DIY CRISPR*

CHRISTI J. GUERRINI, G. EVAN SPENCER & PATRICIA J. ZETTLER**

Although scientists have been manipulating genomes since the 1970s, the recent discovery of Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR") has expanded the possibilities not only for what gene editing might accomplish but also who might accomplish it. Because CRISPR is relatively easy, efficient, and inexpensive, it is accessible to individuals—known as "citizen scientists"—who work in nontraditional laboratory settings and may not have formal scientific training. Prompted by concerns about human applications of CRISPR, the United States is cohosting a series of international summits on human gene editing, while organizations around the world race to issue their own reports and recommendations. For the most part, however, these efforts have focused on the use of CRISPR by professional scientists working in institutional settings who are already subject to layers of formal and informal oversight. They have largely overlooked the do-it-yourself ("DIY") use of CRISPR by citizen scientists—even as instances of self-experimentation with CRISPR are being reported and raising unique concerns.

Drawing on qualitative interviews with almost forty citizen scientists and their supporters, critics, and observers, this Article

** Christi J. Guerrini is an Assistant Professor in the Center for Medical Ethics and Health Policy at Baylor College of Medicine. Evan Spencer is a 2018 graduate of the University of Houston Law Center. At the time this Article was written, Patricia J. Zettler was an Associate Professor at Georgia State University College of Law. She is currently an Assistant Professor at The Ohio State University Moritz College of Law. For their helpful comments and suggestions on earlier drafts of this Article, we thank Paul Enríquez, Erika Lietzan, Alex Pearlman, Lisa Rasmussen, Jacob Sherkow, Anna Wexler, and participants of the *North Carolina Law Review* 2018 Symposium and the 2019 Jaharis Symposium on Health Law and Intellectual Property at DePaul College of Law. We also thank Sameer Sidiq for his research assistance and Isabel Canfield for her assistance preparing this manuscript. We are indebted to the thirty-eight citizen science practitioners, supporters, critics, and observers who informed our understanding of the citizen bioscience landscape during the interview phase of a larger study, which was approved by the Baylor College of Medicine Institutional Review Board (H40925). Individuals cited by name in this Article participated in interviews on a nonconfidential basis. This research was funded in part by an award from the National Human Genome Research Institute (K01-HG009355) (Guerrini, PI).

provides a critical analysis of the practice and governance of DIY CRISPR in the United States. It concludes that existing laws and regulations potentially reach a number of DIY CRISPR activities, although their application to citizen-science contexts is thus far untested. Meanwhile, DIY communities have developed mechanisms of self-regulation that appear to be working reasonably well thus far in discouraging potentially dangerous human applications of CRISPR by citizen scientists. However, we are concerned about the possibility that, as lay understanding of and proficiency with the technology increases, there will be an uptick in risky (if not illegal) human experimentation in the future. Therefore, this Article concludes with suggestions for shoring up the oversight readiness and capacities of regulatory bodies and DIY communities.

INTRODUCTION

On October 3, 2017, a biohacker named Josiah Zayner made headlines when he injected himself with a needle that purportedly contained a gene-editing tool called CRISPR—short for Clustered Regularly Interspaced Short Palindromic Repeats—in front of a live audience.[1] The self-injection occurred during a conference workshop that he was leading titled "A Step-By-Step Guide To Genetically Modifying Yourself with CRISPR."[2] Dr. Zayner, who earned a Ph.D. in molecular biophysics from the University of Chicago, spoke at the front of a packed room near a table that displayed his how-to pamphlets for genetically modifying humans and a syringe filled with CRISPR molecular units, which were designed to promote muscle growth by deactivating a specific gene.[3] Halfway through his talk, which was streamed online, an audience member asked Dr. Zayner what was holding him back from following his own instructions.[4] He responded by picking up the syringe and injecting his forearm. Dr. Zayner told the audience, "I'll let you know how it works out."[5]

1. *See* Josiah Zayner, *DIY Human CRISPR Myostatin Knock-Out*, YOUTUBE (Oct. 6, 2017), https://www.youtube.com/watch?v=o6A9bbDI6fo [https://perma.cc/NT56-K25Z] [hereinafter Zayner, *DIY Human CRISPR*] (showing the self-injection starting at 20:23). For a discussion of the science of CRISPR-Cas9, see *infra* Part I.

2. *Workshop: A Step-by-Step Guide to Genetically Modifying Yourself with CRISPR*, SYNBIOBETA, http://sf2017.synbiobeta.com/sessions/step-step-guide-genetically-modifying-crispr/ [https://perma.cc/GA7Y-LFLZ].

3. *See* Kristen V. Brown, *Genetically Engineering Yourself Sounds Like a Horrible Idea—But This Guy Is Doing It Anyway*, GIZMODO (Nov. 29, 2017, 10:00 AM), https://gizmodo.com/genetically-engineering-yourself-sounds-like-a-horrible-1820189351 [https://perma.cc/RYN3-T7UK] [hereinafter Brown, *Genetically Engineering Yourself*] (describing the workshop during which Dr. Zayner injected himself). More specifically, the CRISPR molecular units were designed to deactivate the gene for the protein myostatin. Animals without a functioning copy of the gene have been observed to develop extra large muscles. *See, e.g.*, Qingyan Lv et al., *Efficient Generation of* Myostatin *Gene Mutated Rabbit by CRISPR/Cas9*, SCI. REP., Apr. 26, 2016, at 1, 1. Dr. Zayner provided additional background on the experiment on his personal website. *See* Josiah Zayner, *The First Attempt at Human CRISPR Gene Editing*, SCI. ART BEAUTY (Oct. 13, 2017), http://www.josiahzayner.com/2017/10/the-first-human-to-attempt-crispr-gene.html [https://perma.cc/4YKL-G6HA].

4. *See* Zayner, *DIY Human CRISPR*, *supra* note 1.

5. *See id.* Dr. Zayner has since expressed regret for at least certain aspects of this demonstration—in particular, that he "didn't make it seem like [he] took it seriously" because observers "didn't see the months of research and 1.5 years of experimentation

Only a few years earlier, Dr. Zayner was working at NASA to engineer bacteria for Mars.[6] By 2015, however, he had grown frustrated with NASA,[7] and so he left to launch an online business called The ODIN, which sells inexpensive genetic-engineering kits and custom genetic material.[8] Dr. Zayner has since emerged as a leading figure in the burgeoning DIY biology movement. His message of self-empowerment and "screw the system" has struck a chord with individuals lacking formal training but who believe in their abilities to learn and do science on their own. His aim of democratizing science also has garnered some respect within the scientific establishment.[9] Dr. Zayner sealed his position as "the mad pirate-king of biotech" by posting videos on YouTube of a number of experiments he conducted on himself that include infusing his skin with fluorescent jellyfish proteins to make it glow.[10]

Although various techniques to manipulate genomes have been in use since the 1970s,[11] the recent development of CRISPR systems to accomplish gene editing has suddenly expanded the possibilities not only for *what* gene editing might accomplish but also *who* might accomplish it.[12] Unlike older editing technologies that require

beforehand." Josiah Zayner, *True Story: I Injected Myself with a CRISPR Genetic Enhancement*, ANTISENSE (Nov. 13, 2018), http://theantisense.com/2018/11/13/true-story-i-injected-myself-with-a-crispr-genetic-enhancement [https://perma.cc/Q3ET-S64B] [hereinafter Zayner, *True Story*]; *see also* Sarah Zhang, *A Biohacker Regrets Publicly Injecting Himself with CRISPR*, ATLANTIC (Feb. 20, 2018), https://www.theatlantic.com/science/archive/2018/02/biohacking-stunts-crispr/553511/ [https://perma.cc/Y36E-BJRY] (reporting Dr. Zayner's expressions of regret about injecting himself with CRISPR).

6. *See About Us*, ODIN, http://www.the-odin.com/about-us/ [https://perma.cc/W3Y6-WP5T].

7. Zayner, *True Story*, *supra* note 5.

8. ODIN, http://www.the-odin.com/ [https://perma.cc/37BN-P4ZG].

9. *See* Brown, *Genetically Engineering Yourself*, *supra* note 3.

10. *See id.* A video of one of these experiments is posted on Dr. Zayner's YouTube channel. Josiah Zayner, *How to Genetically Engineer a Human in Your Garage*, YOUTUBE (Feb. 15, 2017), https://www.youtube.com/watch?v=imTXcEh79lw [https://perma.cc/6U2L-NFQP].

11. *See* Paul Enríquez, *Genome Editing and the Jurisprudence of Scientific Empiricism*, 19 VAND. J. ENT. & TECH. L. 603, 621–33 (2017) (recounting this history and delineating the differences between the technologies).

12. The use of a CRISPR system consisting of Cas9 and an associated guide RNA to target a specific DNA sequence was described for the first time in 2012. *See generally* Martin Jinek et al., *A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 SCIENCE 816 (2012) (describing the molecular function of Cas9 in gene editing). By 2015, understanding and application of CRISPR had matured to the point that its "true power" was revealed. John Travis, *Making the Cut: CRISPR Genome-Editing Technology Shows Its Power*, 350 SCIENCE 1456, 1456 (awarding CRISPR the journal's 2015 Breakthrough of the Year Award). For a description of the twenty-year

sophisticated equipment and are notoriously complicated and error prone, CRISPR is relatively easy, efficient, and inexpensive to use.[13] It can be practiced in school, community, and home laboratories by individuals without doctoral-level training, major research budgets, or state-of-the-art equipment.[14] Even teenagers are redesigning genomes with CRISPR, following protocols described in textbooks, published in journals, or in some cases, developed themselves.[15]

Until recently, the conventional wisdom was that most DIY CRISPR activities did not involve complex organisms.[16] Dr. Zayner's live-streamed demonstration was therefore a wake-up call to the potential for CRISPR to be used in humans outside of traditional scientific institutions, starting with one's own genome. Although some experts have emphasized that self-editing will require more sophisticated materials than those sold by Dr. Zayner,[17] others close

backstory to the discovery of CRISPR as a tool for genetic engineering in mammalian cells, see generally Eric S. Lander, *The Heroes of CRISPR*, 164 CELL 18 (2016).

13. *See* David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCIENCE 36, 36 (2015) (explaining that previous technologies could not make "specific and efficient modifications to a genome," severely limiting the ability to use them); Barry R. Furrow, *The CRISPR-Cas9 Tool of Gene Editing: Cheaper, Faster, Riskier?*, 26 ANNALS HEALTH L. 33, 33 (2017) (explaining that CRISPR is "easily accessible, the equipment is relatively cheap, and not much training is required"); Annie Sneed, *Mail-Order CRISPR Kits Allow Absolutely Anyone to Hack DNA*, SCI. AM. (Nov. 2, 2017), https://www.scientificamerican.com/article/mail-order-crispr-kits-allow-absolutely-anyone-to-hack-dna/ [https://perma.cc/D7AD-75YX] (comparing CRISPR to older gene-editing technologies). *See generally* Jennifer A. Doudna & Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 SCIENCE 1077 (2014) (describing the difficulties of protein design, synthesis and validation associated with older technologies, including zinc-finger nucleases ("ZFNs") and transcription activator-like effector nucleases ("TALENs"), which created barriers to their widespread adoption for routine use).

14. *See* discussion *infra* Part II.

15. *See, e.g.*, ELEONORE PAUWELS & SARAH W. DENTON, WILSON CTR., THE RISE OF THE BIO-CITIZEN 40–41 (Todd Kuiken ed., 2018) (describing high school student Vardhaan Ambat's experiments in a community laboratory using CRISPR to kill cancer cells); *cf.* Emily Baumgaertner, *As D.I.Y. Gene Editing Gains Popularity, 'Someone Is Going to Get Hurt'*, N.Y. TIMES (May 14, 2018), https://www.nytimes.com/2018/05/14/science/biohackers-gene-editing-virus.html [http://perma.cc/J8WU-Q9D6 (dark archive)] (describing teenager Keoni Gandall's genetic experimentation in a home laboratory).

16. *See, e.g.*, Margaret Foster Riley, *CRISPR Creations and Human Rights*, 11 LAW & ETHICS HUM. RTS. 225, 230 (2017) (observing that "sophisticated use of CRISPR in complex organisms is probably out of the reach of an average biohacker right now").

17. *See* Stephanie M. Lee, *This Guy Says He's the First Person to Attempt Editing His DNA with CRISPR*, BUZZFEED NEWS (Oct. 14, 2017, 12:07 PM), https://www.buzzfeed.com/stephaniemlee/this-biohacker-wants-to-edit-his-own-dna?utm_term=.cioZL7N8G6#.xpjg1pvKeJ [https://perma.cc/VV46-8ZYQ] (quoting a CRISPR expert who remarked that "[t]o do real, effective genome-editing, it's going to require a more sophisticated laboratory and more sophisticated materials" than those provided by Dr. Zayner).

to DIY communities are convinced that it is only a matter of time before citizen scientists attain the necessary skills and resources to perform successful human gene editing.[18] In the meantime, and regardless of whether DIY biologists ever achieve their gene-editing objectives, the physical risks associated with making and introducing unregulated gene technologies into one's body, which include infection, immunological reaction, and unintended cellular changes, are frequently noted concerns.[19] Concerns have also been raised about potential copycats and the lack of oversight to ensure that self-experimenters who follow Dr. Zayner's example understand those risks.[20] Indeed, Dr. Zayner has expressed his own worries about self-

18. *See The Ethics of Experimentation with Alex Pearlman*, FUTURE GRIND (Sept. 30, 2017), https://futuregrind.org/podcast-episodes/2018/5/17/ep-7-the-ethics-of-experimentation-with-alex-pearlman [https://perma.cc/RFD7-2BXB]; *see also* Albert C. Lin, *Herding Cats: Governing Distributed Innovation*, 96 N.C. L. REV. 945, 951 (2018) (observing that the capabilities of DIY biologists are improving and their gene-editing activities "cannot be ignored in light of the technology's increasing power and accessibility"); Will Tauxe, *Q&A: Tim Lu, Cocktail Maker*, 528 NATURE S14, S14 (2015) (quoting synthetic biology researcher Tim Lu, who opined that, because CRISPR-Cas systems are so easy to use, "[t]he democratization of biological engineering is inevitable").

19. *See generally* Michael Kosicki, Kärt Tomberg & Allan Bradley, *Repair of Double-Strand Breaks Induced by CRISPR–Cas9 Leads to Large Deletions and Complex Rearrangements*, 36 NATURE BIOTECHNOLOGY 765 (2018) (describing harmful on-target effects of CRISPR in mouse embryonic stem cells); Xiao-Hui Zhang et al., *Off-Target Effects in CRISPR/Cas9-Mediated Genome Engineering*, 4 MOLECULAR THERAPY—NUCLEIC ACIDS, no. e264, Nov. 17, 2015, at 1 (reviewing the basic mechanisms underlying off-target cutting in the CRISPR/Cas9 system); Marcy Darnovsky, *Hacking Your Own Genes: A Recipe for Disaster*, LEAPSMAG (Jan. 17, 2018), https://leapsmag.com/hacking-genes-recipe-disaster/ [https://perma.cc/M9NN-B2B7] (quoting a microbiologist who explained that "[s]crewing up" the purification of what is injected "can kill you from endotoxin"); Eleonore Pauwels, *The Rise of Citizen Bioscience*, SCI. AM. (Jan. 5, 2018), https://blogs.scientificamerican.com/observations/the-rise-of-citizen-bioscience [https://perma.cc/RKT3-WJW5] (noting the potential for infection and immunological reaction from use of unregulated gene therapies).

20. *See* Darnovsky, *supra* note 19 (worrying that Dr. Zayner's demonstration "is likely to encourage emulation" given his "bad-boy celebrity status"). Concerns about copycats have been substantiated by Dr. Zayner himself, who claims to have received "literally hundreds" of emails in the days after his CRISPR self-injection from individuals wanting to do the same. *See* Brown, *Genetically Engineering Yourself*, *supra* note 3. Conversely, one scholar has speculated that public demonstrations like Dr. Zayner's could invite too much oversight and result in severely restricting or even shutting down the broader efforts of citizen scientists seeking to make positive contributions to biomedical research. Pauwels, *supra* note 19; *see also* Steph Yin, *Is DIY Kitchen CRISPR a Class Issue?*, POPULAR SCI. (May 3, 2016), https://www.popsci.com/is-bringing-crispr-to-kitchens-class-issue [http://perma.cc/457T-DAQY] (describing the concerns of a community laboratory founder that Dr. Zayner's generally "cavalier" attitude toward safety practices could "bring about increased regulation which would limit access" to biotechnology).

experimentation with CRISPR, even while he works to facilitate a future of recreational genetic engineering.[21]

Questions about the safety and ethics of human gene editing are not new.[22] In recent years, however, they became a priority when research groups around the world began announcing their use of CRISPR to edit the reproductive cells of nonimplanted human embryos.[23] Responding to an international call to action by prominent genomic scientists,[24] the U.S. National Academies of Sciences, Engineering, and Medicine ("National Academies") joined policymakers in the United Kingdom and China to convene a series of international summits to investigate the social and ethical implications of CRISPR,[25] while organizations around the world raced to issue their own reports and recommendations.[26] In the past

21. *See* Brown, *Genetically Engineering Yourself*, *supra* note 3; Zayner, *True Story*, *supra* note 5 ("I also regret that other people then decided to try and inject themselves with 'gene therapies' that didn't have much scientific basis. I regret that I made people think that doing a gene therapy injection was a stunt that could get them famous, and that I didn't emphasize enough that, to me, this was a serious endeavor.").

22. *See, e.g.*, Joseph Fletcher, *Ethical Aspects of Genetic Control: Designed Genetic Changes in Man*, 285 NEW ENG. J. MED. 776, 776–79 (1971) (exploring ethical justifications for human genetic interventions); Michael J. Reiss, *What Sort of People Do We Want? The Ethics of Changing People Through Genetic Engineering*, 13 NOTRE DAME J.L. ETHICS & PUB. POL'Y 63, 76–90 (1999) (examining the ethical significance of engineering human somatic and germline cells); John A. Robertson, *Procreative Liberty in the Era of Genomics*, 29 AM. J.L. & MED. 439, 473–80 (2003) (discussing ethical issues associated with gene editing of human embryos to achieve various objectives).

23. *See, e.g.*, Xiangjin Kang et al., *Introducing Precise Genetic Modifications into Human 3PN Embryos by CRISPR/Cas-Mediated Genome Editing*, 33 J. ASSISTED REPROD. & GENETICS 581, 583–84 (2016) (reporting the introduction of an HIV-resistance allele into nonviable human embryos); Puping Liang et al., *CRISPR/Cas9-Mediated Gene Editing in Human Tripronuclear Zygotes*, 6 PROTEIN & CELL 363, 366 (2015) (reporting experiments that used CRISPR to cleave the human gene *HBB* in nonviable human embryos). Researchers have also used CRISPR to modify genomes of viable human embryos that were not implanted for birth. *See, e.g.*, Yanting Zeng et al., *Correction of the Marfan Syndrome Pathogenic FBN1 Mutation by Base Editing in Human Cells and Heterozygous Embryos*, 26 MOLECULAR THERAPY 2631, 2635–36 (2018).

24. *See* Baltimore et al., *supra* note 13, at 37–38 (concluding that "the potential safety and efficacy issues arising from the use of CRISPR technology must be thoroughly investigated and understood before any attempts at human engineering are sanctioned, if ever, for clinical testing" and recommending that a "globally representative group" of scientists, policymakers, members of the public, and experts in genetics, law, and bioethics be convened to consider these issues); Edward Lanphier et al., *Don't Edit the Human Germ Line*, 519 NATURE 410, 411 (2015) (urging the international scientific community "to assess whether, and under what circumstances—if any—future research involving genetic modification of human germ cells should take place").

25. *Human Genome Editing Initiative*, NAT'L ACADS. SCI. ENG'G & MED., http://nationalacademies.org/gene-editing/index.htm [https://perma.cc/X9JH-CRXV].

26. *See, e.g.*, NAT'L ACADS. OF SCIS., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 1–2 (2017) [hereinafter NASEM, HUMAN

few months, this work became still more urgent after a Chinese scientist reported editing the genomes of implanted twin human embryos that resulted in the births of the first so-called CRISPR babies.[27] Although it remains unclear whether he succeeded in making the intended edits, the news has sparked heated debate about the adequacy of the existing oversight of CRISPR applications in humans.[28]

Notably, these efforts have focused on the use of CRISPR by credentialed scientists working in institutional settings who are already subject to layers of oversight.[29] Yet the use of CRISPR by citizen scientists working in nontraditional settings introduces new dimensions to ethical and regulatory questions about human gene editing that also merit attention.[30]

This Article makes two primary contributions to the analysis of these questions. First, drawing on qualitative interviews with almost forty citizen scientists and their supporters, critics, and observers, it describes current and possible future applications of CRISPR by citizen scientists.[31] Second, it provides a detailed account of the

GENOME EDITING]; NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING AND HUMAN REPRODUCTION: SOCIAL AND ETHICAL ISSUES, at vii (2018) [hereinafter NUFFIELD COUNCIL 2018].

