication.[108] Thus, the coercion determination is largely rooted in the assessment and treatment decisions of medical personnel, rather than allowing the individual to maintain her dignity in determining the medical treatment she wishes to receive.

Though *Sell* is a case based on criminal law, the standard it sets has broader implications outside the criminal context.[109] The distinction between civil and criminal law in the development of mental health disability law has been significantly blurred, with varying standards being set in each context.[110] "Patent decisional inconsistency" can be seen in the way the Supreme Court's jurisprudence has developed with regard to the Constitutional rights of the mentally ill, and "different substantive and procedural standards have been imposed in [a number of] cases" involving the right to refuse medication.[111] Furthermore, "the Court is equally comfortable with pretextually characterizing what are clearly criminal penalties . . . as civil so as to save them from constitutional challenge."[112] Thus, the implications of *Sell* may extend beyond the trial

[106] *Id.* at 183.
[107] *Id.* at 180.
[108] *See generally, id.* at 184.
[109] Michael L. Perlin, Deborah A. Dorfman & Naomi Weinstein, *"On Desolation Row": The Blurring of the Boarders Between Civil and Criminal Mental Disability Law, and What It Means to All of Us*, 24 TEX. J. ON C.L. & C.R. 59 (2018).
[110] *Id.*
[111] *Id.* at 75.
[112] *Id.* at 86.

competency setting, rendering a patient's ability to refuse medication virtually obsolete where a medical necessity determination has been made.

IV. Regulatory Control Over CRISPR Technology

Given that constitutional bodily autonomy protections are likely insufficient to protect from inappropriate somatic uses of CRISPR in the psychiatric context, state and federal laws and regulations will be relied on to prevent inappropriate use. While state law has the potential to provide greater protection and can serve as a "gap filler" in the niche areas that issues such as CRISPR create, state laws also lack uniformity and have a minimal influence on the scientific community and biomedical industry as a whole.[113] Thus, federal regulation must carry the brunt of the responsibility in shaping and maintaining the legal landscape regarding gene therapy and CRISPR technology.

A. Coordinated Framework

At present, federal regulation fails to sufficiently protect mentally ill patients from improper applications of gene editing technologies such as CRISPR.[114] The Coordinated Framework for the Regulation of Biotechnology was first issued in 1986 by the White House Office of Science and Technology Policy to clarify the roles of major administrative agencies in regulating biotechnology products.[115] While the Coordinated Framework provides "fundamental federal guidance for regulating biotechnology products" and is intended to ensure oversight using already established federal agencies,[116] it is unclear whether these goals are being sufficiently

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[113] *Cf.* M. ARIEL CASCIO & ERIC RACINE, RESEARCH INVOLVING PARTICIPANTS WITH COGNITIVE DISABILITY AND DIFFERENCES: AUTONOMY, INCLUSION, AND INNOVATION, OXFORD UNIVERSITY PRESS (2019), at 255.
[114] *Cf. Advanced Gene Editing: CRISPR-Cas9*, Congressional Research Service Report No. R44824 (last updated Dec. 7, 2018), at 11.
[115] *Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology*, Executive Office of the President: Biotechnology Working Group (2017), at 2–3, https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/2017_coordinated_framework_update.pdf.
[116] *Advanced Gene Editing: CRISPR-Cas9*, *supra* note 114, at 9.

achieved.[117] "Despite recent efforts to update the Coordinated Framework, CRISPR-Cas9 technology and other gene-editing systems raise substantive questions about how (or whether) the products resulting from these technologies are to be regulated, and if so, under what statutory authorities."[118] This confusion has persisted since the 2017 update to the Coordinated Framework, which explicitly left questions regarding genome editing and CRISPR technology to be decided by future regulatory activities.[119]

As CRISPR is an emerging technology, the vast majority of its present use is in an experimental context, leaving it outside of the FDA's product safety regulatory authority. The FDA "can impose requirements on research as a condition for receiving either federal funding or FDA premarket review of a new medical product (such as a drug, device, or biologic);"[120] however, given that CRISPR is in a nascent stage, the FDA has yet to be faced with these challenges in any substantially meaningful way. If the "federal tie" of government funding or premarket review is absent, the FDA lacks jurisdiction over CRISPR research. As suggested earlier, this lack of jurisdiction is not merely hypothetical, as researchers have shown willingness to seek private sources of funding located outside the reach of federal regulation.

