# CRISPR: The New Frontier of Biotechnology Innovation

**By Michael A. Stramiello**

Michael A. Stramiello, PhD, is a life sciences patent attorney in the Washington, DC, office of Paul Hastings LLP. Any opinions expressed herein are his and do not necessarily reflect the views of Paul Hastings or its clients. This article is intended solely for general information purposes and should not be taken as legal advice.

*Practically overnight, we have found ourselves on the cusp of a new age in genetic engineering and biological mastery—a revolutionary era in which the possibilities are limited only by our collective imagination. . . . Within a few decades, we might well have genetically engineered pigs that can serve as human organ donors—but we could also have woolly mammoths, winged lizards, and unicorns. No, I am not kidding.*

—Jennifer Doudna & Samuel Sternberg, *A Crack in Creation* [1]

By now, life sciences IP attorneys have probably heard about *c*lustered *r*egularly *i*nterspaced *s*hort *p*alindromic *r*epeats. In short, they are the signatures of bacterial immune systems that scientists have hijacked into biological tools for editing genomes, the DNA-based instruction manuals from which all living things are built and maintained. This article introduces those tools (collectively, CRISPR) and some of the hot-button IP issues that followed them into the limelight in 2017. Among the areas to watch: disputes over expansive patent rights here and abroad, calls for government intervention in licensing, industry responses to patent pooling efforts, and guidelines on how the FDA will regulate genome editing in humans. Such developments and others, along with the blistering pace of research and development, could make 2018 another exciting and formative year for CRISPR.

## Background

Since 2012, CRISPR has become the genome-editing platform of choice for life scientists around the world, largely due to its simplicity, efficiency, and low cost. Often described as "molecular scissors," CRISPR systems typically have two fundamental components: a strand of guide RNA (gRNA) and a CRISPR-associated endonuclease (e.g., Cas9). Together, they form a search-and-snip complex in which the gRNA takes on a hairpin shape. While one end of that hairpin dangles free to interact with nearby DNA, the other lugs along its endonuclease counterpart. As the complex encounters DNA, it bumps into short sequences (protospacer adjacent motifs), using them as footholds to quickly unzip the double helix and check for a gRNA-DNA match. Upon finding one, the complex undergoes a conformational change that causes its Cas9 component to cut the target DNA. (Put differently, gRNA searches and Cas9 snips.) Otherwise, the complex lets go and continues to hunt.

CRISPR's search-and-snip functionality is especially useful in the presence of natural repair enzymes that lurk near DNA, looking for and patching up breaks. By delivering beneficial DNA fragments to the vicinity of sequences that are targeted and cut, scientists can leverage those repair enzymes to rewrite the genome. In light of this capacity to rapidly create specific mutations, CRISPR has been hailed as "an unprecedented tool" for identifying the genetic basis of disease and reprogramming cellular behavior. [2] CRISPR's beauty lies also in its versatility, which does not stop with genome editing. Researchers have developed alternative, "broken scissors" techniques that focus on delivering molecular cargo rather than cutting. That cargo might serve a simple role, like latching onto a gene and blocking transcription, or it might do more, like inducing gene expression in response to external stimuli (e.g., light or chemicals). CRISPR can also be used to target RNA (which is continuously produced from DNA), greatly reducing any risk of permanent mistakes.

From what we have seen so far, CRISPR has stunning potential to change the future of medicine—some even speculate that "in the not-too-distant future it will cure genetic disease." [3] Still, hurdles remain. For example, scientists have voiced concerns about possible problems with immunogenicity, [4] unintended mutations, [5] and genetic variation across patients. [6] As those concerns are addressed, enthusiasm has mounted over preclinical studies (i.e., studies conducted in animals), which suggest that CRISPR may be used to cure muscular dystrophy, Huntington's disease, hemophilia, and many other genetic diseases, as well as to eliminate antibiotic-resistant bacteria and viruses (e.g., HIV and PERV, the latter of which has long frustrated developments in xenotransplantation). Given those promising results, researchers around the globe are cautiously pressing ahead and have at least 20 clinical trials in the works. [7]

Enthusiasm for CRISPR has also gained steam in other industries. In agriculture, for example, hopes are high that CRISPR will pave the way to hardier livestock and crops (e.g., tuberculosis-resistant cows and canker-resistant oranges). In fact, you might have already seen CRISPR'd, browning-resistant mushrooms at your local grocery. [8] CRISPR has also begun to make its mark on industrial biotechnology. For instance, one company recently began using CRISPR to make hydrogen peroxide for a new line of cleaning wipes, praising the technique as not just environmentally friendly, but also "cheaper and more efficient" than chemical syntheses. [9] Others have made strides toward modifying small organisms such as algae and E. coli into tiny biofuel factories. This broad range of applications sets the stage for wide-ranging and rapid advancements over the coming decades. In fact, recent estimates peg the revenue potential from CRISPR/Cas9 tools at $25–$30 billion by 2030. [10]