27. *See, e.g.*, David Cyranoski & Heidi Ledford, *Genome-Edited Baby Claim Provokes International Outcry*, 563 NATURE 607, 607 (2018).

28. *See, e.g.*, R. Alta Charo, *Rogues and Regulation of Germline Editing*, 380 NEW ENG. J. MED. 976, 977–79 (2019). Since the announcement, the World Health Organization stated that it is establishing an expert panel to assess the "scientific, ethical, social and legal challenges associated with human gene editing (both somatic and germ cell)." *Gene Editing*, WORLD HEALTH ORG. (Dec. 14, 2018), https://www.who.int/ethics/topics/gene-editing/en/ [https://perma.cc/2FJV-3Q6A]. Scientific and medical groups around the world also are in discussions to develop guidelines on the alteration of human germlines. *See* Sharon Begley, *After 'CRISPR Babies,' International Medical Leaders Aim to Tighten Genome Editing Guidelines*, STAT (Jan. 24, 2019), https://www.statnews.com/2019/01/24/crispr-babies-show-need-for-more-specific-rules/ [https://perma.cc/YWH4-SWL2].

29. For example, the National Academies consensus study report includes one mention of gene editing by biohackers. NASEM, HUMAN GENOME EDITING, *supra* note 26, at 25. Similarly, gene editing by "DIY biology enthusiasts" is mentioned once in the Nuffield Council's 2018 report, NUFFIELD COUNCIL 2018, *supra* note 26, at 132, although it receives more attention in the organization's 2016 report, NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING: AN ETHICAL REVIEW 13, 39–40, 92, 99–100, 103 n.483, 107 (2016) [hereinafter NUFFIELD COUNCIL 2016].

30. *Cf.* Henry T. Greely, *Take Care!*, STAT (Mar. 14, 2016), https://www.statnews.com/2016/03/14/crispr-do-it-yourself/#Greely [https://perma.cc/V8FQ-8YNA] ("Universities, research institutes, and big corporations are relatively easy to find and regulate. Finding and regulating do-it-yourself users is much harder and, under our current system, impossible. We urgently need to find a balanced regulatory approach that allows responsible do-it-yourself use while protecting health and the environment.").

31. As noted in the authors' acknowledgment, some interviewees participated on a nonconfidential basis.

oversight of DIY human gene editing by existing external and internal mechanisms. Here, *external oversight* refers to legal and regulatory mechanisms developed and implemented by government authorities, whereas *internal oversight* refers to policies, practices, and norms adopted by DIY biologists. This Article concludes that existing laws and regulations potentially reach a number of DIY human gene-editing activities, although their application to citizen-science contexts is thus far untested. Meanwhile, DIY communities have developed mechanisms of self-regulation that appear to be working reasonably well thus far in discouraging potentially dangerous human applications of CRISPR by citizen scientists. However, this Article presents concerns about the possibility that, as lay understanding of and proficiency with the technology increases, there will be an uptick in risky (if not illegal) human experimentation in the future. Therefore, this Article offers suggestions for shoring up the oversight readiness and capacities of regulatory bodies and DIY communities.

The analysis is subject to several limitations. First, it is focused on DIY applications of CRISPR. It does not address other possible citizen-science activities, such as the manufacture of synthetic DNA or marketed pharmaceuticals, although similar considerations may apply.[32] Second, the analysis is limited to human applications of CRISPR. Although CRISPR can be used to modify the genome of any living cell and important concerns have been raised about nonhuman applications,[33] addressing the complete range of these activities, their consequences, and possible mechanisms for controlling them is outside the scope of this Article. Rather, this Article is focused on one technological application—CRISPR-enabled editing of human genomes—that has received significant attention. Third, although DIY CRISPR is occurring around the world, this Article focuses on activities that are subject to U.S. laws, regulations, institutional rules, and social and scientific norms. The analysis and recommendations therefore may have limited

32. *Cf.* Jenna E. Gallegos et al., *The Open Insulin Project: A Case Study for 'Biohacked' Medicines*, 36 TRENDS BIOTECHNOLOGY 1211, 1212 (2018) (describing the Open Insulin Project, which seeks to develop and release a protocol for manufacturing off-patent insulin).

33. Nonhuman CRISPR applications include altering species in ways that harm the environment and creating viruses, bacteria, and toxins for use as biological weapons. *See, e.g.*, R. Alta Charo & Henry T. Greely, *CRISPR Critters and CRISPR Cracks*, 15 AM. J. BIOETHICS, Dec. 2015, at 11, 11; Diane DiEuliis & James Giordano, *Gene Editing Using CRISPR/Cas9: Implications for Dual-Use and Biosecurity*, 9 PROTEIN & CELL 239, 240 (2018).

applicability to other countries, with the exception that points related to self-governance may be broadly applicable.[34]

This Article proceeds as follows. Part I provides a brief technical description of CRISPR and its human applications to facilitate understanding of the relevant citizen-science activities that are currently underway or that may be possible in the future. Part II then describes the citizen-science contexts in which CRISPR is or might eventually be practiced, as well as some unique risks and benefits associated with these activities. Next, Part III analyzes the external and internal mechanisms that govern or potentially could govern DIY human gene editing in the United States, including laws and regulations, codes of ethics, and biosafety policies and practices. Part IV evaluates the effectiveness of this oversight regime and makes recommendations that we hope, on balance, will improve the ability of regulatory bodies and DIY communities to detect and discourage risky activities with minimal interference to citizen science's educational, creative, and innovative potential.

Because the meanings of many terms used in this Article are evolving, they are identified here to avoid confusion. *Citizen science* broadly describes any scientific endeavor in which members of the public participate as volunteers in one or more activities relevant to the research process other than (or in addition to) allowing personal data or specimens to be collected from them.[35] Such activities might encompass the entirety of the research process.[36] Participants in citizen science are *citizen scientists*.[37] Citizen science occurring in the life sciences is referred to, interchangeably, as *citizen bioscience*, *DIY biology*, and *biohacking*,[38] and citizen scientists engaged in these

34. With respect to countries that have similar laws, regulations, or institutional rules, this Article's analysis and recommendations may still be informative despite not addressing the specific requirements in those other jurisdictions.

35. *See, e.g.*, M.V. Eitzel et al., *Citizen Science Terminology Matters: Exploring Key Terms*, 2 CITIZEN SCI: THEORY & PRAC. 1, 5, 15 (2017) (defining citizen science as "the inclusion of members of the public in some aspect of scientific research"); Jennifer L. Shirk et al., *Public Participation in Scientific Research: A Framework for Deliberate Design*, 17 ECOLOGY & SOC'Y 29, 30 (2012) (defining "public participation in scientific research" as "intentional collaborations in which members of the public engage in the process of research to generate new science-based knowledge").

36. *Cf.* Shirk et al., *supra* note 35, at 32–33 (categorizing kinds of citizen-science research).

37. It should be recognized, however, that there is no consensus regarding what term(s) may or should be used to refer to individuals who engage in citizen science. *See* Eitzel et al., *supra* note 35, at 2, 11–15.

38. This Article also recognizes the debate regarding the relationship between citizen bioscience, DIY biology, and biohacking. One scholar defines DIY biology as "the term life science enthusiasts claim for biology work in laboratories set up outside of

activities are *citizen bioscientists*, *DIY biologists*, and *biohackers*.[39] The CRISPR-enabled editing of genomes by these individuals is *DIY CRISPR*.

I. CRISPR SCIENCE AND APPLICATIONS

Because a basic understanding of CRISPR is necessary to evaluate its oversight, this part provides an overview of the science and human applications of CRISPR. Briefly, CRISPR describes a system that directs a protein to disable or alter specific DNA sequences.

A. CRISPR Science

CRISPR refers to an adaptive immune system found in bacteria and archaea that has been repurposed by humans to conduct gene editing.[40] The process of gene editing using CRISPR encompasses sending a CRISPR associated ("Cas") protein and a guide RNA ("gRNA") to a predetermined location in the DNA of a target cell for the purpose of disabling or altering a specific gene.[41]

The power of CRISPR lies in the Cas protein, which acts as a pair of molecular scissors that cut DNA.[42] Although many Cas proteins are known to be effective in gene editing, Cas9 is a popular

professional science spaces" and having (according to some accounts) the "goals of citizen science," whereas biohacking has a wider range of activities and goals that include bodyhacking. *See* Lisa C. Ikemoto, *DIY Bio: Hacking Life in Biotech's Backyard*, 51 U.C. DAVIS L. REV. 539, 542–43, 548–49 (2017). Others have described DIY biologists as "part of [a] social movement that engages individuals and community groups in the study of the life sciences outside of traditional institutions, often aligning with open science and maker community ideals," whereas biohackers "tend to have a more explicitly political bent to their work." Amelia Fiske et al., *Conceptual and Ethical Considerations for Citizen Science in Biomedicine*, *in* PERSONAL HEALTH SCIENCE 195, 204 (Nils B. Heyen et al. eds., 2019). During interviews with biohackers, we heard these terms distinguished in still other ways. Gabriel Licina suggested doing away with these terms altogether and referring to all biological research activities, regardless of who is conducting them or where they are being conducted, as simply "biology." Telephone Interview with Gabriel Licina, Indep. Biohacker and Chief Research Officer, SciHouse (Aug. 9, 2018) (on file with author); *see also* Telephone Interview with Justin Atkin, Founder, The Thought Emporium (Oct. 15, 2018) (on file with author) ("[My DIY biology activities are] really just biology. We're not hacking anything. We're doing exactly the same thing that every academic lab is.").

39. *See* Daniel Grushkin, *Biohackers Are About Open-Access to Science, Not DIY Pandemics. Stop Misrepresenting Us*, STAT (June 4, 2018), https://www.statnews.com/2018/06/04/biohacker-open-access-science/ [https://perma.cc/7236-69ZN] (observing that these terms are interchangeable).

40. Enríquez, *supra* note 11, at 629.

41. NASEM, HUMAN GENOME EDITING, *supra* note 26, at 65.

42. *See* Doudna & Charpentier, *supra* note 13, at 1258096-2.

choice, especially for editing human genomes.[43] Fully enabled Cas9 cuts both strands of DNA, but the protein can also be modified to cut only a single strand.[44]

In order to be effective, the Cas protein must know exactly which DNA sequence in the genome to cut.[45] This is the job of gRNA, which binds to the Cas protein to form a protein-RNA complex.[46] Just as scientists are able to modify Cas proteins to perform different functions, scientists are able to design gRNA to match any known sequence in the genome.[47]

After Cas9 has cut the DNA that matches the target sequence, the cell deploys its repair machinery, which then works to repair the broken DNA, resulting in a modified gene.[48] In this way, Cas9 can turn off a gene, but it also can be accompanied by instructions from template DNA that have the effect of introducing a new gene at the location of the splice.[49]

To access an organism's DNA, the protein-RNA complex is usually embedded in a delivery system that will survive the protective mechanisms that organisms activate when they detect foreign bodies.[50] Often the delivery system is a viral vector, but nonviral methods also have proven effective in some circumstances.[51]

B. Target Cells

In humans and other organisms that reproduce sexually, target cells of CRISPR are classified as either somatic cells or germ cells. Somatic cells encompass all cells of an organism other than its reproductive cells.[52] Changes to somatic cell DNA alter the functionality of the targeted genes but do not affect genes passed on to offspring.[53]

By contrast, DNA edits to germ cells, which are the reproductive cells of sexually reproducing organisms, are heritable.[54] Germline

43. *Id.* at 1258096-4.

44. *See id.* (explaining that multiple Cas9s that are modified to cut only a single strand can be deployed at the same time to cut DNA in different locations).

45. Jinek et al., *supra* note 12, at 816.

46. Doudna & Charpentier, *supra* note 13, at 1258096-3.

47. NASEM, HUMAN GENOME EDITING, *supra* note 26, at 65.

48. *Id.* at 63–64, 66.

49. *Id.*

50. *See id.* at 96, 246–51.

51. *See id.* at 247–51 (describing advantages and disadvantages of various strategies for delivering gene-editing components to cells).

52. *Id.* at 5.

53. *Id.*

54. *Id.* at 6.

modification can therefore ensure that genes associated with inherited diseases are not passed on to offspring or, conversely, that genes associated with desirable conditions or traits (such as prophylactic protection against disease) are passed on to offspring.[55] For example, CRISPR can potentially rid families of the DNA mutation that causes Huntington's disease, which usually does not manifest prior to adulthood.[56]

Although Huntington's and other inherited diseases are potentially treatable through somatic therapies,[57] germline edits treat both current and future generations. For this reason, edits to germ cells raise different ethical issues than edits to somatic cells.[58] For example, concerns have been raised about the use of the technology to create "superior" individuals who have been genetically enhanced for intelligence, beauty, or strength.[59] There are also concerns about perpetuating changes that harm future generations in ways that cannot yet be appreciated, especially if there is no validated mechanism for reversing those changes.[60]

C. Human Applications

Potential human applications of CRISPR can generally be categorized by primary objective as basic discovery, therapeutic use, performance enhancement, or aesthetic use. While these categories are presented as distinct, they are fluid in practice where, as described below, the objective of a particular application depends on the baseline health of the targeted individual or the application has multiple objectives.[61] Moreover, CRISPR can be applied, at least in

55. *Id.* at 111–12; *see also* Enríquez, *supra* note 11, at 668 ("[C]orrecting gene errors or conferring prophylactic protection to diseases in the germline means the changes can be inherited in a firm and self-perpetuating configuration to subsequent generations.").

56. *See* Peggy C. Nopoulos, *Huntington Disease: A Single-Gene Degenerative Disorder of the Striatum*, 18 DIALOGUES CLINICAL NEUROSCIENCE 91, 92 (2016).

57. *See* Dianne Nicol et al., *Key Challenges in Bringing CRISPR-Mediated Somatic Cell Therapy into the Clinic*, GENOME MED., Sept. 25, 2017, at 1, 1.

58. For a discussion of safety, effectiveness, and ethical concerns that are relevant to the "CRISPR babies," see HENRY T. GREELY, THE END OF SEX AND THE FUTURE OF HUMAN REPRODUCTION 179–84 (2016).

59. Sarah Ashley Barnett, Comment, *Regulating Human Germline Modification in Light of CRISPR*, 51 U. RICH. L. REV. 553, 570–71, 573 (2017) (describing how human germline modification could result in the practice of "positive" eugenics that reinforces stigmas and exacerbates inequalities).

60. *Id.* at 567–69.

61. *See, e.g.*, 2 PRESIDENTIAL COMM'N FOR THE STUDY OF BIOETHICAL ISSUES, GRAY MATTERS: TOPICS AT THE INTERSECTION OF NEUROSCIENCE, ETHICS, AND SOCIETY 28 (2015), https://bioethicsarchive.georgetown.edu/pcsbi/sites/default/files/GrayMatter_V2_508.pdf [http://perma.cc/K2FZ-G3NE] [hereinafter PRESIDENTIAL

theory, to both somatic and germ cells to accomplish any of these objectives.

The first category, basic discovery, describes manipulating DNA in laboratory settings to learn about gene functions and relationships.[62] By turning genes on and off in various combinations, CRISPR enables researchers to understand their roles and interactions.[63] In addition, CRISPR can be utilized to elucidate DNA-repair mechanisms, human development processes, links between genes and disease, and the progression of cancer and other diseases that are influenced by genetics.[64] CRISPR is widely used in research laboratories for these investigative purposes.

By contrast, clinical applications of CRISPR to treat disease remain in the early stages of development. Therapeutic uses, which is the second major category of human CRISPR applications, aim to disable or correct genetic mutations responsible for disease. For example, sickle cell disease, which produces misshapen red blood cells, is caused by a single DNA base mutation and is theoretically curable by replacing the mutated base with the correct base.[65] Conditions like sickle cell disease that are known to be caused by single gene mutations are currently the most promising candidates for therapeutic applications and are the subject of the first CRISPR clinical trials.[66] However, disease treatment for humans might also be

COMM'N] (noting that enhancement and treatment "are not always sharply distinguishable"); H.T. Greely, *Direct Brain Interventions to "Treat" Disfavored Human Behaviors: Ethical and Social Issues*, 91 CLINICAL PHARMACOLOGY & THERAPEUTICS 163, 163 (2012) ("Behaviors do not come naturally labeled as 'disease' and 'nondisease'; humans make those distinctions, and . . . we regularly change them . . . ."). For a critique of the line drawn between drugs used for "legitimate medical purpose[s]" and those that are misused in the Controlled Substances Act, see generally Matt Lamkin, *Legitimate Medicine in the Age of Consumerism* (Aug. 8, 2018), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3228692 [https://perma.cc/C27N-Q375 (staff-uploaded archive)].

62. *See* NASEM, HUMAN GENOME EDITING, *supra* note 26, at 61–82.

63. *See* Patrick D. Hsu, Eric S. Lander & Feng Zhang, *Development and Applications of CRISPR-Cas9 for Genome Engineering*, 157 CELL 1262, 1262 (2014).

64. *See* NASEM, HUMAN GENOME EDITING, *supra* note 26, at 69.

65. *See, e.g.*, Mark A. DeWitt et al., *Selection-Free Genome Editing of the Sickle Mutation in Human Adult Hematopoietic Stem/Progenitor Cells*, SCI. TRANSLATIONAL MED., Oct. 12, 2016, at 1, 1–2 (reporting a CRISPR technique to repair the mutation responsible for sickle cell disease); *see also* Heidi Ledford, *CRISPR Deployed to Combat Sickle Cell Anaemia*, NATURE (Oct. 12, 2016), https://www.nature.com/news/crispr-deployed-to-combat-sickle-cell-anaemia-1.20782 [https://perma.cc/3J5Y-2V5M] (contextualizing the findings).

66. *See A CRISPR Go*, GENOMEWEB (Sept. 4, 2018), https://www.genomeweb.com/scan/crispr-go#.W5_swpNKg0o [https://perma.cc/9NKS-XWC7 (staff-uploaded archive)]. As of the time of writing this Article, the FDA has authorized two clinical trials. Rich Haridy, *FDA Hits Pause on One of the First US Human Clinical Trials to Use CRISPR*,

accomplished by manipulating the DNA of a foreign disease agent. For example, CRISPR has been used experimentally to suppress human immunodeficiency virus 1 ("HIV-1") replication in persistently and latently infected T cells.[67]

Performance enhancement encompasses gene modifications that do not address specific health deficits but rather are intended to improve healthy individuals' cognitive or physical performance to levels beyond the individuals' normal functioning or the statistically normal range for humans.[68] In the future, CRISPR could be used, for example, to modify human genes to stimulate the production of erythropoietin, which increases the supply of red blood cells.[69] While stimulating erythropoietin production is a treatment for anemia, in healthy individuals it can enhance aerobic performance.[70]

NEW ATLAS (May 31, 2018), https://newatlas.com/us-crispr-human-trial-hold-fda/54862/ [https://perma.cc/VSQ5-89M7]. In May 2018, the FDA placed one of the two trials on "clinical hold," which meant the trial could not proceed, although the Agency ultimately lifted the hold in October 2018. *Id.*; Amirah Al Idrus, *FDA Lifts Clinical Hold of Vertex/CRISPR Therapeutics' Sickle Cell Drug*, FIERCEBIOTECH (Oct. 10, 2018, 5:29 PM), https://www.fiercebiotech.com/biotech/fda-lifts-clinical-hold-vertex-crispr-therapeutics-sickle-cell-med [https://perma.cc/8YEF-H5XX]. The FDA has not publicly explained why it put this particular trial on clinical hold, Haridy, *supra*, but the FDA may generally do so for a variety of reasons, including that the subjects would be "exposed to . . . unreasonable and significant risk(s)" or sufficient information to assess the risks to subjects was not provided by the sponsor of the trial, 21 C.F.R. § 312.42 (2018).

67. Youdiil Ophinni et al., *CRISPR/Cas9 System Targeting Regulatory Genes of HIV-1 Inhibits Viral Replication in Infected T-Cell Cultures*, SCI. REP., May 17, 2018, at 1, 2.

68. PRESIDENTIAL COMM'N, *supra* note 61, at 28; *see also* Henry T. Greely, *Remarks on Human Biological Enhancement*, 56 U. KAN. L. REV. 1139, 1140 (2008) ("[Enhancement] is using things not only to repair or bring up the human norm, but also to surpass either the preexisting position or to go to the extreme—to move outside the normal human range."); Maxwell J. Mehlman, *The Law of Above Averages: Leveling the New Genetic Enhancement Playing Field*, 85 IOWA L. REV. 517, 523 (2000) ("A genetic intervention is an 'enhancement,' however, (1) when it is undertaken for the purpose of improving a characteristic or capability that, but for the enhancement, would lie within what is generally accepted as a 'normal' range for humans; or (2) when it installs a characteristic or capability that is not normally present in humans."). The use of CRISPR for enhancement rather than therapy, whether in biohacking or traditional contexts, raises its own social, ethical, and regulatory issues. *See generally* Maxwell J. Mehlman, *How Will We Regulate Genetic Enhancement?*, 34 WAKE FOREST L. REV. 671 (1999).