The FDA's role in regulating CRISPR may remain complicated even within the product safety context, as FDA regulation of a given product depends on whether it falls into one of the specific categories over which the FDA has jurisdiction.[121] The FDA has issued a short statement regarding the self-administration of gene therapy, stating that "FDA considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy" regulated under the category of

[117] *Advanced Gene Editing: CRISPR-Cas9*, *supra* note 114, at 11.
[118] *Id*.
[119] *Modernizing the Regulatory System for Biotechnology Products*, *supra* note 115, at 62.
[120] *Advanced Gene Editing: CRISPR-Cas9*, *supra* note 114, at 17.
[121] *Preparing for Future Products of Biotechnology: The Current Biotechnology Regulatory System*, THE NATIONAL ACADEMIES OF SCIENCE, ENGINEERING & MEDICINE (2017), at 77.

biologics.[122] While courts generally defer to category determinations made by the FDA, deference by the federal courts does not always occur.[123] Furthermore, the FDA's statement notes that "the *sale* of these products is against the law."[124] Thus, in the absence of explicit statutory authority, the door to legal arguments against FDA jurisdiction remains open to challenges based on both statutory definitions and Commerce Clause limitations.[125]

Despite these challenges, the FDA has shown willingness to regulate gene therapies that it *does* determine are within its jurisdiction, and it has recognized a need to keep FDA regulations current with technological advances.[126] For example, FDA guidance released in 1998 expanded the regulatory requirements for clinical trials involving gene therapies so that greater emphasis was placed on the disclosure of potential adverse events.[127] In a moment where researchers appear to be looking for regulatory guidance,[128] the FDA should follow its own precedent. As it has done with similarly controversial technologies, namely recombinant DNA technology, gene therapy and cloning,[129] the FDA must find a way to categorize the CRISPR so that it falls under FDA jurisdiction. While such an assertion may not be failproof, it will provide the guidance the industry is seeking and prevent the technology from falling into a regulatory tailspin.

B. 21st Century Cures Act

In December 2016, the federal regulatory restrictions on emerging technologies, including CRISPR, were relaxed as a result of the enactment of the 21 Century Cures Act (hereinafter, Cures

[122] *Information About Self-Administration of Gene Therapy*, U.S. FOOD & DRUG ADMINISTRATION (Nov. 21, 2017), https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/information-about-self-administration-gene-therapy.
[123] *Id.*
[124] *Information About Self-Administration of Gene Therapy*, *supra* note 122.
[125] *Id.*
[126] Evita V. Grant, *FDA Regulation of Clinical Applications of CRISPR-CAS Gene Editing Technology*, 71 FOOD & DRUG L.J. 608, 621 (2016).
[127] *Id.*
[128] Cui Zhang, *supra* note 35.
[129] Evita V. Grant, *supra* note 126, at 616–26.

Act). "[D]esigned to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently," the Cures Act seeks to reduce bureaucratic impediments to clinical applications of precision medicine technologies.[130] The Cures Act includes a number of measures that, although oriented towards efficiency, will likely have unintended safety consequences.

Sections 2011 through 2014 of the Cures Act are aimed at "Advancing Provision Medicine" and amends the Public Health Service Act, which allows for FDA regulation of biologics.[131] The Cures Act provisions are largely focused on data analysis and patient privacy in the context of biomedical research.[132] While the Cures Act arguably creates greater protections for patients' information by requiring that a certificate of confidentiality is issued to research participants,[133] the Act's overall emphasis on data sharing and interoperability generates concerns regarding data management and abuse.[134] Given that CRISPR applications would likely require sequencing of a patient's genome, research participating in Cures Act-related data sharing places patients at risk of serious harm should genetic data be used inappropriately.[135]

In addition to Sections 2011 through 2014, Section 3023 of the Cures Act addresses the protection of human research subjects. Section 3023 requires the Secretary of Health and Human Services to harmonize human research regulations across federal agencies "[i]n order to simplify