## The IP Landscape

Despite its promise, CRISPR remains hampered by a complex, uncertain IP landscape. In the United States, two key players are locked in an epic battle over how to divvy up foundational patent rights (i.e., those not focused on a specific gene or use), and there may be more to come. Meanwhile, storm clouds are gathering overseas, with foreign patent offices signaling that they may go in different directions. To further complicate domestic matters, some commentators have begun to call for government intervention in licensing. And while early discussion of patent pools brings hope, their viability is another open

question. Finally, the FDA may be gearing up for announcements on how it will regulate CRISPR innovations in human therapeutics. Though true clarity in the CRISPR patent landscape is years away, important developments are on the horizon in 2018.

**CRISPR Battle Lines**

Life sciences patent attorneys might remember 2017 as the year they finally took notice of CRISPR. At the center of their attention was the US Patent and Trademark Office's (USPTO's) Patent Trial and Appeal Board (PTAB), which in February 2017 surprised many by terminating a closely watched patent interference [11] between the University of California (UC, with collaborators University of Vienna and Emmanuelle Charpentier [12] ) and the Broad Institute (Broad, with collaborators Harvard and MIT). Central to that dispute, which the USPTO initiated at UC's request, is the question of which team first invented the claimed applications of CRISPR/Cas9 systems in eukaryotic environments (e.g., human cells). For example, UC argues that its application describes CRISPR/Cas9 systems and how they can be used for gene editing in *any* environment. [13] Broad counters that, among other things, a person of ordinary skill in the art would have had no reasonable expectation that such systems could be successfully applied to eukaryotic cells, as claimed in its own application and patents. [14]

Ultimately, the PTAB was persuaded by Broad's arguments and found that neither party's claims, if considered to be prior art, would have rendered the opposing claims anticipated or obvious, [15] meaning there was no "interference in fact," a threshold requirement rooted in 37 C.F.R. § 41.203(a). The PTAB therefore terminated the proceeding. That the PTAB did not cancel or finally refuse any claims, however, has not stopped some commentators from speculating that the patent landscape will ultimately play out with UC and Broad owning CRISPR rights in prokaryotes and eukaryotes, respectively. [16] The countervailing view, set out in layperson's terms by one of UC's named inventors, boils down to this: "the Broad Institute's patent is for green tennis balls but the patent [UC] will have is for all tennis balls." [17] In any event, UC appealed to the US Court of Appeals for the Federal Circuit, [18] which will likely hear oral arguments in April or May of 2018.

As the UC-Broad interference winds down, CRISPR watchers should not lose sight of the USPTO, where more challenges may wait in the wings. For example, at least one ex parte reexamination against a foundational patent owned by Broad has already been granted (and suspended until the interference concludes). There is also a looming threat of additional interferences, as mentioned in recent USPTO communications [19] and acknowledged in the pre-IPO disclosures of all three CRISPR-centric biotechnology companies publicly traded in the United States (i.e., CRISPR Therapeutics AG, Editas Medicine Inc., and Intellia Therapeutics Inc.). Potential dark horses identified in those filings include: (1) Rockefeller University, a joint applicant on certain Broad applications; (2) ToolGen Inc., whose suggestions of interference against Broad are still pending; and (3) Vilnius University, which has its own US patent for use of CRISPR/Cas9 systems and is party to a cross-licensing agreement with one of UC's licensees. Other entities may also come out of the woodwork with freedom-to-operate strategies that challenge key patents via inter partes review or post-grant review.