69. *See* Dev Mishra, *CRISPR and the Super Athlete*, SIDELINE SPORTS DOC (May 15, 2018), http://www.sidelinesportsdoc.com/crispr-and-the-super-athlete/ [https://perma.cc/L8Q6-B9LP] (discussing the possibility of manipulating the gene responsible for erythropoietin regulation to increase athletic performance).

70. *See generally* Olivier Salamin et al., *Erythropoietin as a Performance-Enhancing Drug: Its Mechanistic Basis, Detection, and Potential Adverse Effects*, 464 MOLECULAR & CELLULAR ENDOCRINOLOGY 75 (2018) (discussing the introduction of erythropoiesis-stimulating agents, development of detection methods, and potential effects of their misuse). *But see* Jules A.A.C. Heuberger et al., *Effects of Erythropoietin on Cycling*

The last category, aesthetic uses, describes gene edits that have the effect of changing a person's physical appearance. For example, eye or skin color might be altered by editing the genes that contribute to these characteristics. As another example, CRISPR could be used to make an individual's metabolism more efficient by altering genes that control the manner in which the body stores and uses fat.[71] If that individual has weight-related health problems and the edit causes weight loss that resolves these problems, the modification would be both aesthetic and therapeutic.

Although the possibility of using CRISPR for human therapeutic, performance enhancing, and aesthetic purposes has attracted widespread attention, the reality is that many of these applications will not be technically feasible for some time. Thus far, the genetic bases of only a small number of conditions and traits have been identified, and most appear to be the result of multiple genes interacting in complex ways with each other and their environment.[72] Until those interactions are fully understood, CRISPR-induced gene changes are unlikely to achieve their intended objectives—even if adverse effects could be controlled.[73] For this reason, commercial interest in CRISPR is currently focused on treating conditions caused by single gene mutations.[74] Nevertheless, the complexities of genetics

Performance of Well Trained Cyclists: A Double-Blind, Randomised, Placebo-Controlled Trial, 4 LANCET HAEMATOLOGY e374, e374 (2017) (concluding that a recombinant human erythropoietin treatment did not affect clinically relevant exercise test performance and road race performance in trained cyclists). Although accomplished by injection of a biologic drug form of erythropoietin, rather than gene-editing techniques, such "blood doping" has been reported as common among elite cyclists, including, most famously, Lance Armstrong. *See, e.g.*, Dave Siebert, *Lance Armstrong Confesses to PEDs: What is Erythropoietin (EPO) Blood Doping?*, BLEACHER REP. (Jan. 16, 2013), https://bleacherreport.com/articles/1471562-lance-armstrong-confesses-to-peds-what-is-erythropoietin-epo-blood-doping [https://perma.cc/GP6U-SXEE].

71. Indeed, scientists are using CRISPR to study a genetic variant associated with obesity. Melina Claussnitzer et al., FTO *Obesity Variant Circuitry and Adipocyte Browning in Humans*, 373 NEW ENG. J. MED. 895, 896–98 (2015).

72. *See, e.g.*, Matthew R. Robinson, Naomi R. Wray & Peter M. Visscher, *Explaining Additional Genetic Variation in Complex Traits*, 30 TRENDS GENETICS 124, 124 (2014) (observing that most "biological phenotypes and many of the characters of interest to humans are complex in that they are determined by many mutations at multiple loci, as well as by many nongenetic factors").

73. *See* Enríquez, *supra* note 11, at 672–85 (dismissing concerns that CRISPR might be used to create "'designer babies' with a panoply of artificial traits," such as enhanced intelligence and tall stature, given that "human knowledge is vastly incomplete concerning the genetics of these complex polygenic traits").

74. *See* Lu Xiao-Jie et al., *CRISPR-Cas9: A New and Promising Player in Gene Therapy*, 52 J. MED. GENETICS 289, 291 (2015) (explaining that, "[c]ompared with polygenic diseases such as cancer, monogenic disorders are more amenable to gene

have not dampened public excitement about the prospect of human gene editing, nor has it discouraged citizen bioscientists from attempting to conduct their own CRISPR experiments for a number of purposes.

II. THE USE OF CRISPR BY DIY BIOLOGISTS

This part describes the use of CRISPR in citizen-bioscience settings. It begins with a brief history of DIY biology and its diverse communities of practitioners and supporters. It then details the private and communal settings in which DIY biology is occurring in the United States with an emphasis on DIY CRISPR. It concludes by considering some unique risks and benefits associated with these activities.

A. The Rise of DIY Biology

Although the term citizen science has only recently entered common usage,[75] there is a long tradition of self-trained "amateurs" conducting research in various scientific fields, including astronomy, ornithology, and agriculture.[76] In the life sciences, famous hobbyists include the monk Gregor Mendel, whose pea-breeding experiments in the mid-1800s uncovered the mechanisms of heredity.[77] There is also a long tradition in medicine of self-experimentation.[78]

In the late 1800s, however, science became less accessible to the general public as it became professionalized.[79] This transformation was the result of several factors that include a rise in "experimentalism" that moved science from the field to the laboratory.[80] In the decades since, the biomedical sciences in particular have largely been restricted to those with advanced

therapies," and so currently their correction "represents the most translatable field in CRISPR-Cas9-mediated gene therapy").

75. Jonathan Silvertown, *A New Dawn for Citizen Science*, 24 TRENDS ECOLOGY & EVOLUTION 467, 470 (2009).

76. *See id.* at 467; *see also* Günter Seyfried, Lei Pei & Markus Schmidt, *European Do-It-Yourself (DIY) Biology: Beyond the Hope, Hype and Horror*, 36 BIOESSAYS 548, 548 (2014); Nora S. Vaage, *Fringe Biotechnology*, 12 BIOSOCIETIES 109, 115–16 (2017).

77. *See* Vaage, *supra* note 76, at 116.

78. *See generally* Allen B. Weisse, *Self-Experimentation and Its Role in Medical Research*, 39 TEX. HEART INST. J. 51 (2012) (discussing instances of self-experimentation by medical researchers over the past 200 years).

79. Fiske et al., *supra* note 38, at 198.

80. Dana Mahr et al., *Watching or Being Watched: Enhancing Productive Discussion Between the Citizen Sciences, the Social Sciences and the Humanities*, *in* CITIZEN SCIENCE: INNOVATION IN OPEN SCIENCE, SOCIETY AND POLICY 99, 104 (Susanne Hecker et al. eds., 2018) (citing the works of Robert E. Kohler).

education and training, as well as access to the sophisticated physical resources that are often necessary to tinker at cellular and molecular levels.

In the past few decades, the internet has helped break down many of these barriers at the same time that it has opened channels for DIY biologists to connect, consult, and collaborate with one another.[81] Today, used or refurbished laboratory equipment can be purchased on eBay or Craigslist, obtained gratis on Freecycle, or even self-manufactured using 3D-printing protocols posted on the internet.[82] As one biohacker explained, "[Y]ou can literally buy almost everything you need off of Ebay. . . . Other than that, the few things that I can't buy, I build because I tend to build a lot of my own tools if I need to."[83] Another interviewee described a different strategy of purchasing equipment at deep discounts from biotechnology companies that have gone bankrupt.[84] Meanwhile, free instruction is available in the form of scientific lectures uploaded to YouTube;[85] courses offered on edX and Coursera and by other biohackers;[86] protocols shared on OpenWetWare;[87] and scientific

81. *See* DANIEL GRUSHKIN, TODD KUIKEN & PEIRS MILLET, WOODROW WILSON CTR., SEVEN MYTHS AND REALITIES ABOUT DO-IT-YOURSELF BIOLOGY 5 (2013), https://www.wilsoncenter.org/sites/default/files/7_myths_final.pdf [https://perma.cc/CX7W-73D5] (providing a brief history of the "DIYbio movement"); Ikemoto, *supra* note 38, at 547 (noting formative events of the DIY biology "movement," including online publication of educational materials and the launch of the DIYbio.org message board).

82. Patrik D'haeseleer, *How to Set Up Your Own DIY Bio Lab*, MAKE: (Apr. 11, 2017, 6:00 AM), https://makezine.com/2017/04/11/how-to-set-up-your-own-lab/ [https://perma.cc/G7HZ-ER9W]. Other sources of equipment are described in Elliot Roth, *A Guide to DIYbio (Updated 2019): Almost Everything You Need to Know About Biohacking (with Links)*, MEDIUM (Feb. 16, 2019), https://medium.com/@ThatMrE/a-guide-to-diybio-updated-2019-abd0956cdf74 [https://perma.cc/D4GD-4UAC].

83. Telephone Interview with Justin Atkin, *supra* note 38.

84. Telephone Interview with Ryan Bethencourt, Partner, Babel Ventures, and CEO, Wild Earth, Inc. (Nov. 15, 2018) (on file with author); *see also* Andrew W. Torrance, *Planted Obsolescence: Synagriculture and the Law*, 48 IDAHO L. REV. 321, 345 (2012) (noting that DIY biology has been encouraged in part by bankruptcies in the biotechnology industry, which "resulted in abundant laboratory equipment available for purchase at steep discounts").

85. *See, e.g.*, *AK Lectures*, YOUTUBE (Aug. 4, 2016), https://www.youtube.com/user/mathdude2012 [https://perma.cc/JNQ8-NQCA]; *Shomu's Biology*, YOUTUBE (May 30, 2016), https://www.youtube.com/user/TheFunsuman [https://perma.cc/M2SR-5SB7]. These lecture series were recommended by biohacker David Ishee. Telephone Interview with David Ishee, Owner, Midgard Kennels (Aug. 10, 2018) (on file with author).

86. *See, e.g.*, BIOHACK ACAD., http://biohackacademy.github.io/ [https://perma.cc/NLK2-4Q7P]; *Biohacker 101 Class*, ODIN, http://www.the-odin.com/biohacker-101-class/ [https://perma.cc/3NYS-V8JQ]; *Principles of Synthetic Biology*, EDX, https://www.edx.org/course/principles-of-synthetic-biology [https://perma.cc/E7AW-C8SN].

87. OPENWETWARE, https://openwetware.org/wiki/Main_Page [https://perma.cc/2CD5-M7XL].

manuscripts available from Sci-Hub, bioRxiv, and other open access libraries.[88]

Numerous websites and online platforms are also now available to support project collaborations—in some cases among individuals who will never meet in person. For example, several years ago, seven individuals with a specific genetic variant codeveloped and executed a protocol to test the effect of different vitamin regimens on their homocysteine levels using the internet platform DIYgenomics.org.[89] As another example, individuals afflicted with amyotrophic lateral sclerosis ("ALS") who met on the website PatientsLikeMe collaborated on testing the effect of lithium carbonate on their symptoms.[90]

In 2008, DIYbio.org was formed to support the efforts of the growing communities of individuals seeking to access and do science outside of traditional scientific institutions.[91] Among the group's early achievements was its organization of two congresses that drafted codes of ethics for DIY biologists.[92] More recently, DIYbio.org launched the DIYbiosphere for sharing information about relevant projects, organizations, and events around the world.[93]

Today, there are over 5000 registered members of the DIYbio.org discussion forum.[94] This represents just a subset of all

88. BIORXIV, https://www.biorxiv.org/ [https://perma.cc/C6UK-7DAL]; SCI-HUB, http://sci-hub.tw/ [https://perma.cc/M4RY-PN5V (staff-uploaded archive)]. We note, however, that Sci-Hub is a "pirate" website.

89. *See* Melanie Swan et al., *Citizen Science Genomics as a Model for Crowdsourced Preventive Medicine Research*, SOC'Y FOR PARTICIPATORY MED. (2010), https://participatorymedicine.org/journal/evidence/research/2010/12/23/citizen-science-genomics-as-a-model-for-crowdsourced-preventive-medicine-research/ [https://perma.cc/X25X-FFYB].

90. *See* Paul Wicks et al., *Accelerated Clinical Discovery Using Self-Reported Patient Data Collected Online and a Patient-Matching Algorithm*, 29 NATURE BIOTECHNOLOGY 411, 411 (2011).

91. *See An Institution for the Do-It-Yourself Biologist*, DIYBIO, https://diybio.org/ [https://perma.cc/G9ZV-3C39].

92. *Codes*, DIYBIO, https://diybio.org/codes/ [https://perma.cc/6X4G-FHWW].

93. Jason Bobe, *Announcing DIYbiosphere: An Open Source Project to Connect DIYbio Related Activities Worldwide*, DIYBIO (Mar. 17, 2018), https://diybio.org/2018/03/17/announcing-diybiosphere-an-open-source-project-to-connect-diybio-related-activities-worldwide/ [https://perma.cc/6GUK-7ZE9]. Events featured on the website include the Global Summit on Community Biotechnology in Cambridge, Massachusetts, an annual gathering of DIY biologists and members of independent and community laboratories sponsored by the MIT Media Lab, GLOBAL COMMUNITY BIO SUMMIT, https://www.biosummit.org [https://perma.cc/96DL-7XS2], and Biohack the Planet in Oakland, California, an annual biohacking convention spearheaded by Dr. Zayner, BIOHACK PLANET, https://www.biohacktheplanet.com [https://perma.cc/J9YH-E8FD].

94. *See DIYbio*, GOOGLE GROUPS, https://groups.google.com/forum/#!forum/diybio [https://perma.cc/967P-5X4V].

DIY biology communities, which Brookings Institution estimated in 2017 to include 30,000 "enthusiasts, followers, biohackers and citizen scientists" in the United States alone.[95]

These communities have proven hard to characterize not only due to their size but also their significant diversity. The formal scientific training of DIY biologists ranges from participation only in high school coursework to completion of PhD programs.[96] Furthermore, DIY biologists have varied objectives that include learning about scientific processes, advancing scientific discovery, commercializing scientific solutions, using science as a medium for artistic expression, and challenging (or even disrupting) traditional scientific practices and norms.[97]

To advance these objectives, some DIY biologists have turned to CRISPR. No data has been collected regarding who exactly is engaged in DIY CRISPR or when, where, or for what purposes it is being practiced. In the only published survey of DIY biologists conducted to date, which involved 359 respondents, the Wilson Center found that almost half of those who answered questions regarding the nature of their experiments reported genetically engineering bacteria or yeast.[98] Respondents were not asked what techniques they used, but it is doubtful that any were using CRISPR because the survey was conducted in 2013 when CRISPR—whose potential to be used for gene editing was first detailed just one year earlier—was still relatively new.[99] As described below, however, reports and anecdotal evidence indicate that in the past few years, CRISPR-enabled gene editing has become a common activity across DIY settings.[100]

95. Bart Kolodziejczyk, *Do-It-Yourself Biology Shows Safety Risks of an Open Innovation Movement*, BROOKINGS INST. (Oct. 9, 2017), https://www.brookings.edu/blog/techtank/2017/10/09/do-it-yourself-biology-shows-safety-risks-of-an-open-innovation-movement/ [https://perma.cc/2JEX-RRCB].

96. *See* GRUSHKIN ET AL., *supra* note 81, at 6.

97. *See id.* at 4; Ikemoto, *supra* note 38, at 548–54.

98. GRUSHKIN ET AL., *supra* note 81, at 6, 10–11. It is unclear exactly how many of the 359 total number of survey respondents answered these particular questions. Percentages of responses to each question were calculated using the number of respondents who answered that specific question as a denominator. *Id.* at 24.

99. *See supra* note 12.

100. *See, e.g.*, Heidi Ledford, *Biohackers Gear up for Genome Editing*, 524 NATURE 398, 398 (2015) (quoting one biohacker's description of CRISPR as "the most amazing tool ever"); Kristen V. Brown, *Inside the Garage Labs of DIY Gene Hackers, Whose Hobby May Terrify You*, PROJECT EARTH (Mar. 29, 2016, 7:00 AM), https://projectearth.us/inside-the-garage-labs-of-diy-gene-hackers-whose-hobby-1796423884 [https://perma.cc/R3JP-DKYL] [hereinafter Brown, *Inside the Garage Labs*] (observing that CRISPR has "galvanized the movement of DIY scientists who want to try their hand

B. CRISPR in DIY Biology Settings

The settings in which DIY CRISPR occurs can broadly be described as private or communal. We define *private settings* as homes, apartments, garages, and other properties owned or leased by individuals. *Communal settings* are properties owned or leased by or on behalf of a (usually nonprofit) collective or entity.

1. Private Settings

The DIY biology movement is said to have originated in homes and apartments, and private settings remain the focus of many media accounts of biohacking. This is perhaps not surprising given the remarkable sophistication of some private laboratories and the resourcefulness of those who built them. Examples of home biologists who have received considerable media attention include Sebastian Cocioba, a college dropout who built a wet laboratory in the spare bedroom of his parent's Long Island City apartment, and David Ishee, a dog breeder from Mississippi who built a genetic-engineering laboratory in his shed.[101]

Many home laboratories are outfitted with second-hand or self-manufactured equipment, although other procurement options are available. For example, Dr. Zayner's retail company, The ODIN, sells a complete genetic-engineering home-lab kit, which includes a thermocycler to amplify segments of DNA, for $1849.[102] Meanwhile, biological materials can be obtained from fellow biohackers[103] or purchased from supply companies.[104]

Although information about how to set up a private laboratory is not hard to find,[105] the number of such laboratories is not known. The

at genetically modifying plants, insects, animals, and, someday, maybe even humans"); Ellen Jorgensen, *DIY Community Can Do Interesting, Useful, Perfectly Respectable Things with CRISPR*, STAT (Mar. 14, 2016), https://www.statnews.com/2016/03/14/crispr-do-it-yourself/#jorgensen [https://perma.cc/V8FQ-8YNA] (describing intense interest in learning and using CRISPR techniques among members of a New York community laboratory).

101. *See* Brown, *Inside the Garage Labs*, *supra* note 100; Kristen V. Brown, *Meet the Guy Biohacking Puppies to Make Them Glow in the Dark*, SPLINTER (Sept. 28, 2016, 11:20 AM), https://splinternews.com/meet-the-guy-biohacking-puppies-to-make-them-glow-in-th-1793862258 [https://perma.cc/DW66-KSMU].

102. *Genetic Engineering Home Lab Kit*, ODIN, http://www.the-odin.com/genetic-engineering-home-lab-kit/ [https://perma.cc/6YB6-4F9W].

103. Brown, *Inside the Garage Labs*, *supra* note 100 (describing how a New York biohacker obtained CRISPR/Cas9 through the mail from a friend in Austria); Telephone Interview with Justin Atkin, *supra* note 38.

104. Telephone Interview with David Ishee, *supra* note 85; Telephone Interview with Gabriel Licina, *supra* note 38.

105. *See, e.g.*, D'haeseleer, *supra* note 82.

Wilson Center survey found that 26% of respondents reporting the location(s) of their DIY work conducted experiments at home in addition to community, institutional, or academic laboratories or other community workspaces, and 8% conducted experiments exclusively at home.[106] However, because the survey was distributed to individuals participating in online forums and known community leaders, the findings could have been biased toward networked individuals who might be less likely to conduct their experiments in private settings.[107]

The extent to which CRISPR is used in private settings is also unknown. In the absence of data, the scope of these activities might be estimated from sales of laboratory equipment and materials to individuals with private laboratories. By late 2017, it was reported that The ODIN had sold over 1000 kits,[108] but it is not known how many were CRISPR kits purchased for home use. Moreover, sales of The ODIN's CRISPR kits that facilitate basic experiments involving bacteria and yeast[109]—which until recently were the only kits sold by the company[110]—may not reflect the actual gene-editing activities of individuals working in relatively sophisticated laboratories that they

106. GRUSHKIN ET AL., *supra* note 81, at 6–7, 9.

107. *Id.* at 24.

108. *See* Sneed, *supra* note 13.

109. For a short time, The ODIN sold a kit marketed as enabling consumers to genetically engineer yeast to make glow-in-the-dark beer. Stephanie M. Lee, *DNA Biohackers Are Giving the FDA a Headache with Glow-In-The-Dark Booze*, BUZZFEED NEWS (Dec. 6, 2016, 9:42 AM), https://www.buzzfeednews.com/article/stephaniemlee/biohacking-booze#.xeeD8r8Gp [https://perma.cc/DKE6-QUNX]. It stopped selling that kit after Dr. Zayner spoke with FDA officials who reportedly expressed concern that the yeast was an unsafe color additive for food. *Id.* Color additives are "material[s]" that "when added or applied to a food . . . [are] capable . . . of imparting color," 21 U.S.C. § 321(t) (2012), and must be approved by the FDA as safe before marketing, *id.* § 379e. Several sources offer an overview of FDA requirements related to color additives. *See, e.g.*, PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, FOOD AND DRUG LAW: CASES AND MATERIALS 617–26 (2013); *see also* Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 ADMIN. L. REV. 431, 447 (2008) (describing the status of the FDA's review of color additives); *cf.* Lars Noah & Richard A. Merrill, *Starting from Scratch?: Reinventing the Food Additive Approval Process*, 78 B.U. L. REV. 329, 351 n.94 (1998) (explaining that Congress declined to exempt from FDA review those color additives that are "generally recognized as safe").