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[130] U.S. Food & Drug Administration, *21st Century Cures Act* (last visited Feb. 14, 2020), https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act. *See also* Michael Gabay, *21st Century Cures Act*, 52 HOSP. PHARM. 264 (2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5424829/pdf/i0018-5787-52-4-264.pdf; Betty Lengyel-Gomez, *21st Century Cures Act – A Summary*, Healthcare Information and Management Systems Society, Inc. (last updated Nov. 20, 2018) https://www.himss.org/resources/21st-century-cures-act-summary.
[131] 114 P.L. 255 §§ 2011-14 (2016).
[132] *Id.*
[133] Leslie E. Wolf, *et al*., *The Web of Legal Protections for Participants in Genomic Research*, 29 Health Matrix 1, 20–21 (2019).
[134] Anthony W. Orlando & Arnold J. Rosoff, *The New Privacy Crisis: What's Health Got to Do with It?*, 123 Am. J. of Med. 127–28 (2019), https://www.amjmed.com/action/showPdf?pii=S0002-9343%2818%2931025-8.
[135] *Id.*

and facilitate compliance by researchers with applicable regulations."[136] The Cures Act further requires that the harmonization "reduce regulatory duplication and unnecessary delays."[137] This requirement resulted in the 2019 update to the Common Rule, discussed below.

C. Common Rule

The largely experimental nature of present CRISPR uses allows the Common Rule to play a substantial role in regulating the technology's use. The Common Rule (the Federal Policy for the Protection of Human Subjects) was created in response to the *Belmont Report*, published in 1979,[138] which outlined the main ethical principles to be safeguarded in conducting biomedical and behavioral research with human participants.[139] These main principles include (1) respect for persons, (2) beneficence, and (3) justice, and they correlate to three practical measures that researchers can take: informed consent, assessment of risk and potential benefits, and selection of participants.[140] The *Belmont Report* led to a revision of FDA regulations that "placed primary emphasis on obtaining and documenting voluntary and informed consent, but provided little guidance on assessment of risk and potential benefit or the selection of research participants."[141] In addition to the *Belmont Report* and the associated FDA revisions, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research called for standardization of research regulations across government agencies.[142] Following this call, the

[136] 114 P.L. 255 § 3023(a) (2016).
[137] 114 P.L. 225 § 3023(b) (2016).
[138] Committee on the Use of Third Party Toxicity Research with Human Research Participants, *Intentional Human Dosing Studies for EPA Regulatory Purposes: Scientific and Ethical Issues*, NATIONAL RESEARCH COUNCIL 50 (2004) (citing *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, National Commission (1979)), https://www.ncbi.nlm.nih.gov/books/NBK215886/pdf/Bookshelf_NBK215886.pdf.
[139] *Belmont Report Anniversary and Oral History*, Kennedy Institute of Ethics: Bioethics Research Library (Nov. 13, 2018), https://bioethics.georgetown.edu/library-materials/archives/belmont-report-anniversary-and-oral-history/.
[140] Committee on the Use of Third Party Toxicity Research with Human Research Participants, *supra* note 138, at 50.
[141] *Id.*
[142] *Id.*

Common Rule was created to codify the goals set forth by the *Belmont Report* and ensure their application throughout the biomedical and behavioral research fields.[143]

The initial version of the Common Rule was created in 1981 and set out compliance guidelines in accordance with the ethical principles of the *Belmont Report*;[144] however, the Rule suffers from limitations of its own. It is limited in its reach—the Common Rule applies only to those studies that "(1) meet certain jurisdictional requirements[], (2) involve 'research,' and (3) involve the use of 'human subjects.'"[145] As with FDA restrictions, the Common Rule jurisdictional requirement involves a federal tie (e.g., federal funding) for the Rule to apply:[146] "[i]f federal funds are not involved or if regulatory approval is not required, research activities involving humans might not be subject to any form of oversight."[147] While it may be difficult to imagine a large-scale study where a federal tie is not present, regulators should not discount private actors. Since CRISPR technology is relatively affordable, it will be accessible to individuals without the jurisdictional "hook".[148] For instance, an activist "biohacker" has already begun DIY CRISPR experimentation on his own body while selling "kits" to online purchasers.[149]

The most recent update to the Common Rule was published in 2019[150] and focuses on requirements for informed consent. Since the Rule is intended to ensure "(1) respect for the autonomous decision-making of those capable of providing it and (2) []protection for persons with