Additional CRISPR disputes will happen overseas in 2018—and if patent grants are any indicator, foreign agencies might not simply follow the USPTO's lead. The European Patent Office's (EPO's) Opposition Division (OD) will kick things off on January 16, when it hears oral arguments in oppositions

lodged against a foundational patent owned by Broad. Among other things, challengers have attacked the purported novelty of Broad's claims, a determination that may hinge on whether Broad validly claimed priority to two of its early applications. If it did not, at least seven of Broad's other opposed patents may be vulnerable too. The OD has already issued a preliminary opinion indicating that it expects the oppositions to succeed. [20] While that opinion is nonbinding, European analysts have stressed that it is usually "very difficult" to sway the OD from its preliminary views. [21] In any event, Broad will not be the only foundational patent holder fighting to keep its rights alive across the pond in 2018, as the EPO has also granted noteworthy patent rights to UC, Sigma-Aldrich, and Cellectis, thus opening nine-month windows for would-be challengers to file post-grant oppositions. The fight over UC's patent, which controversially covers use of CRISPR in both prokaryotes and eukaryotes, may be especially heated. It has already withstood over a half dozen third-party observations (including some filed by Broad), [22] and at least two groups have now filed post-grant oppositions. [23]

China, home to the world's second-busiest CRISPR patent landscape (after the United States), may host similar turf wars in 2018. UC and Broad, among many others, are already on the scene and may be drawing up battle plans. While Broad's applications remain pending, China's State Intellectual Property Office announced in June its intention to grant UC a patent covering CRISPR/Cas9 methods and compositions for applications in any environment. One of UC's key licensees in human therapeutics praised the decision as "further global recognition that [UC and its collaborators] are the pioneers in the application of CRISPR/Cas9 in all cell types." [24] Not missing a beat, Broad issued an ominous reminder that "[i]n China, patents are subject to invalidation proceedings after they are issued." [25]

**Agency Invasion**

CRISPR tangles in the United States have already sparked calls for government intervention per the Bayh-Dole Act of 1980. This law generally allows recipients of federal funds to license the fruits of their labor, providing commercialization opportunities that fuel innovation and public access to technologies made possible by taxpayer dollars. A more controversial aspect of Bayh-Dole, however, provides federal agencies with "march-in rights." Under specific circumstances, those rights—which have never been exercised [26] —confer on the executive branch the power to compel "nonexclusive, partially exclusive, or exclusive license[s]" to "responsible applicant[s]." [27]

Other commentators have more generally advocated for "updating Bayh-Dole's pro-commercialization safeguards," apparently out of concern "that courts [will] let overly broad patent rights emerge." [28] Their critics, however, ponder how agencies would properly determine whether patents are "overly broad," [29] also pointing out a placid statement from the federal government's premier funder of medical research, the National Institutes of Health (NIH):

While *we have not received any inquiries or complaints about lack of access* to the CRISPR-CAS9 technology for research or commercial development from those who are in a position to use the technology, *we continue to monitor access* and use of the CRISPR technology that was funded by NIH with respect to public access and compliance with NIH principles and policies. *At this time, we do not believe that a new NIH policy to address the licensing of CRISPR patented technology is necessary*. [30]

In arriving at that conclusion, the NIH considered and reported no violation of its long-standing "Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources." Among other things, those recommendations discourage exclusive licensing, "except in cases where the licensee undertakes to make the research tool widely available to researchers through unrestricted sale, or [where] the licensor retains rights to make the research tool widely available." [31]

**Patent Pool: Oasis or Mirage?**

As CRISPR marches on, there may be an elegant solution for making it widely available without government intervention in licensing: patent pools. These joint licensing platforms enable owners to combine their IP rights into bundles that are made accessible, nonexclusively, to a broad range of users via a single transaction with predictable terms. As a result, licensors and licensees can concentrate on innovation and commercial development, respectively, while minimizing transaction costs and litigation risk. [32] This model was popularized in the 1990s, when the consumer electronics industry adopted it to facilitate deployment of the MPEG-2 digital video standard, which has yielded about $5 trillion in worldwide product sales since 1997. [33] A key coordinator of that effort, MPEG LA LLC, now invites CRISPR/Cas9 patent holders to participate in their own pool.

MPEG LA has been gauging interest from CRISPR rights holders since at least April 2017. [34] Broad and Rockefeller University announced that they had submitted nearly two dozen "key CRISPR-Cas9 patents," [35] from 10 families, "for evaluation of eligibility to participate in discussions facilitated by MPEG LA regarding creation of a CRISPR Joint Licensing Platform." [36] UC reportedly has no plans to follow suit, citing potential conflicts with its existing licenses. [37] The effect that pooling would have on such arrangements may remain unclear until contributors finalize pool terms, which could take years. Early efforts might focus on pooling foundational patents, and there has also been speculation about specialized pools geared toward particular CRISPR applications (e.g., agriculture and industrial biotechnology). [38] Pooling may prove to be more of a challenge with respect to human therapeutics, a field where rights holders typically expect exclusivity as a reward for their enormous investment in rigorous clinical trials.