110. In 2018, The ODIN began selling for the first time a kit to alter frog genomes that includes six live frogs, cages, and food. *Frog Genetic Engineering Kit–Learn to Genetically Modify Animals*, ODIN, http://www.the-odin.com/frog-ge-kit/ [https://perma.cc/BS49-8RKV]. The ODIN also sells a plasmid that expresses Cas9 and a gRNA that targets the human myostatin gene, although it is not "injectable or meant for direct human use." *Human Myostatin Knock-Out Targeting CRISPR-Cas9 Plasmid*, ODIN, http://www.the-odin.com/human-myostatin-knock-out-targeting-crispr-cas9-plasmid/ [https://perma.cc/S8YL-VANN].

built on their own. Yet, the activities of these DIY biologists may be especially important to track to the extent they demonstrate more proficiency with CRISPR and potential for editing human genetic material.[111] Others have observed that citizen bioscientists working in private settings may include those most suspicious of government authority and "likely to explore the margins of ethical or legal conduct."[112]

But even those who use CRISPR exclusively in private settings are not necessarily working in secret. Because biohackers' access to materials and information is generally limited, consulting each other and sharing resources can be critical to the success of their experiments.[113] It is therefore not surprising that only 6% of the Wilson Center survey respondents who answered the question, "What are your feelings about transparency and sharing your work?," favored privacy, and of the 8% who reported conducting experiments exclusively at home, many, according to the authors, "avidly discuss their work online."[114] Such is the case, for example, with Dr. Zayner. Although he has conducted experiments behind closed blinds so as not to alarm his neighbors,[115] Dr. Zayner also has invited friends and journalists to observe his work in person and regularly discusses and posts videos of his activities on his blog and YouTube channel.[116]

2. Communal Settings

As an alternative to private settings, some citizen bioscientists work in community laboratories, which provide members access to

111. A Stanford University infectious disease expert has expressed concern that use of even basic CRISPR kits "'will help enable users to become proficient more generally with this technology,' . . . so that they could someday become skilled enough to use advanced tools to introduce less benign genes." Lisa M. Krieger, *Playing God at Home with a Gene Editing Kit*, CHI. TRIB., Feb. 10, 2016, at 3.

112. CTR. FOR GLOB. SEC. RESEARCH, LAWRENCE LIVERMORE NAT'L LAB., INDEPENDENT BIOTECHNOLOGY: THE INNOVATION-REGULATION DILEMMA 7 (2016), https://cgsr.llnl.gov/content/assets/docs/Independent_Biotechnology_Workshop_SummaryNOV2016.pdf [https://perma.cc/KN3F-TNWJ].

113. Telephone Interview with David Ishee, *supra* note 85; *see also* CTR. FOR GLOB. SEC. RESEARCH, *supra* note 112, at 7 (noting that much of biotechnology is collaborative in nature so isolation can be an impediment to DIY biology).

114. *See* GRUSHKIN ET AL., *supra* note 81, at 8, 15. The number of individuals responding to the question regarding one's preference for transparency was not reported.

115. *See* Krieger, *supra* note 111.

116. SCI. ART BEAUTY, http://www.josiahzayner.com/ [https://perma.cc/R5VQ-BJAG]; Josiah Zayner, *Homo Sapien Mutagensis*, YOUTUBE (Jan. 18, 2017), https://www.youtube.com/channel/UC-aCKd4djOAf_0BzyUMJ5FA [https://perma.cc/7KH3-D657].

laboratory space, materials, and instruction.[117] In contrast to private settings, much is known about community laboratories and the gene-editing activities occurring within them. There are an estimated fifty community laboratories and similar biohacking spaces dispersed throughout the United States,[118] although they appear to be concentrated on the East and West Coasts.[119] Some of the oldest and most well-established laboratories include Genspace in Brooklyn, New York;[120] Baltimore Under Ground Science Space ("BUGSS") in Baltimore, Maryland;[121] BioCurious in Santa Clara, California;[122] and Counter Culture Labs in Oakland, California.[123]

Most community laboratories are run by small teams that include at least one professionally trained scientist, and their members represent a spectrum of ages, professions, scientific backgrounds, and commercial intentions. In part due to limited funds, community laboratories are sometimes located in industrial parks or warehouse districts or share space with nonscientific groups.[124] Furthermore, like home laboratories, community laboratories generally are outfitted with second-hand equipment, although unlike home laboratories,

117. DIY biology also takes place in traditional scientific settings, which encompass academic, commercial, and government laboratories. GRUSHKIN ET AL., *supra* note 81, at 6–7. This Article does not address these activities because they are subject to many of the well-known oversight mechanisms that govern scientific work in those settings. *Cf.* CTR. FOR GLOB. SEC. RESEARCH, *supra* note 112, at 6 (noting that scientists working in institutional settings, whether or not federally funded, are subject to formal and ad hoc regulatory mechanisms, as well as institutional norms and liabilities, "that make it more likely that many 'eyes' will scrutinize a project during planning and execution—and intervene if necessary").

118. Kolodziejczyk, *supra* note 95.

119. *See* DIYBIOSPHERE, http://sphere.diybio.org/ [https://perma.cc/5V5K-FXL7] (providing a listing and map of community laboratories).

120. GENSPACE, https://www.genspace.org/ [https://perma.cc/YBQ8-9UPA]. Founded in 2009, Genspace describes itself as "the world's first community lab." *Id.*

121. BALT. UNDER GROUND SCI. SPACE, http://www.bugssonline.org/ [https://perma.cc/7BJG-7NNS].

122. BIOCURIOUS, http://biocurious.org/ [https://perma.cc/M5YM-5P8G].

123. COUNTER CULTURE LABS, https://www.counterculturelabs.org/ [https://perma.cc/8H6V-TA63].

124. For example, BUGSS shared spaced in its early years, Lisa Z. Scheifele & Thomas Burkett, *The First Three Years of a Community Lab: Lessons Learned and Ways Forward*, 17 J. MICROBIOLOGY & BIOLOGY EDUC. 81, 83 (2016), while Counter Culture Labs is housed in Omni Commons, a community center in Oakland that is home to eleven other collectives, OMNI COMMONS, https://omnicommons.org/index.html# [https://perma.cc/L9UQ-JBHH].

such equipment might be donated directly to them by academic or commercial laboratories.[125]

Although each community laboratory has a distinct ethos, a common objective is to promote education and experimentation.[126] Thus many community laboratories offer instruction on laboratory techniques and specific areas of scientific interest. Among these educational programs, training in the use of CRISPR with bacteria and yeast has become popular in recent years. For example, a CRISPR class series is offered multiple times a year at both Genspace[127] and BUGSS.[128]

Community laboratories also offer members the opportunity to contribute to community research or conduct their own research using laboratory-owned or approved equipment, disposables, and biological materials. Some of these research projects involve CRISPR. For example, BioCurious and Counter Culture Labs are co-leading a project that uses CRISPR called Real Vegan Cheese, which aims to turn yeast into milk protein factories.[129] Members are also using CRISPR on their own to edit bacteria and yeast genomes.[130]

Although nonmembers generally have access to courses and lectures, only members may conduct research at community laboratories. Sometimes access is tiered by membership type. At Genspace, for example, "community members" may participate in community projects, "individual members" may conduct independent research, and "premium members" may use the laboratory for

125. For example, HiveBio, a community laboratory in Seattle, solicits equipment donations. *Equipment Wish List*, HIVEBIO, https://hivebiolab.wordpress.com/equipment-wish-list/ [https://perma.cc/WB9T-U7XE].

126. *See* Scheifele & Burkett, *supra* note 124, at 82.

127. *Classes*, GENSPACE, https://www.genspace.org/classes/ [https://perma.cc/W249-66GJ] (describing a four-part course titled "Genome Editing with CRISPR-Cas9").

128. *Build-a-Gene Course (Now More CRISPR)*, BALT. UNDER GROUND SCI. SPACE, http://www.bugssonline.org/build-a-gene-now-more-crispr/ [https://perma.cc/CJ5U-M5PX].

129. REAL VEGAN CHEESE, https://realvegancheese.org/ [https://perma.cc/TLL5-52AB].

130. *See, e.g.*, Sneed, *supra* note 13 (describing the independent CRISPR projects of a BioCurious member).

entrepreneurial purposes.[131] Fees for these memberships range from $100 to $800 per month.[132]

Whether working on community or individual projects, members are expected to comply with laboratory policies, which might be developed with input from members. The content of these policies varies, but most laboratories have adopted rules related to safety that endeavor to strike an appropriate balance between minimizing potential risks to members and helping members realize their educational, expressive, and scientific objectives.

C. Potential Risks and Benefits of DIY CRISPR

While the risks of CRISPR-enabled gene editing conducted by professional scientists in institutional settings are the subject of a robust literature and ongoing public conversations,[133] uses of CRISPR by citizen bioscientists present additional human health and societal considerations. Assessment of these risks encompasses three questions: What are the potential outcomes? How likely are they? What are the consequences?[134]

Focusing on negative outcomes related to safety, the use of CRISPR in *ex vivo* experimentation poses health risks to citizen bioscientists performing this work that are likely minimal and not unlike those present in other laboratory work involving mammalian cells. Using CRISPR to edit human cells *in vivo*, however, poses risks that include immunological reaction, infection, and other unintended health effects that may be more likely to occur when conducted by

131. *Join the Lab*, GENSPACE, https://www.genspace.org/join-the-lab/ [https://perma.cc/5WEZ-8JFB]. BUGSS also recognizes various membership categories, including a membership category for students and teachers. BALTIMORE UNDER GROUND SCIENCE SPACE (BUGSS) MEMBERSHIP APPLICATION AND AGREEMENT 2 [hereinafter BUGSS MEMBERSHIP APPLICATION], http://www.bugssonline.org/wp-content/uploads/2018/05/BUGSSmembership-agreement.pdf [https://perma.cc/A7JT-FD5S].

132. *Join the Lab*, *supra* note 131. Some community laboratories also offer ways to reduce membership fees. *See, e.g.*, BUGSS MEMBERSHIP APPLICATION, *supra* note 131, at 2 (offering a "starving hacker" membership option); *Join Counter Culture!*, COUNTER CULTURE LABS, https://www.counterculturelabs.org/join.html [https://perma.cc/F2SD-92S9] (offering sponsored memberships at reduced rates).

133. *See supra* notes 22–28 and accompanying text.

134. Stanley Kaplan & B. John Garrick, *On the Quantitative Definition of Risk*, 1 RISK ANALYSIS 11, 13 (1981); *see also* Ortwin Renn, *Concepts of Risk: A Classification*, *in* SOCIAL THEORIES OF RISK 77 (Sheldon Krimsky & Dominic Golding eds., 1981) (conceptualizing risk to also include ways that undesirable outcomes might come to pass). Both definitions are cited by the National Academies' Committee on Future Biotechnology Products and Opportunities to Enhance Capabilities of the Biotechnology Regulatory System. NAT'L ACADS. OF SCIS., ENG'G, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 69, 107 (2017).

individuals who do not have extensive experience with this technique or knowledge of the underlying science.[135] In addition, individuals who attempt gene editing on themselves in an effort to cure disease or treat disease symptoms could suffer negative health outcomes if they stop taking prescribed medications or forego treatments known to be safe and effective.[136] It is possible that some of these individuals will not appreciate the health risks of their gene-editing activities, and even if they do, there is the danger that they might be pressured by others into accepting those risks. Finally, self-experimentation does not, by design, yield generalizable information and so its outcomes are of limited usefulness to population health. Yet dissemination of information about those outcomes could lead others to try such experiments based on a misunderstanding that they are likely to achieve similar outcomes.

In assessing the likelihood that these undesirable outcomes will come to pass, it is important to note that there have been few reports of human applications of DIY CRISPR thus far. The majority of CRISPR activities in home and community laboratories appear to be limited to editing bacteria and yeast genomes.[137] Aside from Dr. Zayner's highly publicized self-injection, there are also few known instances in which individuals have self-experimented with CRISPR, and all of them involved somatic cells.[138] While discussions on a biohacking forum indicate interest in self-experimenting with CRISPR, these discussions are infrequent and might not reflect the activities that posters actually have undertaken or will undertake in the near future.[139]

135. For a description of the risks of immunological reactions, infection, and potential on-target and off-target effects of CRISPR, see *supra* note 19 and accompanying text.

136. *Cf.* Jessica Lussenhop, *Why I Injected Myself with an Untested Gene Therapy*, BBC NEWS (Nov. 21, 2017), https://www.bbc.com/news/world-us-canada-41990981 [https://perma.cc/UQ8B-T2TJ] (describing the live-streamed self-injection of an unregulated HIV therapy by a biohacker who had stopped taking conventional antiretroviral drugs two years earlier).

137. *See supra* notes 98, 109, 129–130 and accompanying text.

138. While it was reported that one biohacker added DNA constructs to a sample of his own sperm, Antonio Regalado, *The DIY Designer Baby Project Funded with Bitcoin*, MIT TECH. REV. (Feb. 1, 2019), https://www.technologyreview.com/s/612838/the-transhumanist-diy-designer-baby-funded-with-bitcoin/ [https://perma.cc/3KWU-5JTD], he did not use CRISPR to conduct germline editing, Email from David Ishee, Owner, Midgard Kennels, to Christi Guerrini, Assistant Professor, Baylor Coll. of Med. (Mar. 1, 2019, 3:09 PM) (on file with author).

139. For example, in an online discussion of self-experimentation using CRISPR, one poster described plans for self-experimentation using CRISPR to be performed by the person and "close friends." Cha0sthe0rist, *Playing with Viruses*, BIOHACK.ME (Mar. 2018), https://forum.biohack.me/index.php?p=/discussion/comment/26480#Comment_26480

Still, there is reason to believe that instances of attempted self-experimentation with CRISPR might increase in coming years. In particular, the recent news that a Chinese researcher used CRISPR to alter the genomes of twin babies in an effort to confer HIV resistance could embolden some DIY biologists to attempt more human CRISPR experiments.[140] Summarizing the implications of the news, which came on the eve of the Second International Summit on Human Genome Editing in November 2018, a Harvard geneticist remarked that "the genie [is] really out of the bottle."[141] Increased human applications of CRISPR by citizen bioscientists generally will heighten concerns about the associated risks, especially if DIY CRISPR experiments are conducted on germ cells because the genomic alterations or disruptions will be heritable and any harmful effects may be more difficult to identify and mitigate in DIY settings than in traditional settings.

Yet there are benefits to human applications of DIY CRISPR that include the potential for expanding scientific knowledge.[142] Recent examples of important breakthroughs by DIY biologists include the development of an inexpensive diagnostic system to detect malaria from a drop of blood and a genetic test to determine vulnerability to hemochromatosis.[143] Given the realities of the modern research environment, some of these breakthroughs might not occur in traditional research settings if, for example, the investigation is not considered "fundable" because it is too speculative or has limited translational potential. In addition, DIY CRISPR has the potential to increase genetic literacy, where public education about genetics has been identified as both a major challenge and a priority given the

[https://perma.cc/X2PY-2T48]. In another discussion, a poster described efforts to improve on Dr. Zayner's CRISPR/Cas9 myostatin knockout materials and asked individuals to contact the poster if interested in self-experimenting with them. LifeForAll, *Myostatin Knock-out and More*, BIOHACK.ME (Mar. 2018), https://forum.biohack.me/index.php?p=/discussion/comment/26268#Comment_26268 [https://perma.cc/FVY7-LHZZ].

140. Cyranoski & Ledford, *supra* note 27. The news also serves as a reminder that such experiments may not be disclosed to the public until long after they are completed.

141. Sharon Begley, *Claim of CRISPR'd Baby Girls Stuns Genome Editing Summit*, STAT (Nov. 26, 2018), https://www.statnews.com/2018/11/26/claim-of-crispred-baby-girls-stuns-genome-editing-summit/ [https://perma.cc/M55X-PAHQ] (quoting Dr. George Church).

142. *Cf.* Telephone Interview with Keoni Gandall, Research Assistant, Stanford Univ. (Sept. 1, 2018) (on file with author) ("I feel strongly that the future of biotechnology is not going to be made by large companies making proprietary products. It's going to be influenced and created . . . by grassroots movements, the individuals who are trying to help each other.").

143. Sharona Hoffman, *Citizen Science: The Law and Ethics of Public Access to Medical Big Data*, 30 BERKELEY TECH. L.J. 1741, 1755–56 (2015).

increasingly personalized approach to medicine in the United States.[144]

Finally, self-experimentation with CRISPR is consistent with the cultural value that Americans generally place on allowing individuals to make decisions concerning their own bodies.[145] Notions of bodily freedom have particular salience in the context of patients with serious or terminal conditions who lack traditional treatment options—either because there are no validated therapies or those therapies that are validated are too expensive or inaccessible for other reasons.[146] Indeed, citizen bioscientists sometimes emphasize the challenges faced by such patients in conversations about the potential benefits of DIY biology.[147] In the case of therapies that are

144. *See, e.g.*, Lynn G. Dressler et al., *Genomics Education for the Public: Perspectives of Genomic Researchers and ELSI Advisors*, 18 GENETIC TESTING & MOLECULAR BIOMARKERS 131, 131–32, 138 (2014).

145. *See generally* Lewis A. Grossman, *The Origins of American Health Libertarianism*, 13 YALE J. HEALTH POL'Y L. & ETHICS 76 (2013) (providing an overview of therapeutic libertarianism attitudes between the American Revolution and the Civil War). Notions of bodily freedom animate other, sometimes overlapping, DIY movements. *See, e.g.*, Anna Wexler, *The Social Context of "Do-It-Yourself" Brain Stimulation: Neurohackers, Biohackers, and Lifehackers*, FRONTIERS HUM. NEUROSCIENCE, May 2017, at 1, 2–3. Although bodily freedom has deep roots in American jurisprudence, there is no absolute legal right to bodily freedom. *See* Meghan Boone, *The Autonomy Hierarchy*, 22 TEX. J.C.L. & C.R. 1, 17–19 (2016); *cf.* Abigail All. for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 697 (D.C. Cir. 2007) (declining to find a constitutional right for terminally ill patients to access experimental drugs).

146. Famous examples of movements premised, at least in part, on the intersection of bodily freedom and serious illness include AIDS activists' protests of the FDA in the 1980s, seeking quicker access to promising but unproven drugs intended for HIV—after which the Agency updated its policies—and more recently, the "right to try" movement seeking a pathway for patients to access unapproved drugs without FDA authorization, which ultimately led to the 2018 enactment of a federal law creating such a pathway. *See, e.g.*, Lewis A. Grossman, *AIDS Activists, FDA Regulation, and the Amendment of America's Drug Constitution*, 42 AM. J.L. & MED. 687, 688 (2016); Holly Fernandez Lynch, Patricia J. Zettler & Ameet Sarpatwari, *Promoting Patient Interests in Implementing the Federal Right to Try Act*, 320 JAMA 869, 869 (2018); Patricia J. Zettler & Henry T. Greely, *The Strange Allure of State "Right to Try" Laws*, 174 JAMA INTERNAL MED. 1885, 1885 (2014).

147. *See, e.g.*, Josiah Zayner (@jzayner), INSTAGRAM (Dec. 17, 2018), https://www.instagram.com/p/Brf0pOKFl9z/ [https://perma.cc/7QGF-XUBU]; *see also* David Ishee, *The People Who Fall Through the Cracks*, ANTISENSE (Nov. 12, 2018), http://theantisense.com/2018/11/12/the-people-who-fall-through-the-cracks/ [https://perma.cc/L9AV-LBQ9] (explaining that individuals with genetic diseases and parents of children with genetic diseases regularly approach biohackers who have appeared in the media to ask for help finding cures); Josiah Zayner, *Biohack the Planet Day 2018 – Day 2-Sept 1*, YOUTUBE (Sept. 1, 2018), https://www.youtube.com/watch?v=CHQleUE-Iwk [https://perma.cc/WPX3-FMRY] [hereinafter Zayner, *Biohack the Planet*] (conversation between Tristan Roberts and one of the authors—Patricia J. Zettler—including discussion of this issue).

known to be effective and relatively easy to manufacture, DIY biology might provide an avenue for patients who cannot afford the marketed therapies to make their own.[148] Moreover, and regardless of whether DIY CRISPR ultimately produces safe and effective therapies, or products with enhancing or aesthetic uses, it may have societal value as a medium for political and creative expression.[149]

III. OVERSIGHT OF DIY CRISPR

The oversight of DIY CRISPR should aim to strike an appropriate balance between preventing its potential harms and promoting its potential educational, expressive, and scientific benefits. Assessment of this balance requires an understanding of the relevant oversight mechanisms. To that end, this part describes the external legal and regulatory mechanisms, as well as the internal mechanisms adopted by DIY biology communities and suppliers of biological materials, that apply or potentially could apply to DIY CRISPR.