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[143] *Id.* at 51.
[144] *History of Research Ethics*, University of Missouri-Kansas City, https://ors.umkc.edu/research-compliance/institutional-review-board-(irb)/history-of-research-ethics.
[145] CARL H. COLEMAN, JERRY A. MENIKOFF, JESSE A. GOLDNER & NANCY NEVELOFF DUBLER, THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS (2005) § 3.02.
[146] Committee on the Use of Third Party Toxicity Research with Human Research Participants, *supra* note 138, at 46.
[147] *Id.* at 52.
[148] *Cf.* Patrick Griffin, *Edit Thyself: Biohacking in the Age of CRISPR*, Harvard University Graduate School of Arts and Sciences (Feb. 14, 2018), http://sitn.hms.harvard.edu/flash/2018/edit-thyself-biohacking-age-crispr/.
[149] Sigal Samuel, *A Celebrity Biohacker Who Sells DIY Gene-Editing Kits is Under Investigation*, Vox (May 19, 2019, 8:00 AM), https://www.vox.com/future-perfect/2019/5/19/18629771/biohacking-josiah-zayner-genetic-engineering-crispr.
[150] 45 C.F.R. §§ 46, *et seq.* (2019).

diminished autonomy . . . the Common Rule seeks to ensure voluntary participation through informed consent."[151] The 2019 revisions sought to redesign consent standards in an attempt to streamline the informed consent process.[152] As a result, the updated Common Rule requires that informed consent procedures involve the application of a "'reasonable person' standard for research disclosure, require[s] informed consent forms to begin with a 'concise and focused presentation' of 'key information,' and authorize[s] individuals to provide 'broad consent' to future research with identifiable data and biospecimens."[153] Whether these provisions will reduce "administrative burden" while maintaining protections for human research subjects is debatable, and the changes may open participants up to even greater vulnerability.[154]

In addition to the changes to informed consent protocols, the Revised Common Rule contains definitional adjustments, including in its references to persons with mental impairments. The term "mentally disabled persons" has been removed and replaced with "individuals with impaired decision-making capacity."[155] Arguably, this change means that those diagnosed with psychiatric disorders are no longer explicitly included as a "vulnerable population" under the Rule.[156] It is unclear what impact this will have on participants with mental illness involved in psychiatric research.[157] Notably, the Revised Common Rule fails to address *Belmont Report* goals other than informed consent. Further guidance on selection of participants would have been

[151] Foulkes, *et al.*, *supra* note 56, at 1391.
[152] Carl H. Coleman, *Symposium Introduction*, 47 J.L. MED. & ETHICS 189 (2019).
[153] *Id.*
[154] *Id.* (citing Rebecca Dresser, *The Reasonable Person Standard for Research Disclosure: A Reasonable Addition to the Common Rule*, 47 J.L. MED. & ETHICS 194 (2019); Nancy M. P. King, *Key Information in the New Common Rule: Can It Save Research Consent?*, 47 J.L. MED. & ETHICS 203 (2019); and Holly Fernandez Lynch, Leslie E. Wolf & Mark Barnes, *Implementing Regulatory Broad Consent Under the Revised Common Rule: Clarifying Key Points the Need for Evidence*, 47 J.L. MED. & ETHICS 213 (2019)).
[155] Gary L. Chadwick, *Final Rule Material: New and Revised Definitions*, CITI Program: A Division of BRANY (2018), https://about.citiprogram.org/wp-content/uploads/2018/07/Final-Rule-Material-New-and-Revised-Definitions.pdf.
[156] Foulkes, *et al.*, *supra* note 56, at 1392.
[157] *Id.*

particularly pertinent in the psychiatric research context, as these patients are particularly vulnerable to coercion in the consent process.[158]

D. Other Sources of Guidance and Potential Solutions

While a thorough examination of the international debate on CRISPR research is outside the scope of this article, the ideas arising out of that debate may provide important insights to consider in the development of domestic CRISPR policy. Several international organizations have begun working on CRISPR policy. For example, the World Health Organization has established an advisory committee to examine genome editing issues, but the committee's work is still developing.[159] In addition to the WHO Committee, the International Commission on Clinical Use of Heritable Human Genome Editing is also developing guidance,[160] and the UK Fertilization and Embryology Authority, though dedicated to assisted reproductive technology, may be an important resource regarding how to approach bioethics questions regarding genetics.[161] Notably, however, as in the United States, the primary concern of the international discussion has been germ-line editing.[162] Thus, the international community has largely ignored the use of genetic editing in somatic cell lines, which would likely be a major component of psychiatric CRISPR applications.[163]

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[158] *Id.*

[159] *Cf. WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing*, WORLD HEALTH ORGANIZATION, https://www.who.int/ethics/topics/human-genome-editing/committee-members/en/; Emmanuelle Tuerlings, *Background Paper Governance 1 Human Genome Editing*, WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (Mar. 2019), https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Governance-1-paper-March-19.pdf.