**Toward the Clinic**

In June 2017, an FDA senior policy advisor announced that the agency has begun building the capacity to regulate treatments that use CRISPR/Cas9 technologies. [39] Hammering out the details will take time, but related approvals, market exclusivities, and patent scuffles may be governed by the Biologics Price Competition and Innovation Act (BPCIA). Though gene therapies are not expressly included in the BPCIA's definition of "biological product[s]," [40] the FDA has made clear that marketing of "genetic material to modify or manipulate the expression of a gene product or to alter the biological properties of living cells for therapeutic use" requires an approved biologics license application. [41]

As regulatory channels take shape, do-it-yourself CRISPR kits have already become available for purchase, pitched with a warning that they are "not injectable or meant for direct human use." [42] The CEO founder of one such vendor recently made headlines by publicly injecting a CRISPR concoction after announcing: "This will modify my muscle genes to give me bigger muscles." [43] The FDA quickly

responded with a statement expressing its "concern[] about the safety risks" of such products and noting that their sale "is against the law." [44] It said nothing, though, of whether or how it would enforce that law. Either way, heavily invested patent owners may see traditional infringement litigation as a means to shield their nascent technologies from bad press as they wind their way toward the market.

## Conclusion

All things considered, 2018 is poised to be another defining year for CRISPR patent landscape. While the interference saga between UC and Broad may be nearing an end, it might be replaced by a similarly important ex parte reexamination and perhaps more interferences. Tremors may be felt overseas too, with high-profile opposition proceedings set to begin at the EPO and additional post-grant battles looming in Europe and possibly China. Adding to that uncertainty are (1) the possibility of government intervention in licensing, and (2) lingering questions about patent pooling efforts, which have been successful in other contexts and could dramatically simplify the CRISPR licensing. Finally, the FDA may soon issue guidelines for human therapeutics, which could either fuel or dampen enthusiasm for CRISPR-based medicine. While many of these questions (and others) will likely remain at the end of 2018, what happens between now and then may fundamentally shape the evolution of what many consider to be one of the most important scientific discoveries of the twenty-first century.

## Endnotes

1. JENNIFER A. DOUDNA & SAMUEL H. STERNBERG, A CRACK IN CREATION: GENE EDITING AND THE UNTHINKABLE POWER TO CONTROL EVOLUTION 117–18 (2017).

2. Arlene Weintraub, *Editing Genes with a More Precise Alternative to CRISPR*, FIERCEBIOTECH (Nov. 16, 2017), https://www.fiercebiotech.com/research/editing-genes-a-more-precise-alternative-to-crispr.

3. Megan Molteni, *CRISPR May Cure All Genetic Disease—One Day*, WIRED (June 7, 2017), https://www.wired.com/2017/06/crispr-may-cure-genetic-disease-one-day/; *see also* Andrew Griffin, *Gene Editing Could Bring an End to All Inherited Disease and Cancer, Expert Says*, INDEPENDENT (Feb. 16, 2017), http://www.independent.co.uk/life-style/gadgets-and-tech/news/cancer-inherited-disease-dna-crispr-gene-genome-edze-westra-exeter-university-a7584111.html.

4. *See, e.g.*, Carsten Trevor Charlesworth et al., *Identification of Pre-Existing Adaptive Immunity to Cas9 Proteins in Humans*, BIORXIV (Jan. 5, 2018), https://www.biorxiv.org/content/early/2018/01/05/243345.

5. *See, e.g.*, Kellie A. Schaefer et al., *Unexpected Mutations after CRISPR-Cas9 Editing In Vivo*, 14 NATURE METHODS 547 (2017). Notably, these findings drew widespread criticism, *see, e.g.*, Caleb Lareau et al., *"Unexpected Mutations after CRISPR-Cas9 Editing In Vivo" Are Most Likely Pre-Existing Sequence Variants and Not Nuclease-Induced Mutations*, BIORXIV (July 5, 2017), https://www.biorxiv.org/content/early/2017/07/05/159707, prompting editors to supplement the original article with an "Editorial Expression of Concern."

6. *See, e.g.*, Samuel Lessard et al., *Human Genetic Variation Alters CRISPR-Cas9 On – and Off-Targeting Specificity at Therapeutically Implicated Loci*," 114 PROC. NAT'L ACAD. SCI. USA E11257 (2017).

7. Michael Le Page, *Boom in Human Gene Editing as 20 CRISPR Trials Gear Up*, NEW SCIENTIST (June 7, 2017), https://www.newscientist.com/article/2133095-boom-in-human-gene-editing-as-20-crispr-trials-gear-up/.