A. External Oversight

Many reports of DIY CRISPR note that its regulation by federal and state authorities is an important issue, but the scope of regulation has not yet been examined in detail. This section provides this critical information by explaining how, exactly, existing regulations relevant to biotechnology and scientific research apply to DIY CRISPR. The specific regulatory schemes that are addressed are: (1) the regulation of biological drug products by the FDA; (2) the regulation of genetic research by the National Institutes of Health ("NIH") and state and local governments; (3) the regulation of clinical laboratories by the Centers for Medicare and Medicaid Services ("CMS"); (4) federal

148. *See, e.g.*, Gallegos et al., *supra* note 32, at 1211. Marketed therapies can be very expensive. For example, the three currently approved gene therapies each cost hundreds of thousands of dollars. Rachel Salzman et al., *Addressing the Value of Gene Therapy and Enhancing Patient Access to Transformative Treatments*, 26 MOLECULAR THERAPY 2717, 2718 (2018) (stating that approved therapies cost between $373,000 to $850,000). Of course, drug pricing and health care costs more generally are pressing and complicated problems that ideally would be solved through reforms to the overall system rather than through patients attempting individual work-arounds. *See generally* Aaron S. Kesselheim, Jerry Avorn & Ameet Sarpatwari, *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 JAMA 858 (2016); Rachel E. Sachs, *Delinking Reimbursement*, 102 MINN. L. REV. 2307 (2018).

149. *See* NUFFIELD COUNCIL 2016, *supra* note 29, at 100 (describing the use of CRISPR in bioactivism and bioart).

and state protections of human subjects in research; (5) federal patent law; and (6) state tort law.

This section concludes that the standard account that regulation is largely dependent on federal funding does not tell the whole story.[150] The FDA in particular has broad authority to regulate a number of activities relevant to DIY human gene editing, and state tort law is a potentially important constraint on activities that cause harm. To date, however, these regulations remain almost entirely untested in DIY biology contexts.

1. FDA Requirements

The FDA is perhaps the most obvious choice to regulate DIY CRISPR because of the Agency's expertise in evaluating the safety and effectiveness of medical technologies.[151] It does indeed have the potential to reach a variety of DIY CRISPR activities through its authority to regulate the "articles"—that is, the products, materials, or things—used in these activities.[152] In November 2017, the FDA stated that it "considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy," including self-administered materials and materials intended for performance-enhancing and aesthetic uses, subject to the requirements for biological drug products.[153] These

150. *See, e.g.*, CTR. FOR GLOB. SEC. RESEARCH, *supra* note 112, at 4–5 (explaining that risk and regulation of biotechnologies generally "rel[y] on the control of federal funding as a mechanism to enforce 'voluntary' standards and guidelines for ensuring public health, human subject protections, and environmental safeguards").

151. *See* EXEC. OFFICE OF THE PRESIDENT, MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS: FINAL VERSION OF THE 2017 UPDATE TO THE COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY 1 (2017), https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/2017_coordinated_framework_update.pdf [https://perma.cc/U4VE-5TCS]; *see also* Alex Philippidis, *Gene Therapy Briefs*, 28 HUM. GENE THERAPY CLINICAL DEV. 1, 1 (2017) (describing the FDA's "product-focused, science-based regulatory policy" approach to gene-editing technologies and applications); *cf.* Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1826 (1996) (explaining that the FDA's position is that the "fundamental principles underlying evaluation of any therapeutic intervention, whether it is a drug [or a] device . . . are the same" (quoting FINAL REPORT OF THE FDA COMMITTEE FOR CLINICAL REVIEW (1993), *reprinted in* SUBCOMM. ON OVERSIGHT & INVESTIGATIONS, HOUSE COMM. ON ENERGY & COMMERCE, 103D CONG., LESS THAN THE SUM OF ITS PARTS: REFORMS NEEDED IN THE ORGANIZATION, MANAGEMENT, AND RESOURCES OF THE FOOD AND DRUG ADMINISTRATION'S CENTER FOR DEVICES AND RADIOLOGICAL HEALTH 98, 105 (Comm. Print 1993))).

152. *Cf.* 21 U.S.C. § 321 (2012) (defining the "articles" within the FDA's jurisdiction).

153. *Information About Self-Administration of Gene Therapy*, FDA (Nov. 21, 2017), https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm586343.htm [https://perma.cc/J7Z6-FWJA].

requirements are extensive and include, among other things, good laboratory practice requirements for preclinical research, requirements for FDA authorization of clinical trials (which must be well designed and conducted in compliance with human research subject protections), good manufacturing practices, postapproval safety monitoring and restrictions on advertising and promotion, and, in some cases, risk-mitigation programs.[154] Likely most important for DIY biologists, and put most simply, biological drug products—including gene therapies intended for self-administration—cannot legally be sold without the FDA's authorization.[155]

Notwithstanding the FDA's clear statement on the use of CRISPR in humans, there are nuances to the scope of the FDA's jurisdiction that are important for understanding which DIY CRISPR materials the Agency can regulate.[156] First, the key to understanding what counts as a biological drug product is determining the "intended use" of the material. This is because the Federal Food, Drug, and Cosmetic Act ("FDCA") broadly defines drugs subject to FDA jurisdiction as "articles *intended for use* in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" or "*intended* to affect the structure or any function of the

154. *See, e.g.*, Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WIS. L. REV. 929, 937 (describing the FDA as "responsible for analyzing information related to a drug's risks and benefits throughout the lifecycle of a drug").

155. 21 U.S.C. §§ 331(d), 355(a), (i) (2012); 42 U.S.C. § 262(a) (2012).

156. There are similar, although not identical, issues with respect to the scope of the FDA's jurisdiction over other emerging DIY or direct-to-consumer technologies. *See, e.g.*, Dianne Hoffmann et al., *Improving Regulation of Microbiota Transplants*, 358 SCIENCE 1390, 1390 (2017); Margaret F. Riley & Bernat Olle, *FDA's Pathway for Regulation of FMT: Not So Fraught*, 2 J.L. & BIOSCIENCES 742, 743–44 (2015); Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. & BIOSCIENCES 396, 397–98 (2015); Anna Wexler, *A Pragmatic Analysis of the Regulation of Consumer Transcranial Direct Current Stimulation (TDCS) Devices in the United States*, 2 J.L. & BIOSCIENCES 669, 671–73 (2015); Patricia J. Zettler, *What Lies Ahead for FDA Regulation of tDCS Products?*, 3 J.L. & BIOSCIENCES 318, 322–23 (2016); *see also* Barbara J. Evans, *The Limits of FDA's Authority to Regulate Clinical Research Involving High-Throughput DNA Sequencing*, 70 FOOD & DRUG L.J. 259, 261–65 (2015) (considering FDA regulation of DNA sequencing); Barbara J. Evans, *The First Amendment Right to Speak About the Human Genome*, 16 U. PA. J. CONST. L. 549, 551 (2014) (exploring "whether the First Amendment can help clear away old laws that limit genomic speech"); Erika Lietzan, *Access Before Evidence and the Price of FDA's New Drug Authority*, 53 U. RICH. L. REV. (forthcoming 2019) (manuscript at 19–24), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3346574 (exploring the implications of applying FDA approval authorities to fecal microbiota materials); W. Nicholson Price II, *Regulating Black-Box Medicine*, 116 MICH. L. REV. 421, 438 (2017) (considering FDA regulation of medical algorithms).

body of man or other animals."[157] The Agency can take the position that any use of CRISPR in humans makes those CRISPR materials a biological drug product because gene editing is, by design, intended to affect the structure or function of the body. Indeed, since 1986 the FDA has said that human gene therapies are biological drug products.[158]

The question in DIY contexts, however, will be which CRISPR materials and kits are intended for use in humans and nonhuman animals given that many materials and kits are expressly described as intended for basic discovery or educational uses. Importantly, the FDA is not limited to considering express, public statements in making this determination.[159] Courts have concluded, and the FDA has agreed, that the Agency may consider "any relevant source" of evidence of a product's intended use.[160] Most controversially, the FDA has taken the position that, in certain circumstances, it can rely on a manufacturer's, seller's, or distributor's knowledge about how consumers intend to use the product as evidence of statutory intended

157. 21 U.S.C. § 321(g)(1) (2012) (emphasis added). Within this broad category of drugs, certain types of items—any "virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man"—must also meet the definition of a biological product under the Public Health Service Act ("PHSA"). 21 C.F.R. § 600.3 (2018). Different statutory and regulatory provisions govern the regulation of biological and traditional, small-molecule drug products—for example, the approval standard for biological drug products is "safe, pure, and potent," while that for small-molecule drugs focuses on safety and effectiveness. 42 U.S.C. § 262(i) (2012). But the FDA has interpreted many of the requirements to be essentially the same. This Article therefore focuses on the statutory and regulatory requirements for the more broadly defined drugs, rather than biological products.

158. Statement of Policy for Regulating Biotechnology Products, 51 Fed. Reg. 23,309, 23,311 (June 26, 1986); Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248, 53,249 (Oct. 14, 1993).

159. *See* 21 C.F.R. § 201.128 (2018).

160. *See, e.g.*, Nat'l Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 334 (2d Cir. 1977) ("[T]he FDA is not bound by the manufacturer's subjective claims of intent .... Such intent also may be derived or inferred from labeling, promotional material, advertising, and 'any other relevant source.'"); Clarification of When Products Made or Derived from Tobacco are Regulated as Drugs, Devices, or Combination Products, 82 Fed. Reg. 2193, 2199 (Jan. 9, 2017) (to be codified at 21 C.F.R. pts. 201, 801, and 1100) ("[T]he Agency may look to any relevant source to determine intended use."); *cf.* FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 156 (2000) (rejecting the FDA's attempt to regulate tobacco products as drugs and devices, without disagreeing with the argument that the tobacco products' design was evidence of their intended use). For more detailed discussion of the kinds of evidence that the FDA might rely on to demonstrate a product's intended use, see, for example, Patricia J. Zettler, Natalie Hemmerich & Micah L. Berman, *Closing the Regulatory Gap for Synthetic Nicotine Products*, 59 B.C. L. REV. 1933, 1952–70 (2018).

use.[161] Therefore, even if a person or company manufacturing, selling, or distributing DIY CRISPR products expressly describes them as intended for educational or basic science uses, the FDA might rely on (or try to rely on), for example, elements of product design that suggest an intended human use,[162] online videos of company executives using the products on themselves,[163] or even mere knowledge that consumers are acquiring the products for self-experimentation as evidence that the materials are "gene therapies" intended for human use.[164]

A second relevant nuance to the FDA's authority over DIY CRISPR materials and kits is that the Agency has jurisdiction over only those products that move in interstate commerce or include a component that moves in interstate commerce.[165] In most contexts, the requirement that a product or one of its components have moved in interstate commerce does not significantly limit FDA jurisdiction. Modern supply chains are complex, and products and their components generally travel across state and national lines at many points.[166] For example, DIY CRISPR products sold through a website to consumers all over the United States or the world would clearly be products moving in interstate commerce such that the FDA would have jurisdiction.[167] But the connection with interstate commerce need not be so obvious for the FDA to have jurisdiction. For instance,

161. Whether the Agency can rely on manufacturer, seller, and distributor knowledge of consumer intent is at the heart of a dispute over the FDA's 2017 attempt to revise its regulatory definition of intended use. As of the time of writing this Article, the Agency's intended use regulations continue to permit it to rely on such knowledge as evidence of intended use. § 201.128; Clarification of When Products Made or Derived from Tobacco are Regulated as Drugs, Devices, or Combination Products, 82 Fed. Reg. at 2198, 2200 (providing the January 2017 Final Rule); Clarification of When Products Made or Derived from Tobacco are Regulated as Drugs, Devices, or Combination Products; Further Delayed Effective Date; Request for Comments, 82 Fed. Reg. 14,319, 14,320 (Mar. 20, 2017) (to be codified at 21 C.F.R. pts. 201, 801, and 1100) (delaying the effective date of the January 2017 Final Rule).

162. *Cf.* Clarification of When Products Made or Derived from Tobacco are Regulated as Drugs, Devices, or Combination Products, 82 Fed. Reg. at 2208 (describing circumstances in which the FDA has relied on product design as evidence of intended use).

163. *Cf.* Brown, *Genetically Engineering Yourself*, *supra* note 3 (describing Dr. Zayner's live-streamed self-injection).

164. *See* § 201.128.

165. 21 U.S.C. § 331 (2012). Moving in interstate commerce requires crossing state, territory, or national borders at some point. *Id.* § 321(b).

166. *Cf. id.* § 379a (providing that the FDA may presume the necessary connection between a product and interstate commerce).

167. *Cf.* ODIN, *supra* note 8 (selling biohacking products for various uses, including educational and nonhuman animal uses).

interventions derived from patients' own stem cells—but including an ingredient that had previously crossed state lines—have the necessary intersection with interstate commerce.[168]

Moreover—and importantly for DIY biologists who distribute or provide materials to one another—money likely does not need to change hands to trigger FDA jurisdiction in many instances.[169] Most provisions of the FDCA do not expressly require a sale to trigger FDA jurisdiction. For example, the FDCA prohibits introducing into interstate commerce any adulterated, misbranded, or unapproved drug without reference to a "sale."[170]

The FDA therefore could reasonably conclude that many manufacturers, sellers, or distributors of DIY CRISPR materials and kits intended for human (or nonhuman animal) use are or include biological drug products that fall within the Agency's jurisdiction. The

168. United States v. Regenerative Scis., LLC, 741 F.3d 1314, 1320 (D.C. Cir. 2014); *see also* United States v. Allgyer, No. Civil Action No. 11-02651, 2012 WL 355261, at *4 (E.D. Pa. Feb. 3, 2012); 21 C.F.R. § 1240.61(a) (2018); Sean O'Conner & Erika Lietzan, *The Surprising Reach of FDA Regulation of Cannabis, Even After Descheduling*, 68 AM. U. L. REV. 823, 908–09 (2019) (discussing the FDA's position on raw milk and cannabis products' connection with interstate commerce); *Food Safety and Raw Milk*, FDA (Nov. 1, 2011), https://web.archive.org/web/20120103191250/www.fda.gov/Food/FoodSafety/Product-SpecificInformation/MilkSafety/ucm277854.htm [https://perma.cc/NVM5-38WJ].

169. *See* Patti Zettler, *Decoding FDA's Statement on DIY Gene Therapies*, OBJECTIVE INTENT BLOG (Dec. 11, 2017), https://objectiveintent.blog/2017/12/11/decoding-fdas-statement-on-diy-gene-therapies/ [https://perma.cc/KGP7-E7HL].

170. 21 U.S.C. § 331 (2012). The main exception is that the FDCA prohibits actions that misbrand or adulterate drugs (or other articles) "while held for sale after shipment in interstate commerce." *Id.* § 331(k). This provision allows the FDA to reach *intra*state distribution of products that have a connection to *inter*state commerce earlier in the supply chain, such as the distribution of fentanyl to individuals in the same state that the drug was manufactured in, when the ingredients to make the fentanyl crossed state lines. *See, e.g.*, Baker v. United States, 932 F.2d 813, 816 (9th Cir. 1991) ("We hold that wholly intrastate manufactures and sales of drugs are covered by 21 U.S.C. § 331(k) as long as an ingredient used in the final product travelled in interstate commerce."). Courts have concluded that a sale has occurred under the meaning of this provision of the FDCA in a broad range of settings, even if the recipient does not directly pay the distributor. *See, e.g.*, United States v. Kaplan, 836 F.3d 1199, 1208 (9th Cir. 2016), *cert. denied*, 137 S. Ct. 1392 (2017); United States v. Evers, 643 F.2d 1043, 1049 (5th Cir. 1981); United States v. Rhody Dairy, L.L.C., 812 F. Supp. 2d 1239, 1244 (W.D. Wash. 2011). The major limitation on this broad interpretation is that, in *United States v. Geborde*, 278 F.3d 926 (9th Cir. 2002), the Ninth Circuit found that a man who made a recreational drug (GHB) that he then gave to "several" friends for free at a house party was engaged in "wholly non-commercial" distribution that did not involve a product being held for sale under the meaning of the FDCA. *Id.* at 927. Where biohackers distribute DIY CRISPR products without charging money, that conduct may be neither as noncommercial as distributing homemade drugs to a small group of friends in a residential setting nor as commercial as a physician treating patients. In other words, it is not clear that giving away DIY CRISPR materials for free will be sufficient to escape FDA jurisdiction—absent a court concluding that such distribution is wholly noncommercial, analogous to the circumstances in *Geborde*.

fact that the Agency can potentially reach materials and kits that are not expressly described as for human or nonhuman animal use and that are freely distributed are particularly salient takeaways for DIY communities. The FDA also could—and likely would—determine that CRISPR products within its jurisdiction can be used only with a prescription from a licensed health care provider and cannot be sold directly to consumers for their own use.[171]

At the same time, the FDA likely cannot reach DIY CRISPR activities when users make and self-administer interventions themselves, without having purchased products for which there is evidence that the products were intended for human (or nonhuman animal) use. The FDA also cannot regulate instructions for self-administering interventions that are not tied to a product or provided on behalf of a manufacturer, seller, or distributor of DIY CRISPR products. Although the FDA regulates the advertising and promotion of prescription drugs, including prescription biological drug products, the Agency's authority reaches only those statements made by or on behalf of product manufacturers, sellers, and distributors.[172] Together, these exceptions describe narrow but clear gaps in the FDA's oversight of the safety and effectiveness of human applications of DIY CRISPR.

Moreover, even for those products within the FDA's jurisdiction, it is not clear how extensively the Agency will enforce its requirements. The FDA generally has discretion to decide whether to enforce its requirements for any particular product or category of product,[173] and despite the FDA's November 2017 statement about the dangers of DIY genetic engineering, it has not yet publicly initiated significant enforcement activities in this space. This lack of enforcement may reflect, among other things, that the Agency does not consider DIY gene editing to be a public health priority. It is also possible that the Agency has concerns about its ability to demonstrate that DIY CRISPR products are biological drugs (for example, in the absence of express claims that the products address disease or affect the structure or function of the body). In sum, the FDA's authority likely could intersect with many—although certainly not all—DIY

171. 21 U.S.C. § 353(b) (2012).

172. *Cf.* 21 C.F.R. § 201.128 (2018).

173. *See, e.g.*, Heckler v. Chaney, 470 U.S. 821, 837–38 (1985); Nathan Cortez, *Regulating Disruptive Innovation*, 29 BERKELEY TECH. L.J. 175, 221 (2014); Lars Noah, *The Little Agency That Could (Act with Indifference to Constitutional and Statutory Strictures)*, 93 CORNELL L. REV. 901, 902 (2008); Jordan Paradise, *Regulatory Silence at the FDA*, 102 MINN. L. REV. 2383, 2388 (2018).

CRISPR activities, but it remains to be seen whether the FDA will enforce its authority in this space.

2. NIH, State, and Local Research Requirements

While countries like Germany prohibit gene editing (including the use of DIY CRISPR kits) outside of licensed facilities,[174] there are no federal laws in the United States that limit gene editing to approved individuals or settings. However, since 1976, the NIH has regulated the conduct of research involving recombinant or synthetic nucleic acid molecules that is funded by the NIH or is conducted at or sponsored by institutions that receive NIH funds for research involving such molecules.[175] Those rules, which are set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"), require approval of nonexempt research by an Institutional Biosafety Committee ("IBC") (or at least notification to the IBC), and sometimes also approval by the NIH Director, NIH Office of Science Policy, or an Institutional Review Board ("IRB"), possibly with input from the Recombinant DNA Advisory Committee ("RAC").[176] The NIH Guidelines also require researchers to adhere to biosafety containment procedures

174. *See, e.g.*, Gesetz zur Regelung der Gentechnik [Gentechnikgesetz – GenTG] [Act on the Regulation of Genetic Engineering], Dec. 16, 1993, § 8(1) (Ger.) (prohibiting "genetic engineering operations" except in authorized facilities); *see also* Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, *Genetic Engineering with Biology Kits: Simple but Possibly Punishable*, BVL.BUND.DE (Jan. 25, 2017), https://www.bvl.bund.de/DE/06_Gentechnik/04_Fachmeldungen/2017/2017_01_25_DIY-Kits.html [https://perma.cc/WWS4-64L4]. Although these regulations may make it impossible for German biohackers to conduct gene editing in private settings, they can do so in authorized community laboratories. *See* Kristen V. Brown, *Germany is Threatening Biohackers with Prison*, GIZMODO (Feb. 9, 2017, 8:46 AM), https://gizmodo.com/germany-is-threatening-biohackers-with-prison-1792143993 [https://perma.cc/2A4D-RMT5].

175. U.S. DEP'T OF HEALTH & HUMAN SERVS., NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES 9–10 (2016) [hereinafter NIH GUIDELINES]. It is the responsibility of institutions covered by the NIH Guidelines and those associated with them to adhere to the general intent and specific requirements of the NIH Guidelines. *Id.* at 24.