[160] *International Commission on Clinical Use of Heritable Human Genome Editing*, National Academies of Sciences, Engineering & Medicine, http://nationalacademies.org/gene-editing/international-commission/index.htm.

[161] *How We Regulate*, Human Fertilisation & Embryology Authority, https://www.hfea.gov.uk/about-us/how-we-regulate/.

[162] Brokowski, *et al.*, *supra* note 58.

[163] *Id.*

There is presently no *binding* international consensus on the use of CRISPR technology;[164, 165] however, the creation of laws and policies at the national level can act as an important influence in guiding corporate research and development decisions:

> There are government guidelines in other areas as well. These provisions technically are not enforceable, and yet they are very strongly persuasive because complying with them creates what essentially is a safe haven for companies. They know that if they stay within the guidelines, they are not going to run afoul of some actual regulation or law. These guidelines also create strong social norms . . . from which nations feel free to deviate only when they can provide justification that it is necessary to achieve some public benefit.[166]

Government-created, binding guidelines are therefore essential.[167] While ethical discussions within the scientific community are important to foster debate and establish some social consensus, these discussions, as evidenced by Professor He's "CRISPR babies", do little to ensure actual adherence.[168] Clear and straightforward regulation from domestic governments might create sufficient industry pressure to keep rogue experiments like He's from reoccurring.

In the United States, the requisite clarity would ideally come from Congress in the form of a statute outlining strict limitations on both somatic and germline applications of CRISPR technology; however, present legislative paralysis suggests that a federal statute is unlikely at any point in the near future.[169] In the meantime, the FDA should seek to provide greater informal guidance to industry, outlining how CRISPR fits into the current regulatory scheme and prohibiting its use on individuals under sixteen and other vulnerable populations. In addition, the

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[164] Annalisa Choy, *Rewriting the Human Genome: CRISPR and an International Gene-Editing Standard*, CORNELL INT'L L.J. (Nov. 3, 2017), http://cornellilj.org/rewriting-the-human-genome-crispr-and-an-international-gene-editing-standard/.
[165] R. Alta Charo, *The Legal and Regulatory Context for Human Gene Editing*, 32 ISSUES IN SCI. & TECH. (2016), https://issues.org/the-legal-and-regulatory-context-for-human-gene-editing/.
[166] *Id.*
[167] *Cf. id.*
[168] *Cf. id.*
[169] Ella Nilsen, *House Democrats Have Passed Nearly 400 Bills. Trump and Republicans Are Ignoring Them.*, VOX (Nov. 29, 2019, 7:00 AM), https://www.vox.com/2019/11/29/20977735/how-many-bills-passed-house-democrats-trump.

FDA should require that clinical trials involving CRISPR employ a "Common Rule *plus*" approach to informed consent, where researchers must show that they have outlined the potential risks associated with CRISPR treatment and provided the patient with adequate time to consider his or her options. Furthermore, as CRISPR is first and foremost a *methodology*, states should seek to pass legislation or professional board guidance limiting somatic use of CRISPR to patients over the age of sixteen, where strict informed consent procedures are followed, the treatment is medically necessary, and alternative treatment options prove substantially deficient in managing the patient's illness. Such state laws will allow for regulation of the *practice* of medical applications of CRISPR, not just the sale of a product (which may not even be necessary to perform CRISPR edits), and prevent a legal vacuum should federal law prove insufficient.

V. Conclusion

Many of the more concerning applications of CRISPR technology are still far off in reality; however, leaders should take this opportunity to get ahead of the science in a realm where policy is often far outpaced by technology. As the psychiatric context makes clear, somatic applications may be just as problematic as germ-line uses of CRISPR, and we must carefully consider the consequences of engaging in biological manipulations that cut to the core of an individual's personhood. It is doubtful Constitutional protections will be sufficient once gene editing becomes widespread, especially as applied to mentally ill persons who are civilly committed or otherwise institutionalized. As used in the experimental context, clear regulatory guidance from the FDA, NIH, and similar agencies would not only serve American researchers, but could help to shape industry standards and encourage the development of international policies that carry more weight. CRISPR must be taken seriously, even in its somatic applications, and the government should seek

to develop ironclad protections that enable those patients desperate for novel treatments to receive care without being unnecessarily placed at risk.