176. *See id.* at 15–23. The RAC is the public advisory committee that advises the U.S. Department of Health and Human Services ("HHS") Secretary, HHS Assistant Secretary for Health, and NIH Director on recombinant and synthetic nucleic acid molecule research. *Id.* at 11. A proposal to eliminate RAC review of human gene transfer research was recently published in the Federal Register. *See generally* National Institutes of Health (NIH) Office of Science Policy (OSP) Recombinant or Synthetic Nucleic Acid Research: Proposed Changes to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), 83 Fed. Reg. 41,082 (Aug. 17, 2018). For a discussion of the evolution of RAC responsibilities, see Francis S. Collins & Scott Gotlieb, *The Next Phase of Human Gene-Therapy Oversight*, 379 NEW ENG. J. MED. 1393, 1395 (2018).

that depend on the risks presented by the biological agents involved in specific studies.[177] Risk is determined based on an assessment of each agent's ability to cause disease in humans, the available treatments for such disease, and how the agent will be manipulated.[178]

Because the vast majority of DIY biologists appear to be self-funded and do not conduct work in NIH-funded institutions, the NIH Guidelines do not apply to them.[179] This means that DIY biologists are not obligated to set and adhere to containment conditions for, or to obtain external approval of, their CRISPR activities in accordance with the NIH Guidelines. The exception is if those activities take place in a state or local jurisdiction that has elected to enforce the NIH Guidelines. New York State and the City of Cambridge, Massachusetts, for example, prohibit certain activities involving recombinant DNA without a state or local permit, where approval is conditioned on compliance with the NIH Guidelines.[180]

Also unlike other countries,[181] the United States has not adopted a federal ban on germline editing. However, a number of legal provisions have the effect of severely limiting the ability of researchers to edit human germlines. As noted above, genetic-engineering products subject to FDA oversight require the Agency's authorization for research or distribution. Since 2016, however, Congress has effectively prohibited the FDA from approving any intervention that involves human germline modification or taking any action that would allow clinical trials of such therapies to proceed.[182] Additionally, the NIH is prohibited

177. *See* NIH GUIDELINES, *supra* note 175, at 12–15.

178. *Id.* at 12.

179. Nevertheless, the NIH Guidelines encourage uncovered individuals and institutions to follow the prescribed standards and procedures and to affiliate with institutions that have approved IBCs. *Id.* at 34.

180. New York restricts the conduct of recombinant DNA activities to institutions certified by the New York State Commissioner of Health. *See* N.Y. PUB. HEALTH LAW §§ 3220–3223 (McKinney 2018); N.Y. COMP. CODES R. & REGS. tit. 10, subpt. 61-1 (Westlaw through 2018). To obtain certification, an institution must provide written assurance that it will comply with the NIH Guidelines. N.Y. COMP. CODES R. & REGS. tit. 10, § 61-1.3. Similarly, all persons and entities who wish to conduct research using recombinant DNA in Cambridge, Massachusetts, must first obtain a permit from the Cambridge Commissioner of Health and Hospitals, which requires the applicant's written agreement to comply with the NIH Guidelines. CAMBRIDGE, MASS., MUNICIPAL CODE ch. 8.20.050 (2017).

181. *See* Melanie Senior, *UK Funding Agencies Weigh in on Human Germline Editing*, 33 NATURE BIOTECHNOLOGY 1118, 1119 (2015) (noting that at least twenty-five countries prohibit human germline modification).

182. *See* I. Glenn Cohen & Eli Y. Adashi, *The FDA is Prohibited from Going Germline*, 353 SCIENCE 545, 546 (2016) (describing the history and effect of the

from funding the creation of human embryos for research purposes or research in which human embryos are destroyed, discarded, or subjected to risk of serious injury or death.[183] Finally, for researchers who are covered by the NIH Guidelines, the NIH will not entertain proposals for human germline alterations.[184]

3. Federal Clinical Laboratory Requirements

Although federal requirements related to gene editing do not apply to most DIY biologists who are self-funded and do not work in NIH-funded institutions, other requirements might reach the settings in which they conduct their research. The most relevant requirements govern clinical laboratories. In particular, the Clinical Laboratory Improvement Amendments of 1988 ("CLIA") and implementing regulations require certification (or waiver of certification) of all laboratories where human specimens are examined for the purpose of providing information for the diagnosis, prevention, or treatment of disease or the assessment of health.[185] Such laboratories must satisfy quality control, documentation, personnel, and proficiency testing requirements that are intended to help ensure the accuracy, reliability, and timeliness of clinical test results.[186] However, the regulations do not apply to laboratories where testing on others is performed if the results are not reported back to those individuals or their clinicians. In such circumstances, the laboratories fall under a research exception to CLIA.[187]

Because clinical testing generally does not take place in community laboratories—and indeed would be prohibited by the

prohibition, which was first introduced as a rider to the Consolidated Appropriations Act of 2016). The rider continues to be renewed, most recently in the Consolidated Appropriations Act, 2018, Pub. L. No. 115-141, § 734, 132 Stat. 348, 389.

183. Francis S. Collins, *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT'L INSTITUTES HEALTH (Apr. 28, 2015), https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos [https://perma.cc/X4XF-ZG83] (referencing the Balanced Budget Downpayment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996)).

184. NIH GUIDELINES, *supra* note 175, at 100.

185. 42 U.S.C. § 263a(a) (2012); 42 C.F.R. §§ 493.2–.3 (2018).

186. 42 U.S.C. § 263a(f)(1) (2012).

187. *See* 42 C.F.R. § 493.3(b)(2) (2018); CENTERS FOR MEDICARE & MEDICAID SERVICES, RESEARCH TESTING AND CLINICAL LABORATORY IMPROVEMENT AMENDMENTS OF 1988 (CLIA) REGULATIONS (2014), https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/Research-Testing-and-CLIA.pdf [https://perma.cc/AR86-EJ25] (stating that "facilities performing research testing on human specimens that do not report patient-specific results may qualify to be excepted from CLIA certification" (emphasis omitted)).

safety policies of many[188]—it is unlikely that community laboratories are governed by CLIA. Although it is possible that clinical testing is performed in some private laboratories, we are not aware of any instance of this. Accordingly, federal clinical laboratory regulations do not appear to provide effective oversight of DIY human gene-editing activities.

4. Federal and State Human Research Subject Protections

Yet clinical applications of DIY CRISPR could be subject to federal rules intended to protect the safety and welfare of research participants. For one, if a product qualifies as an FDA-regulated drug, its use in clinical studies must comply with FDA human research-subject protections.[189] Independent of whether FDA rules apply, clinical studies involving CRISPR could be subject to federal protections detailed in the Federal Policy for the Protection of Human Subjects (known as the Common Rule).[190] Like FDA human research-subject protections, the Common Rule requires IRB approval of research involving human participants, which is based on the determination that the anticipated risks to participants are minimized and reasonable in relation to the anticipated benefits and that participants provide their informed consent to participate.[191] However, the Common Rule is limited to studies involving human participants or their identifiable private information or biospecimens that are federally funded or supported.[192] We are not aware of any DIY CRISPR activities that satisfy these conditions and therefore are regulated by the Common Rule.[193]

188. *See* discussion *infra* Section III.B.1.b.

189. Protection of Human Subjects; Prisoners Used as Subjects in Research, 45 Fed. Reg. 36, 386, 36,390 (May 30, 1980) (to be codified at 21 C.F.R. pt. 50); Protection of Human Subjects; Standards for Institutional Review Boards for Clinical Investigations, 46 Fed. Reg. 8958, 8975 (Jan. 27, 1981) (to be codified at 21 C.F.R. pt. 56).

190. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7150 (Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46).

191. 21 C.F.R. §§ 50.20, .25, 56.103, .109, .111 (2018); 45 C.F.R. §§ 46.109, .111, .116 (2018). According to both rules, informed consent is legally effective when consent is sought in circumstances that provide the prospective subject or her representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion, and where information about the risks and benefits of the study (among other things) is provided in a language understandable to the subject or her representative. 21 C.F.R. § 50.20; 45 C.F.R. § 46.116(a).

192. 45 C.F.R. §§ 46.101(a), .102(e), (l) (2018).

193. Some institutions interpret the Common Rule as applicable to researchers' participation in their own experiments. *See, e.g.*, Johns Hopkins Med. Office of Human Subjects Research, *Investigators as Study Participants (Self-Experimentation)*, JOHNS HOPKINS MED. (July 2005), https://www.hopkinsmedicine.org/institutional_review_board/

Some states, however, have adopted protections for research participants that do not turn on funding source and so potentially reach some DIY CRISPR activities.[194] Among them, California, which is home to a number of community laboratories, has adopted protections for participants in "medical experiment[s]," which are defined to include the

> severance or penetration or damaging of tissues of a human subject or the use of a drug or device . . . in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject.[195]

The few published court opinions that have interpreted California's human research subject protections have done so in contexts involving interventions having therapeutic purposes and found that the rules did not apply.[196] It is therefore unclear when gene editing conducted by DIY biologists might qualify as regulated medical experimentation in California. Self-experimentation would surely not be covered by virtue of the statute's provisions for damages since one cannot sue oneself.[197] On the other end of the spectrum, DIY clinical studies conducted as "pure" research would likely be

guidelines_policies/guidelines/self_experimentation.html [https://perma.cc/T8AV-U2JM]. However, these institutional policies and guidelines will not reach self-experimentation and other activities that have no connection to those institutions.

194. *See, e.g.*, CAL. HEALTH & SAFETY CODE §§ 24170–24179.5 (West 2006 & Supp. 2019); MD. CODE. ANN. HEALTH–GEN. §§ 13-2001 to -2004 (Westlaw through legislation effective Apr. 18, 2019, from the 2019 Reg. Sess.); N.Y. PUB. HEALTH LAW §§ 2440–2446 (McKinney 2019); VA. CODE ANN. §§ 32.1-162.16 to -162.20 (2015 & Supp. 2018).

195. § 24174(a). "Medical experiments" also include investigational uses of drugs or devices conducted in accordance with FDA or state regulations applicable to clinical trials. *Id.* § 24174(b).

196. *See, e.g.*, Perez v. Nidek Co., 711 F.3d 1109, 1114–16 (9th Cir. 2013) (finding that eye surgery had a therapeutic purpose and so was not medical experimentation and observing that California's human research subject protections did not apply to physicians' therapeutic off-label uses of drugs or devices, which the legislature had intentionally excluded from the definition of medical experimentation); *In re* Ariz. Theranos, Inc., Litig., 256 F. Supp. 3d 1009, 1044–45 (D. Ariz. 2017), *partial reconsideration*, Nos. 2:16-cv-2138-HRH, 2:16-cv-2373-HRH, 2:16-cv-2660-HRH, 2:16-cv-2775-HRH, 2:16-cv-3599-HRH, 2017 WL 4337340 (D. Ariz. Sept. 29, 2017) (holding that blood testing had a therapeutic purpose and was not medical experimentation where the tested individual's physician prescribed medication based on the results of those tests).

197. *See* § 24176 (providing for damages against any person "primarily responsible for the conduct of a medical experiment" and any "representative or employee of a pharmaceutical company, who is directly responsible for contracting with another person for the conduct of a medical experiment," in violation of the regulations).

covered[198] and individuals would be required to provide their informed consent to participate.[199]

Maryland, on the other hand, extends the Common Rule to all human subjects research occurring in the state.[200] In so doing, Maryland adopts the Common Rule's definition of regulated "research" as a "systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge."[201] The scope of Maryland's regulations is therefore broader than California's and likely would cover all DIY CRISPR human applications (although perhaps not self-experimentation) regardless of whether they have any therapeutic purpose.[202] Maryland also explicitly requires both independent review of protocols and the informed consent of participants.[203] However, we are not aware of any judicial opinions that apply Maryland's regulations, consistent with the relatively slender body of precedent interpreting state human research subject protections. Especially because these protections are not well tested in traditional research scenarios, it is unclear whether they might provide effective oversight of DIY CRISPR.

5. Patent Law

Patent law provides an interesting—but also likely ineffective—governance mechanism for DIY CRISPR. Foundational patents have been obtained on CRISPR's basic technology, and many of those patents already have been licensed to biotechnology and pharmaceutical companies.[204] Meanwhile, researchers are seeking

198. *See* Trantafello v. Med. Ctr. of Tarzana, 227 Cal. Rptr. 84, 87 n.2 (Cal. Ct. App. 1986) (describing California's protections as limited to "experiments on human subjects in the course of pure research").

199. CAL. HEALTH & SAFETY CODE §§ 24172–24173, 24175 (West 2006).

200. MD. CODE. ANN. HEALTH–GEN. § 13-2002 (Westlaw through legislation effective Apr. 18, 2019, from the 2019 Reg. Sess.).

201. *Id.* § 13-2001(e) (adopting the definition of "research" from 45 C.F.R. § 46.102(l) (2018)).

202. The regulations are enforced by Maryland's Office of Attorney General, *id.* § 13-2004, and it is unclear whether the office would both interpret the regulations to cover self-experimentation and apply them to enjoin these activities.

203. *Id.* § 13-2002 (requiring that all human subjects research comply with the Common Rule).

204. *See* Jorge L. Contreras & Jacob S. Sherkow, *CRISPR, Surrogate Licensing, and Scientific Discovery*, 355 SCIENCE 698, 698 (2017). The owner of the foundational patent on CRISPR in eukaryotic cells has been the subject of a protracted legal battle, which was recently settled in favor of the Broad Institute. *See generally* Regents of the Univ. of Cal. v. Broad Inst., 903 F.3d 1286 (Fed. Cir. 2018) (holding that there was no interference-in-fact); Heidi Ledford, *Pivotal CRISPR Patent Battle Won by Broad Institute*, NATURE

patent protection for numerous, narrower CRISPR components and applications.[205] From 2000 to 2015, patent applications were filed around the world on over 600 CRISPR discoveries, with the majority filed in the United States.[206]

The owner of an issued patent has a legal right to stop others from making, using, selling, or offering to sell the patented discovery for twenty years from the application date.[207] Those who conduct any of these activities without the patent owner's permission are liable for direct patent infringement, which is a strict liability offense.[208] This means that one's knowledge (or lack of knowledge) of the patent is generally irrelevant; an individual can be liable for infringing a patent about which she is completely ignorant.[209] One's reasons for infringing a patent, even if innocent and noncommercial, also are generally irrelevant.[210]

Applying these rules to the large and still expanding CRISPR patent landscape, many individuals using CRISPR in DIY settings may be infringing one or more CRISPR patents.[211] If sued for infringement, however, they may be able to rely on an experimental

(Sept. 10, 2018), https://www.nature.com/articles/d41586-018-06656-y [https://perma.cc/46GJ-TBCW] (discussing the outcome of the litigation).

205. *See* Knut J. Egelie et al., *The Emerging Patent Landscape of CRISPR–Cas Gene Editing Technology*, 34 NATURE BIOTECHNOLOGY 1025, 1028–29 (2016).

206. *See id.* at 1027–29.

207. *See* 35 U.S.C. § 154 (2012 & 2017 Supp.) (defining patent term); *id.* § 271 (2012) (defining patent infringement).

208. Jurgens v. CBK, Ltd., 80 F.3d 1566, 1570 n.2 (Fed. Cir. 1996) (explaining that a court must award damages for direct patent infringement "regardless of the intent, culpability or motivation of the infringer"); Robert P. Merges, *A Few Kind Words for Absolute Infringement Liability in Patent Law*, 31 BERKELEY TECH. L.J. 1, 3 (2016) ("Put simply, patent infringement is an absolute liability regime.").

209. Tun-Jen Chiang, *The Reciprocity of Search*, 66 VAND. L. REV. 1, 10 (2013) (noting that "anyone who makes, uses, or sells something that is covered by a patent will infringe, even if he is unaware of the patent").

210. There are exceptions to this rule for medical practitioners whose infringing activities constitute medical activities, 35 U.S.C. § 287(c) (2012); individuals whose infringing activities are for the purpose of obtaining regulatory approval of drugs or medical devices, *id.* § 271(e)(1); and individuals whose infringing activities are for the purpose of amusement or curiosity, *infra* text accompanying notes 212–214. In addition, liability for *indirect* patent infringement "requires the patentee to establish that the accused infringer acted with some measure of intentionality or scienter." Merges, *supra* note 208, at 3 n.1.

211. However, they would not infringe patents on CRISPR materials obtained from providers like Addgene that distribute exclusively pursuant to Material Transfer Agreements. *Information for Tech Transfer Offices (TTOs)*, ADDGENE, https://www.addgene.org/techtransfer/tto/#request-process [https://perma.cc/LW6Q-9M6E]; *see also* Jacob S. Sherkow, *Patent Protection for Microbial Technologies*, 364 FEMS MICROBIOLOGY LETTERS, Sept. 25, 2017, at 1, 2.

use defense, which is an exception to the rule of strict liability. That defense excuses patent infringement where the purpose is "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry."[212] Although the defense has been characterized as narrow[213] and inapplicable where the alleged infringement "is in any way commercial in nature,"[214] many DIY biology activities might qualify.

But it is unlikely that citizen bioscientists will ever need to invoke this defense given the strong tradition in the life sciences of not enforcing patents against those conducting noncommercial research. For example, the Broad Institute, which is an assignee of several foundational CRISPR patents, has publicly committed to making its patents and other intellectual property freely available for noncommercial uses.[215] That patent litigation is expensive and patentees may be unlikely to recover significant damages from citizen bioscientists are additional reasons why patent law may not be a reliable constraint on DIY CRISPR.[216] Because entrepreneurs are a growing constituency of community laboratories, however, it will be interesting to follow whether any companies that incubate in these spaces are sued for patent infringement.

6. Tort Law

Finally, state tort law indirectly governs DIY CRISPR by providing a mechanism for DIY biologists harmed during these activities to recover damages from those who might be responsible. For example, persons injured in the course of using DIY CRISPR materials and kits expressly described as intended for educational or basic discovery purposes could bring tort claims against the manufacturers or distributors of the products, notwithstanding a lack

212. Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000) (quoting Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984)).

213. Madey v. Duke Univ., 307 F.3d 1351, 1361 (Fed. Cir. 2002); *see also* Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 87 (observing that "the experimental-use exemption has been reduced to a mere *de minimis* exception").

214. *Madey*, 307 F.3d at 1362.

215. *See Principles for Disseminating Scientific Innovations*, BROAD INST., https://www.broadinstitute.org/principles-disseminating-scientific-innovations [https://perma.cc/W3Y6-J4AX]; Issi Rozen, *Licensing of IP to Maximize Public Benefit*, BROAD INST. (Dec. 16, 2016), https://www.broadinstitute.org/node/35316 [https://perma.cc/N4LP-2SYV].

216. *See* Telephone Interview with Josiah Zayner, Founder and CEO, The ODIN (Aug. 6, 2018) (on file with author) ("Here's the thing is most people who do biohacking don't have much money."); *cf.* Gallegos et al., *supra* note 32, at 1214 (considering infringement of insulin patents by individuals practicing those patents at home and concluding that infringement actions would be exceedingly rare given, among other things, the high cost of such lawsuits).

of evidence that they intended the products to be used in humans.[217] As another example, individuals who are injured in the course of following instructions describing how to edit one's genetic material could bring state tort claims against those who provided the instructions.[218]

A full examination of biohackers' potential tort liability under state law, including an analysis of the likely success of such claims, is beyond the scope of this Article. Nevertheless, it has the potential to be an important mechanism for encouraging safe practices in DIY biology and the full disclosure of risks associated with DIY CRISPR activities. Indeed, during interviews with biohackers, concerns that individuals who replicate their experiments might be injured, and interviewees' potential liability in such circumstances, were frequently raised. These concerns also have factored into interviewees' decisions regarding when and how to disclose some of their activities on social media sites and YouTube.

However, like patent law, state tort law is enforced in civil litigation, which can be expensive. Moreover, because injured individuals will not be able to recover damages from those citizen bioscientists who lack significant financial resources, lawsuits may be limited as a practical matter to those involving commercial defendants or others with deep pockets. We are not aware of any U.S. tort cases alleging injuries resulting from DIY biology activities, but if such a case is pursued, its outcome will depend on the scope of and remedies provided by the governing state's laws and, of course, on the precise facts giving rise to the action.

B. Internal Oversight

The foregoing examination of potential external oversight mechanisms for DIY CRISPR reveals that there are gaps both in the scope of regulatory authority and the extent to which regulators and rights holders may choose to enforce the authority that they do have. Over the years, citizen bioscientists have filled some of these gaps through mechanisms of self-regulation that address ethical and safety concerns. In addition, many commercial suppliers of biological materials have adopted practices that have the effect of restricting

217. *See, e.g.*, RESTATEMENT (THIRD) OF TORTS: PRODS. LIAB. § 2 (1998).

218. *Cf.* RESTATEMENT (SECOND) OF TORTS § 302 (1965) ("A negligent act or omission may be one which involves an unreasonable risk of harm to another through . . . the foreseeable action of the other"); *id.* § 302A ("An act or an omission may be negligent if the actor realizes or should realize that it involves an unreasonable risk of harm to another through the negligent or reckless conduct of the other . . . .").

sales to those who are considered trustworthy. This section describes these and other internal oversight mechanisms for DIY CRISPR.

1. Self-Regulation by DIY Biologists

a. Ethics Standards and Practices

Ethical conduct, or at least the avoidance of unethical conduct, is a stated priority for many DIY biologists. One of the earliest accomplishments of DIYbio.org was its organization of two congresses in 2011 that developed an ethical framework for DIY biology communities.[219] That framework is embodied in similar (but distinct) codes of ethics for North America and Europe, both of which endorse "transparency" and "peaceful purposes," among other values.[220] At the local level, some community laboratories and individual projects also have endorsed statements with ethical foundations. For example, the project wiki for Real Vegan Cheese includes a "Statement of Ethics" that describes the project's commitment to education, tinkering, and access to tools and technical knowledge.[221]

Far trickier than agreeing on general ethical principles and values has been determining when and how to review the ethical implications of specific projects. As explained above, every study protocol involving human participants that is federally funded or supported, or that constitutes a clinical investigation under the purview of the FDA, must be reviewed for compliance with ethical standards by an IRB.[222] In addition, some institutions provide research-ethics services that scientists can consult independent of, or complementary to, IRB review.[223] However, federal IRB regulations generally do not apply to the activities of DIY biologists, and DIY biologists who nevertheless would like some sort of ethics guidance (even if they are not legally obligated to obtain it) may not have access to an institution-based IRB or ethics consultation service.

219. *See Codes*, *supra* note 92.

220. *See id.*

221. *Ethical, Legal, and Social Implications*, REAL VEGAN CHEESE, https://web.archive.org/web/20170222164858/https://wiki.realvegancheese.org/index.php/Ethical,_Legal,_and_Social_Implications [https://perma.cc/S539-SQ6M]. In furtherance of its commitment to decentralized access to biotechnology, the project plans to obtain a patent on its discoveries and then abandon the patent to the public domain. *Id.*

222. *See supra* notes 189–191 and accompanying text.

223. *See* Mildred K. Cho et al., *Strangers at the Benchside: Research Ethics Consultation*, AM. J. BIOETHICS, Mar. 2008, at 4, 4.

As an alternative, DIY biologists might constitute (and even register with the federal government) their own ethics review boards or pay independent, for-profit boards, such as WIRB-Copernicus, to review their plans for ethical concerns. However, the creation of ethics review boards by DIY biologists does not appear to be common,[224] and we are not aware of any instance in which a DIY biologist obtained an ethics opinion from an independent, for-profit board. This may be due to limited resources, but it also may reflect a libertarian spirit that is common in DIY biology. BioCurious, for example, informs members that it will not "exercise editorial control over the science done in the lab" and therefore will not make "judgment calls" as to whether members' experiments are—or are not—ethical.[225]

New models of ethics review have been proposed that may better align with the practice and ethos of citizen bioscience. One model invites "citizen ethicists" to conduct nonbinding ethical assessments of proposed research and post their opinions online.[226] On DIYgenomics.org, an online platform that facilitates collaboration on studies that citizen bioscientists design and execute themselves, two citizen ethicists were identified in connection with studies, although it is unclear whether the citizen ethicists completed any ethical assessments of specific protocols.[227] Additionally, at least one

224. An example of a citizen bioscience group that has constituted and registered its own ethics review board is Citizen Science Belleville ("CSB"). CSB's review board has adopted procedures that diverge in many ways from those followed by institution-based IRBs. For example, CSB's review board issues written decisions of reviews that resemble judicial decisions. For more information, see *Citizen Science Belleville IRB Procedures*, OPEN SCI. FRAMEWORK, https://osf.io/6hyd7/ [https://perma.cc/Q74W-RFC6].

225. *See* BIOCURIOUS SAFETY RULES 2 (version 2.6) [hereinafter BIOCURIOUS SAFETY RULES], https://docs.google.com/document/d/1NrAOBsKgPDZiE1la_g6USZU-9iuNFqFlSAEoU3lurPw/edit [https://perma.cc/P32N-F2ZP]. However, BioCurious requires strict compliance with its safety rules. *Id.* at 1 (stating that the laboratory "will not compromise on safety").

226. *See* Amy Dockser Marcus, *The Ethics of Experimenting on Yourself*, WALL ST. J. (Oct. 24, 2014), https://www.wsj.com/articles/the-ethics-of-experimenting-on-yourself-1414170041?KEYWORDS=amy+dockser+marcus [https://perma.cc/XU8U-ZWL8]; *see also* Effy Vayena & John Tasioulas, *The Ethics of Participant-Led Biomedical Research*, 31 NATURE BIOTECHNOLOGY 786, 787 (2013) (discussing the potential for crowdsourced ethics review).

227. However, they did post answers to two questions regarding the handling of study risks. *See DIYgenomics Citizen Ethicist Review*, DIYGENOMICS, http://diygenomics.pbworks.com/w/page/53826289/Ethical_Review [https://perma.cc/6U57-YZX6]; *see also Welcome to DIYgenomics!*, DIYGENOMICS, http://diygenomics.pbworks.com/w/page/23041784/Welcome%20to%20DIYgenomics%21 [https://perma.cc/GE5W-DHQ5] (discussion under "DIYgenomics citizen science ethics and standards").

biohacker informed us that he has cobbled together an informal "ethics board" of trusted individuals whom he consults on an as-needed basis.[228] Meanwhile, some support the development of ethics toolkits and guidance for DIY communities.[229]

b. Safety Standards and Practices

Although DIY biologists have not reached a consensus regarding management of ethical issues, there is broad agreement that safety issues should be managed by reference to a guidance document developed by the NIH and the Centers for Disease Control and Prevention ("CDC"). Considered the cornerstone of biosafety practices in the United States, *Biosafety in Microbiological and Biomedical Laboratories* ("BMBL") describes recommended microbiological practices, safety equipment, and facility safeguards that correspond to four levels of containment known as biosafety levels ("BSLs").[230] BSL 1 describes a basic level of protection and is appropriate for handling biological agents "not known to consistently cause disease in immunocompetent healthy adults."[231] Individuals working in BSL 1 laboratories are advised to use personal protective equipment when appropriate and have access to a sink, but research may be conducted at open benches.[232] The BSL 2 designation is appropriate for handling moderate-risk agents that cause human disease of varying severity by ingestion or skin or mucous membrane exposure.[233] It is recommended that BSL 2 laboratories follow additional precautions, such as routine decontamination of equipment and use of physical containment devices.[234] BSL 3 and 4 laboratories

228. Telephone Interview with Sebastian Cocioba, Founder and CEO, N.Y. Botanics (Sept. 7, 2018) (on file with author).

229. *See* TODD KUIKEN, ELEONORE PAUWELS & SARAH W. DENTON, WOODROW WILSON CTR., THE RISE OF THE NEW BIO-CITIZEN: ETHICS, LEGITIMACY, AND RESPONSIBLE GOVERNANCE IN CITIZEN-DRIVEN BIOMEDICAL RESEARCH AND INNOVATION 7–9 (2018), https://www.wilsoncenter.org/sites/default/files/7.3.18_chi_workshop-report__1.pdf [https://perma.cc/K57X-UKXG] (describing consensus among workshop participants that ethical considerations must be included in toolkits to assist "biocitizens" who initiate or conduct health research).

230. U.S. DEP'T OF HEALTH & HUMAN SERVS., PUB. NO. 21-1112, BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES, at iii, 4, 30–59 (Deborah E. Wilson & L. Casey Chosewood eds., 5th ed. 2009) [hereinafter BMBL]. The BMBL was first published in 1984 and last revised in 2009. *Id.* at iii.

231. *Id.* at 4, 30.

232. *Id.* at 30–33.

233. *Id.* at 4, 33.

234. *Id.* at 33–38. In addition, the BMBL states that individuals working in BSL 2 laboratories should be supervised by scientists "competent in handling infectious agents

handle the most dangerous materials and therefore are advised to follow the most stringent containment procedures.[235]

Compliance with the BMBL is generally voluntary.[236] However, it is broadly respected across laboratory settings. Community laboratories in particular usually adhere to BMBL standards, with most designating themselves as BSL 1, although at least one community laboratory appears to maintain space designated as BSL 2.[237] Interviewees who operate home laboratories also informed us that they are aware of and make an effort to comply with BMBL standards.[238]

The containment practices of community laboratories are often set forth in safety policies, some of which explicitly reference BSL levels.[239] These policies describe requirements related to protective wear and procedures for handling, transporting, and disposing of materials. They also detail limits, and in some cases outright prohibitions, on certain activities. For example, at BioCurious, work with human samples is generally not allowed except that members may analyze buccal and saliva samples under certain conditions.[240] BioCurious also allows genetic manipulation and recombination, although members may not deliberately work to create organisms

and associated procedures," *id.* at 33, whereas supervision in BSL 1 laboratories may be conducted by scientists trained generally in microbiology or a related science, *id.* at 30.

235. *Id.* at 38–58. For BSL 4 laboratories, these materials include exotic agents that pose a high individual risk of life-threatening disease for which no treatment is available. *Id.* at 45.

236. *See id.* at iii (emphasizing the BMBL's status as an "advisory document recommending best practices" rather than a regulatory document); *see also* Rebecca Emerson, Comment, *Biosafety Regulations: Who's Watching the Lab? Safety in High Risk Infectious Disease Research*, 25 TEMP. J. SCI. TECH. & ENVTL. L. 213, 218 n.44 (2006). However, compliance with or consideration of the BMBL might be required in certain circumstances. *See* BMBL, *supra* note 230, at iii. For example, it is required of federal grant recipients. *See* FRANK GOTTRON, CONG. RESEARCH SERV., R45491, SCIENCE AND TECHNOLOGY ISSUES IN THE 116TH CONGRESS 32 (2019).

237. *See About Us*, COUNTER CULTURE LABS, https://www.counterculturelabs.org/info--history.html [https://perma.cc/T2EB-JBUV] (identifying BSL 1 and 2 areas on site map).

238. *See, e.g.*, Telephone Interview with Sebastian Cocioba, *supra* note 228 (stating that, in his home laboratory, he "stick[s] to materials and organisms that are within biosafety level 1 confines"). *But see* Yin, *supra* note 20 (reporting criticism of Dr. Zayner's laboratory practices as noncompliant with "basic biosafety protocols").

239. *See, e.g.*, BALT. UNDER GROUND SCI. SPACE, BUGSS SAFETY MANUAL (version 1.1, July 2012) [hereinafter BUGSS SAFETY MANUAL], http://www.smilesaidtheriver.com/bugsswordpress2/wp-content/uploads/2017/08/bugss_safety_manual_v_1.1.pdf [https://perma.cc/5AFY-48NF].

240. *See* BIOCURIOUS SAFETY RULES, *supra* note 225, at 8.

that would be pathogenic to humans.[241] The safety manual adopted by BUGSS includes similar restrictions.[242]

In addition to adopting safety policies and designating individuals responsible for compliance, some community laboratories require that members' projects pass a safety review before they are allowed to begin. The directors of Genspace, for example, conduct mandatory safety reviews of proposed projects, sometimes in consultation with the laboratory's safety advisory committee.[243] HiveBio, a Seattle community laboratory, similarly mandates unanimous approval of new projects by a safety review board.[244]

While a grant-funded effort is currently underway to improve and standardize safety policies and practices across DIY communal settings,[245] the effectiveness of these policies and practices depends, at least in part, on their enforcement. It is not uncommon for community laboratories to require members to demonstrate their safety knowledge by passing a test or completing a class.[246] In at least one case, a prospective member who failed the required safety test multiple times was reported to other community laboratories as a safety risk.[247] In addition, designated safety officers generally monitor compliance with laboratory policies and may even be required to be on site during hours of operation.[248] The design of community laboratories as open—and usually small—spaces also facilitates peer

241. *Id.*

242. BUGSS SAFETY MANUAL, *supra* note 239.

243. These procedures are described in GRUSHKIN ET AL., *supra* note 81, at 19.

244. *About*, HIVEBIO, http://www.hivebio.org/about/ [https://perma.cc/8NEN-ELKB]. Approval of new projects also requires documented review of lab safety protocol. *Id.*

245. Led by the former executive director of Genspace and a scholar at North Carolina State University, this work, which is funded by a $700,000 grant from the Open Philanthropy Project, comprises identifying existing safety practices at community laboratories and establishing early career biosafety officers at select community laboratories for the purpose of nurturing biosafety specialization in those settings. *See* Patti Mulligan, *Upgrading Biosafety and Biosecurity: Open Philanthropy Awards $700K for DIYbio*, N.C. ST. U. (Sept. 22, 2017), https://research.ncsu.edu/ges/2017/09/upgrading-biosafety-biosecurity-at-diybio-labs/ [https://perma.cc/ENP3-S28H].

246. *See, e.g.*, BUGSS MEMBERSHIP APPLICATION, *supra* note 131, at 2 (requiring that members who want to work independently in the laboratory first complete a biosafety course); *What Happens After Joining?*, BIOCURIOUS, https://biocuriosity.wordpress.com/join/what-happens-after-joining/ [https://perma.cc/6KAW-2JUD] (requiring that new members achieve a 100 percent on a safety quiz before being allowed to work in the laboratory).

247. *See* CTR. FOR GLOB. SEC. RESEARCH, *supra* note 112, at 7.

248. *See, e.g.*, *About*, *supra* note 244.

support and monitoring.[249] Finally, many community laboratories require their members to sign agreements or contracts that describe member responsibilities and penalties for engaging in prohibited activities. For example, the BUGSS membership agreement states that disregard for personal safety, reckless endangerment of others, and use of equipment for illegal purposes can result in restrictions on or even termination of one's membership.[250] Community laboratories' enforcement practices have not yet been systematically described, although we suspect that enforcement actions are rare given that members self-select into communities for which safety is an explicit priority.

Of course, laboratories' safety policies and practices are not binding on DIY biologists who work in private settings. One does not need to pass a biosafety test—or even be aware of biosafety standards—to tinker at home. Further, for those with safety questions, professional advice is not readily available. Responding to this need, in 2013, DIYbio.org launched an online "Ask a Biosafety Professional" forum through which volunteer biosafety experts answered questions posed by citizen bioscientists, who were allowed to participate anonymously.[251] In 2014, however, the forum was closed to new questions.[252]

Although there do not currently appear to be any other structured mechanisms for DIY biologists working in private settings to obtain professional safety advice, they frequently discuss safety issues in discussion groups dedicated to DIY biology, such as the DIYbio Google Group and Biohack.me, as well as on Facebook, Twitter, and other social media platforms.[253] While many of these conversations are directed to sharing and helping, social shaming also

249. *See* Scheifele & Burkett, *supra* note 124, at 84 (noting that, "due to their limited space and communal nature, community labs can actually guard against clandestine activities and enable safety and regulatory oversight of amateur scientists").

250. *See* BUGSS MEMBERSHIP APPLICATION, *supra* note 131, at 3; *see also BioCurious Membership Agreement*, BIOCURIOUS (June 7, 2017), https://docs.google.com/document/d/e/2PACX-1vQHZZvoERCqR1HJuGTq2-xga-Pip_kl4x5kzMtx08wQAvg6tNE8yxtYjTBTesaE3akEmh7dJJfTkKjj/pub [https://perma.cc/E4J5-VJDK] (providing that "[l]ying or misleading the Safety Officer is grounds for immediate membership termination").

251. *Ask a Biosafety Professional Your Question*, DIYBIO, http://ask.diybio.org/ [https://perma.cc/X4DU-8TC2].

252. *See Ask a Biosafety Officer—Closed*, DIYBIO, https://diybio.org/ask-biosafety-notice/ [https://perma.cc/MNU9-5XLB].

253. For example, one discussion on the DIYbio Google Group forum concerns how to safely dispose of old cultures. *Safely Disposing of Old Cultures?*, GOOGLE GROUPS (Mar. 4–21, 2017), https://groups.google.com/forum/#!searchin/diybio/%22is$20it$20safe%22%7Csort:date/diybio/lT9JlRSsKMQ/a-LXT0-rCQAJ [https://perma.cc/KM8F-R8EA].

takes place when individuals are perceived to be engaging in unsafe conduct.[254] This is consistent with the general observation of one interviewee that some biohackers "will quite happily call people out" if they do not respect community norms.[255]

2. Self-Regulation by Suppliers

a. Screening Protocols and Practices

To conduct gene editing, DIY biologists must have the necessary biological materials—including Cas proteins and gRNA—to execute their experiments. Many major commercial suppliers compete in this market. Except with respect to materials that qualify as regulated toxins or select agents,[256] there are generally no legal restrictions on

254. For example, on Biohack.me, one poster warned of the dangers of attempting to transform one's skin cells to bioluminesce:

> [Y]ou should probably learn a lot more biology before messing with your DNA. . . . Take it very seriously and give it the respect it deserves or run the risk of very seriously [messing] yourself up. People are getting all excited about gene mods and wanting to just jump in cause they saw others do it. IT'S NOT A GOOD IDEA unless you know what you're doing."

Chironex, Comment to *Fluorescent & Luminescent Modification*, BIOHACK.ME (Sept. 2018), https://forum.biohack.me/index.php?p=/discussion/comment/26495#Comment_26495 [https://perma.cc/CF3Z-NB7H]; *see also* Chironex, Comment to *Playing with Viruses*, *supra* note 139 (publishing a response to another poster's announcement of plans to conduct DIY CRISPR in the near future: "If you don't know what you're doing, you shouldn't even consider using crispr on yourself. Hell even if you do, you probably still shouldn't. . . . Crispr is brand new tech and every week more papers come out showing we don't know enough about how it works and risk of unintended mutations can be very high without proper thought, and even if things have been carefully considered because of the complexity of biology. It's cute that you read about crispr, but evidently you haven't taken a . . . biology class.").

255. *See* Telephone Interview with Tristan Roberts, Researcher, Transcendence Sys. (Aug. 8, 2018) (on file with author) (commenting on informal penalties for failure to respect community norms related to attribution and ownership).

256. All U.S. research must comply with federal regulations that apply to the handling of select agents and toxins, which are substances identified by HHS or the U.S. Department of Agriculture ("USDA") as having the potential to pose a severe threat to public health and safety or to animal or plant health or products. *See* 7 C.F.R. § 331.2 (2018); 9 C.F.R. § 121.2 (2018); 42 C.F.R. § 73.2 (2018). HHS and USDA currently regulate over sixty select agents and toxins, including ricin and the Ebola virus, by restricting their possession, use, and transfer to only individuals and entities holding certificates of registration approved by the Federal Select Agent Program ("FSAP"). *See Select Agents and Toxin List*, FED. SELECT AGENT PROGRAM, https://www.selectagents.gov/selectagentsandtoxinslist.html [https://perma.cc/RL7V-SN3A] (identifying regulated select agents and toxins). These restrictions are detailed in 7 C.F.R. § 331.7 (2018), 9 C.F.R. § 121.7 (2018), and 42 C.F.R. § 73.7 (2018). We are not aware of any instance in which a DIY biologist attempted to register with FSAP, although such an

who can purchase biological materials. Yet, concerns have long been raised about the potential misuse of synthesized genetic material to design pathogens or introduce mutations that harm public health or the environment.[257]

In recent years, policies have been developed to address these concerns. Specifically, in 2010, the U.S. Department of Health and Human Services ("HHS") released screening guidance for double-stranded DNA synthesis companies.[258] Around the same time, companies representing 80% of the global commercial gene synthesis capacity formed the International Gene Synthesis Consortium ("IGSC") and developed its own screening protocol for members.[259] The IGSC protocol, which was recently updated, describes a two-step process.[260] First, orders of synthetic double-stranded DNA sequences are checked against a database of regulated pathogens.[261] Second, buyers are screened against multiple national watch lists and checked for institutional affiliations.[262] In some cases, buyers are also investigated to ensure that they are bona fide end users and may be required to explain their proposed experiments.[263]

Importantly, neither protocol is legally binding.[264] Many suppliers may nevertheless choose to comply with HHS or similar screening protocols.[265] But there is scant data on the screening procedures that

application would surely be denied if submitted given the stringent security and safety conditions that must be met for approval.

257. *See supra* note 33 and accompanying text.

258. *See generally* Screening Framework Guidance for Providers of Synthetic Double-stranded DNA, 75 Fed. Reg. 62,820 (Oct. 13, 2010).

259. INT'L GENE SYNTHESIS CONSORTIUM, HARMONIZED SCREENING PROTOCOL V. 2.0, ¶ 1 (2017) [hereinafter IGSC PROTOCOL].

260. *Id.* ¶¶ 2–3.

261. *Id.* ¶ 2. In 2015, it was reported that approximately 5% of orders are flagged for further review based on this screen. *See* SARAH R. CARTER & ROBERT M. FRIEDMAN, DNA SYNTHESIS & BIOSECURITY: LESSONS LEARNED AND OPTIONS FOR THE FUTURE 11–12 (2015).

262. *See* IGSC PROTOCOL, *supra* note 259, ¶ 3; CARTER & FRIEDMAN, *supra* note 261, at 10.

263. IGSC PROTOCOL, *supra* note 259, ¶¶ 3.3, 3.5. Notably, if a citizen bioscientist informs a supplier that she plans to use the materials for self-experimentation (or on other humans or nonhuman animals), that might cause the material to be a biological drug product subject to FDA regulation. *See* discussion *supra* Section III.A.1.

264. Further, neither protocol applies to short, single-stranded DNA orders, which can be used to construct genes and gene fragments, or DNA synthesizers. CARTER & FRIEDMAN, *supra* note 261, at 19–21.

265. *See id.* at 13.

have been adopted by suppliers of biological materials or how closely they are adhering to those procedures.[266]

It is also unclear what effect suppliers' screening procedures are having on DIY biologists in particular. Assuming that the vast majority of orders placed for DIY CRISPR activities do not include materials listed in any pathogen database, the main hurdle that biohackers face is customer screening. Yet there is anecdotal evidence that this hurdle is not always difficult to overcome. Given the various CRISPR activities that are taking place in community laboratories,[267] it does not appear that DIY biologists who work in these settings are having trouble obtaining materials for their CRISPR experiments. Meanwhile, DIY biologists who work in private settings have identified ways to pass customer screening. For example, biohacker David Ishee registered a company in his home state in part to satisfy suppliers that only ship to institutional addresses.[268] Although IGSC at one point flagged Mr. Ishee, his order was ultimately approved after he was able to convince the screener that he "wasn't a crazy person."[269]

b. Pricing Mechanisms

Another approach to screening customers—albeit an indirect one—is through price. Biological materials purchased from commercial suppliers are expensive; they run into hundreds and even thousands of dollars for some protocols. Grant-funded researchers budget for these costs in funding applications, and commercial researchers can pass them on to customers. But the typical biohacker is self-funded and may not be able to afford materials from commercial suppliers.[270]

To facilitate free access to materials, in late 2017, the nonprofit BioBricks Foundation launched the Free Genes Project, which coordinates the synthesis and distribution of DNA sequences to

266. *See id.* at 8 (observing that "details of how any one company has reviewed or will review any specific order remain unclear").

267. *See supra* text accompanying notes 127–130.

268. Telephone Interview with David Ishee, *supra* note 85; *see also Where Do DIY Biologists Get Things Like CRISPR or Genes*, GOOGLE GROUPS (Oct. 2017), https://groups.google.com/forum/#!searchin/diybio/CRISPR%7Csort:date/diybio/lbuIYFdUW0c/2HNq9rqDAQAJ [https://perma.cc/EB4J-6LA2] (forum discussion on obtaining CRISPR materials).

269. Telephone Interview with David Ishee, *supra* note 85.

270. *Cf.* Telephone Interview with Josiah Zayner, *supra* note 216.

anyone who requests them at no cost.[271] Meanwhile, a number of biohackers are avoiding institutional suppliers altogether when possible and sharing materials with each other. For example, in September 2018, a Florida biohacker gave away approximately $25,000 worth of gene lines to attendees of a biohacking convention.[272] This same individual is spearheading the development of a free library of biological materials.[273]

IV. FUTURE OVERSIGHT POSSIBILITIES

Our examination of the existing regulatory framework for DIY CRISPR reveals that it is potentially more robust than is commonly believed but certain activities remain outside its reach. Yet, because no regulatory scheme can be perfectly effective nor completely comprehensive, the existence of such gaps in oversight does not necessarily compel the conclusion that regulatory changes are needed. Accordingly, this part evaluates whether existing oversight mechanisms, considered collectively rather than individually, succeed in minimizing the potential risks of DIY CRISPR without unduly interfering with the realization of its potential educational, expressive, and scientific benefits. It concludes that the current regulatory framework seems to be working reasonably well thus far in discouraging especially worrisome human applications of DIY CRISPR. However, we are concerned about a possible future uptick in risky (if not illegal) human experimentation as lay understanding of and proficiency with the technology increases. We therefore offer suggestions for shoring up the oversight readiness and capacities of regulatory bodies and DIY communities.

A. Evaluating Existing Oversight Mechanisms

Given the absence of a coordinated and comprehensive regulatory framework, it is perhaps remarkable that there have not yet been any confirmed reports of DIY CRISPR activities that raise ethical concerns of the magnitude of those raised by the alleged "CRISPR babies" announced in November 2018.[274] The reported

271. *The Free Genes Project*, BIOBRICKS FOUND., https://biobricks.org/freegenes/ [https://perma.cc/S65H-M3DP].

272. *See* Christi J. Guerrini, *A Gathering of Biohackers: The Future of Science?*, BAYLOR C. MED.: POLICYWISE (Sept. 14, 2018), https://blogs.bcm.edu/2018/09/14/a-gathering-of-biohackers-the-future-of-science/ [https://perma.cc/7CVF-98BT].

273. *See* Zayner, *Biohack the Planet*, *supra* note 147 (starting at 47:54, Gabriel Licina explains the development).

274. *See, e.g.*, *supra* notes 27–28 and accompanying text.

human applications of DIY CRISPR have involved only somatic—not germline—cells, and they seem to have been voluntarily undertaken.[275] However, it may be that such activities are being conducted in secret and have not yet been disclosed.

There also have not been any confirmed reports of physical injuries resulting from DIY gene-editing activities. Of course, it is possible that such injuries have occurred but have not yet been reported. Citizen bioscientists who prefer to work in secret, for example, may be unlikely to share this kind of news. It is also possible that citizen bioscientists who have been injured do not understand that their injuries were caused by their gene-editing activities.

On the other hand, the absence of reported injuries may reflect that no injuries have occurred because gene editing outside of professional research settings is not a particularly dangerous activity. Although this is plausible with respect to basic *ex vivo* experiments involving nonpathogenic biological materials, it is less plausible with respect to *in vivo* experiments, whose potential harms include infection, immunological reaction, and cellular changes that range from mild to life threatening.[276] In such cases, individuals may be taking appropriate precautions to avoid injury when they engage in DIY CRISPR. While this probably helps explain the safety record of community laboratories, where *ex vivo* experiments must comply with safety rules and self-experimentation is prohibited, it is less clear how well it explains the safety record (as far as it is known) of DIY CRISPR undertaken in private settings. In the end, the question is an empirical one that has not yet been studied.

We suspect, however, that the absence of confirmed reports of human applications of DIY CRISPR raising grave ethical questions or resulting in known injuries is in large part a function of the current infrequency of these activities. Although experimentation with CRISPR on bacteria and yeast genomes is popular across DIY settings,[277] there are few known instances in which individuals have self-experimented with CRISPR,[278] and we are not aware of any confirmed instance in which citizen bioscientists attempted to conduct gene editing on others.

The infrequency of human applications of DIY CRISPR is likely the result of a number of factors. For one, the FDA's jurisdiction

275. *See supra* note 138 and accompanying text.
276. *See supra* text accompanying note 19.
277. *See supra* notes 98, 109, 129–130 and accompanying text.
278. *See supra* notes 138–139 and accompanying text.

over, and requirements for, biological drug products have almost certainly discouraged widespread distribution of DIY CRISPR materials intended for *in vivo* human use, as well as DIY CRISPR activities akin to clinical trials. General confusion about how various federal and state laws apply to DIY biology may also have prompted some to err on the side of caution and steer clear of these activities.[279] Other factors that likely have contributed to the low incidence of human applications of DIY CRISPR include the safety policies and practices of community laboratories;[280] the active discouragement of these activities by individuals posting in online forums;[281] and general concerns about CRISPR's safety or the ethical implications of its human applications. Finally, and perhaps most importantly, the sophisticated knowledge and skills necessary to use CRISPR in humans is probably out of reach of most biohackers at this time.[282]

In the end, there is probably some truth to each of these explanations. That is, the existing regulatory framework has worked to discourage the kinds of DIY gene-editing activities—e.g., *in vivo* human applications—that are most likely to raise serious ethical concerns and result in injury. At the same time, only a small number of biohackers currently have the knowledge, skills, and resources to attempt using CRISPR in humans. These individuals might also be reluctant to publicly disclose their gene-editing activities or resulting injuries, making it difficult to assess the impact of the current regulatory framework on the current state of affairs.

But as DIY biologists become more adept at using CRISPR, safe human applications are discovered and detailed in the literature, and some consensus is reached about ethical questions raised by these applications; thus, it is not unreasonable to expect more DIY biologists to attempt human gene editing. It is therefore worth considering ways to improve the existing oversight regime.

B. Improving Oversight of DIY CRISPR

At the broadest level of analysis, and especially with respect to self-experimentation, the current regulatory framework relies heavily on internal oversight. In the near term, continued reliance on self-regulation seems appropriate. There is a long tradition of self-regulation in science that includes the voluntary guidelines that were

279. *Cf.* Telephone Interview with Sebastian Cocioba, *supra* note 228 (discussing the lack of clarity regarding the application of laws and regulations to DIY biology activities).

280. *See supra* text accompanying notes 240–242.

281. *See supra* notes 253–255 and accompanying text.

282. Ledford, *supra* note 100, at 399; Riley, *supra* note 16, at 230.

developed in 1975 at the Asilomar Conference Center in California to ensure the safe conduct of research involving recombinant DNA technology.[283] Likewise, internal oversight has long played a key role in the conduct of DIY biology.[284] While the ability of DIY biologists to effectively regulate themselves has been questioned,[285] self-regulation is politically well-suited to biohacking communities given some members' distrust of government and the scientific establishment.[286] Indeed, because self-regulation is consistent with the emphasis that DIY communities place on autonomy and flexibility, it is an approach that likely has and can retain broad buy in. Moreover, self-regulation may be an especially appropriate oversight mechanism for activities like DIY gene editing involving new technologies that are thus far not widespread nor, importantly, widely commercialized. Unlike external regulatory mechanisms, which can be slow to change, internal oversight mechanisms can be quickly adjusted to respond to new issues raised by emerging technologies. Finally, the costs associated with external intervention do not seem justified at this time given the low incidence of confirmed human applications of DIY CRISPR.

Still, we appreciate that internal oversight has significant weaknesses, including vulnerability to underenforcement or, in the case of ethics codes, nonenforcement. Internal oversight also can be inconsistent—for example, different laboratories might address problems in different ways—and inefficient—for example, different laboratories might each work to develop policies for the same issues independently without the opportunity to learn from each other's experiences. Moreover, the effectiveness of self-regulation is likely to change as DIY biology communities evolve, scientific understanding

283. Paul Berg et al., *Summary Statement of the Asilomar Conference on Recombinant DNA Molecules*, 72 PROCEEDINGS NAT'L ACAD. SCI. 1981, 1981 (1975).

284. *See* discussion *supra* Sections II.A, III.B.1.

285. *See, e.g.*, Gaymon Bennett et al., *From Synthetic Biology to Biohacking: Are We Prepared?*, 27 NATURE BIOTECHNOLOGY 1109, 1110 (2009) (arguing that DIY biology enthusiasts are insistent that policymakers trust them to self-regulate yet "are often unwilling to frankly address dangers posed by easy-to-engineer and open source biology"). However, as the November 2018 announcement of the "CRISPR babies" demonstrated, self-regulation by institution-based scientists is also imperfect. *Cf.* Furrow, *supra* note 13, at 42–43 (expressing skepticism about the effectiveness of self-regulation of CRISPR by both traditional scientific and DIY biology communities).

286. Others have suggested, however, that successful self-regulation of biotechnologies may not be possible if their users expand beyond "elite academic research scientists" who have been disciplined in a common responsibility to include "scientifically literate but not scientifically socialised ('disciplined') amateurs and dilettantes" who may not share that sense of common responsibility. NUFFIELD COUNCIL 2016, *supra* note 29, at 107.

of gene-editing progresses, and, if hopes for DIY CRISPR are realized, a robust market for it develops.[287] It will therefore be important for DIY biologists and regulatory bodies to regularly reevaluate whether, in light of these developments, primary reliance on self-regulation continues to be appropriate.

To facilitate this effort, DIY biologists should be encouraged to coordinate their practices in partnership with regulatory bodies. Recently, the Wilson Center conducted a workshop attended by citizen bioscientists, academics, and regulators that established an agenda of legal and ethical issues associated with DIY biology.[288] This is a good start to what we hope will be a continuing and inclusive effort to develop best practices in DIY biology that will inform governance of gene editing in particular.

One DIY activity that requires careful consideration is self-experimentation. The slow pace of traditional research, the extraordinary cost of marketed gene therapies, and the reality that, for many conditions, we simply do not have good therapies, may drive some patients to attempt DIY interventions.[289] These activities are generally not subject to external regulatory mechanisms and are not always discouraged by social norms. But the absence of oversight may assume that individuals engaged in self-experimentation appreciate the potential risks of their activities, when in fact they do not. While we are, at this time, reluctant to endorse extending existing regulations to self-experimentation, we support the development of tools to help individuals who self-experiment make more informed—and therefore autonomous—choices.

287. Declining to increase external regulatory authorities (or enforcement) without more evidence of harm, in some ways, would be consistent with the history of public health regulation and, in particular, the history of FDA regulation, which is often described as having expanded in response to specific crises. *See, e.g.*, HUTT ET AL., *supra* note 109, at 641–42. This approach, of course, has a downside in that waiting until a foreseeable harm occurs to change regulation to address that harm permits at least some individuals to be harmed, arguably unnecessarily. For example, in the context of stem cell clinics—which have rapidly expanded in the United States and offer a range of interventions sometimes associated with serious risks and with little to no evidence supporting their effectiveness—the FDA has been criticized for waiting until a robust market developed before taking clear action to assert its authority. *See, e.g.*, Paul S. Knoepfler & Leigh G. Turner, *The FDA and the US Direct-to-Consumer Marketplace for Stem Cell Interventions: A Temporal Analysis*, 13 REGENERATIVE MED. 19 (2018); Amy Zarzeczny et al., *The Stem Cell Market and Policy Options: A Call for Clarity*, J.L. & BIOSCIENCES, Nov. 20, 2018, at 1, 4–5.

288. *See* KUIKEN ET AL., *supra* note 229, 11–12.

289. *See supra* notes 147–148 and accompanying text.

This Article also encourages different factions within citizen bioscience to reach across the aisle and collaborate with each other. During interviews, it was not uncommon to hear members of community laboratories dismiss some biohackers who work in private settings as reckless or attention-seeking. On the other hand, biohackers working in private settings have been known to dismiss community laboratories as hierarchical and elitist.[290] While these groups can have very different reasons for engaging in DIY biology, we were struck during interviews by the consistency of their priorities, which included transparency, doing good science, and having fun. Although some biohackers working in private settings may have a higher risk tolerance than those working in community laboratories, it also was apparent that safety remains a concern among both groups. In the end, the different factions of DIY biologists likely have more in common with each other than they think and can help each other better anticipate and mitigate potential harms. Collaborations among various factions would also likely have the benefit of yielding information about the scale of and trends related to DIY human gene editing.

With respect to external regulations, although other countries and some U.S. states and municipalities prohibit the conduct of certain genetic research outside of licensed facilities or by anyone other than licensed individuals and entities,[291] this Article does not recommend that the U.S. federal government adopt a licensing program at this time. For one, there is no obvious authority to develop and enforce such a program. The U.S. regulatory body with perhaps the most relevant responsibilities is the NIH Office of Science Policy, which coordinates all activities related to the NIH Guidelines. However, that office does not have experience implementing a licensing program. Another possibility is the Federal Select Agent Program, which issues certificates to individuals and entities authorizing their handling of select agents and toxins, but the focus of that program is on biological materials, not scientific techniques.[292] In any event, a federal licensing program seems unnecessary at this time given that attempts to edit human genes outside of traditional scientific settings seem to be rare. Moreover, as noted by other commentators, taking such a strong regulatory approach could have the effect of driving this activity into the

290. *See, e.g.*, Yin, *supra* note 20.
291. *See supra* notes 174, 180 and accompanying text.
292. *See supra* note 256 and accompanying text.

shadows where it will be even more difficult to monitor.[293] For now, it seems more appropriate to encourage disclosure and close monitoring of these activities.

Finally, the FDA—the federal regulator with potentially far-reaching jurisdiction over activities related to DIY CRISPR—should proactively work to help DIY communities better understand the scope of its authority, its requirements, and its plans for enforcement. Although the FDA has already made clear that it views "any use of CRISPR/Cas9 gene editing in humans to be gene therapy" subject to the requirements for biological drug products,[294] many DIY biologists are not well versed in the intricacies of food and drug law and do not have access to sophisticated legal representation. Partly for those reasons, there is value in the Agency engaging with individual citizen bioscientists. Through ongoing dialogue with DIY communities, the FDA can help demystify its regulations and help citizen bioscientists understand the ways that the Agency seeks not only to prevent harm but also to encourage high-value innovation.[295]

The FDA should also consider issuing guidance on its views about which DIY CRISPR activities are within the Agency's jurisdiction and, of those, for which activities the Agency intends to enforce relevant requirements. Consistent with the Agency's risk-based approach to its enforcement priorities, it should focus on those DIY CRISPR activities within its jurisdiction that pose significant risks to public health.[296] For example, the FDA might clarify that certain DIY CRISPR kits sold for educational purposes are not biological drug products within the Agency's jurisdiction. It might also explain that it does not intend to closely examine the free exchange of raw biological materials that are not pathogenic but that it will prioritize CRISPR products distributed for use in others.

In sum, although there are few confirmed instances of human applications of DIY CRISPR, there are several things that DIY

293. *See, e.g.*, Sarah Kellogg, *The Rise of DIY Scientists: Is It Time for Regulation?*, WASH. LAW., May 2012, at 21, 21 (quoting a bioentrepreneur who opined that a "strong regulatory approach" will "only create a situation where people are afraid of the authorities, so they'll do it behind closed doors," which "is far more dangerous because [the authorities] may not know when [DIY scientists] are about to do something dangerous").

294. *See Information About Self-Administration of Gene Therapy*, *supra* note 153.

295. *Cf.* Nathan G. Cortez, I. Glenn Cohen & Aaron S. Kesselheim, *FDA Regulation of Mobile Health Technologies*, 371 NEW ENG. J. MED. 372, 376 (2014) (discussing the ways that FDA oversight can produce high-value innovation in the digital health context).

296. Some scholars have described this approach as "regulatory parsimony." Amy Guttman & Jonathan D. Moreno, *Keep CRISPR Safe: Regulating a Genetic Revolution*, 97 FOREIGN AFFS. 171, 172, 176 (2018).

biologists and regulatory bodies can do to prepare for a future in which that is no longer the case. These include creating opportunities to meaningfully engage with one another to enhance mutual understanding and developing best practices that have buy in from both groups. At the same time, regulatory bodies and DIY communities, working together, should regularly reevaluate the effectiveness of the existing regulatory framework as facts on the ground change.

CONCLUSION

Academic and policy discussions about the risks, responsibilities, and appropriate regulation of emerging technologies go back many decades[297] and include the landmark contributions of David Collingridge, who in 1980 described a paradox associated with social control of technologies: "When change is easy, the need for it cannot be foreseen; when the need for change is apparent, change has become expensive, difficult, and time-consuming."[298]

This paradox describes the basic problems with regulatory approaches at extreme ends of the temporal possibilities. On one end are preemptive approaches animated by the precautionary principle, which advises taking measures early in the development of a technology to prevent future threats.[299] But because the technology has not yet been deployed and integrated into society, those threats are not yet known and so it is difficult to identify oversight mechanisms that will effectively manage them. On the other end are reactionary approaches that advise waiting to learn the undesirable impacts of a technology before intervening.[300] At this point, however, there may be stakeholders in the technology who strongly resist the imposition of limits on its use.

To manage the current safety and ethical concerns raised by DIY CRISPR, this Article proposes an approach that falls somewhere in the temporal middle. This approach is focused on encouraging the disclosure of information to better understand how CRISPR is, and soon might be, used in DIY settings, as well as promoting robust communication and collaboration among various citizen bioscience

297. Audley Genus & Andy Stirling, *Collingridge and the Dilemma of Control: Towards Responsible and Accountable Innovation*, 47 RES. POL'Y 61, 61 (2018).

298. DAVID COLLINGRIDGE, THE SOCIAL CONTROL OF TECHNOLOGY 11 (1980).

299. *See* Oliver Todt & José Luis Luján, *Analyzing Precautionary Regulation: Do Precaution, Science and Innovation Go Together?*, 34 RISK ANALYSIS 2163, 2166 (2014); *see also* Anupam Chander, *Future-Proofing Law*, 51 U.C. DAVIS L. REV. 1, 3 (2017).

300. Chander, *supra* note 299, at 3–4.

factions and regulatory bodies to build their capacities to identify, prevent, and mitigate harms. Importantly, these recommendations assume that it will not be too late to implement new mechanisms to address the most serious harms should the need for doing so arise. The recommendations also reflect the hope that those new mechanisms, once implemented, will be more effective than they otherwise would have been because they were developed with robust input from the regulated communities.

Critically, that development process will require confronting difficult questions regarding what constitutes scientific expertise and who is entitled to participate in scientific knowledge production. The answers not only have the potential to disrupt established scientific practices, institutions, and norms, but, for some biohackers, they also implicate fundamental individual freedoms. As explained by one interviewee: "[I]f [regulators] tell me I need to get a permit, I will happily get a permit. If they tell me I can't do it at home, I'll try to figure that out. But if they tell me I need a PhD, I will riot in the streets."[301] In the end, decisions regarding the regulation of DIY CRISPR will need to resolve not only safety, effectiveness, and ethical issues related to specific applications but also issues of epistemic justice that could be equally challenging and significant.

301. *See* Telephone Interview with Sebastian Cocioba, *supra* note 228.