8. *See* Letter from Michael J. Firko, Animal & Plant Health Inspection Serv. Deputy Adm'r, USDA, to Yinong Yang, Pa. State Univ. (Apr. 13, 2016), https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-321-01_air_response_signed.pdf.

9. Alex Knapp, *These Sustainably Produced Cleaning Wipes Herald a Manufacturing Revolution*, FORBES (Oct. 24, 2017), https://www.forbes.com/sites/alexknapp/2017/10/24/these-sustainably-produced-cleaning-wipes-herald-a-manufacturing-revolution/.

10. Reenita Das, *Gene Editing with CRISPR-Cas9: The Next Step in Human Evolution Will Be Worth $25 Billion by 2030*, FORBES (Dec. 14, 2017), https://www.forbes.com/sites/reenitadas/2017/12/14/gene-editing-with-crispr-cas9-the-next-step-in-human-evolution-to-be-worth-25-billion-by-2030/.

11. A patent interference is essentially a trial over who invented what first.

12. While university researchers are typically required to assign IP rights to their employer, Charpentier reportedly retained hers due to "a quirk of Swedish law," as she was employed by Sweden's Umeå University at the time of her contributions to the involved claims. Joe Stanganelli, *Interference: A CRISPR Patent Dispute Roadmap*, BIO-IT WORLD (Jan. 9, 2017), http://www.bio-itworld.com/2017/1/9/interference-a-crispr-patent-dispute-roadmap.aspx.

13. Brief for Appellants at 14, Regents of Univ. of Cal. v. Broad Inst., Inc., No. 17-1907 (Fed. Cir. July 25, 2017).

14. Broad et al. Reply 2, at 1, Broad Inst., Inc. v. Regents of Univ. of Cal., No. 106,048 (P.T.A.B. Sept. 28, 2016), https://acts.uspto.gov/ifiling/PublicView.jsp?identifier=106048&identifier2=null&tabSel=4&action=filecontent&replyTo=PublicView.jsp (Doc. No. 866).

15. Broad Inst., Inc. v. Regents of Univ. of Cal., No. 106,048, 2017 WL 657415 (P.T.A.B. Feb. 15, 2017).

16. Jef Akst, *UC Berkeley Receives CRISPR Patent in Europe*, SCIENTIST (Mar. 24, 2017), https://www.the-scientist.com/?articles.view/articleNo/48987/title/UC-Berkeley-Receives-CRISPR-Patent-in-Europe/.

17. Sarah Buhr, *CRISPR-Cas9 Inventor Jennifer Doudna's Plans on Moving Forward, Genetically Modifying Humans*, TECHCRUNCH (Feb. 15, 2017), https://techcrunch.com/2017/02/15/crispr-cas9-inventor-jennifer-doudnas-plans-on-moving-forward-genetically-modifying-humans/.

18. Brief for Appellants, *supra* note 13.

19 *See, e.g.*, Office Communication in U.S. Patent Application No. 15/435,233, dated Dec. 15, 2017.

20. *CRISPR in Europe: The Patent Landscape for 2018*, LIFE SCI. INTELL. PROP. REV. (Nov. 30, 2017), https://www.lifesciencesipreview.com/news/crispr-in-europe-the-patent-landscape-for-2018-2595.

21. Alexander Esslinger, *CRISPR EP Update: Oral Hearing at EPO in Opposition Case against Broad Patent Is Scheduled for 16 January 2018. Preliminary Opinion Negative for Broad*, PATENTLY GERMAN (Apr. 25, 2017), https://patentlygerman.com/2017/04/25/crispr-ep-update-oral-hearing-at-epo-in-opposition-case-against-broad-patent-is-scheduled-for-16-january-2018-preliminary-opinion-negative-for-broad/.

22. Akst, *supra* note 16.

23. Jonathan Wosen, *Cellectis Granted T Cell CRISPR Patent in Europe*, GENETIC ENGINEERING & BIOTECHNOLOGY NEWS (July 25, 2017), https://www.genengnews.com/gen-news-highlights/cellectis-granted-t-cell-crispr-patent-in-europe/81254707.

24. Press Release, Intellia Therapeutics, Intellia Therapeutics Announces Patent for CRISPR/Cas Genome Editing in China (June 19, 2017), https://globenewswire.com/news-release/2017/06/19/1025667/0/en/Intellia-Therapeutics-Announces-Patent-for-CRISPR-Cas-Genome-Editing-in-China.html.

25. Sydney Johnson, *China Will Grant CRISPR Patent to UC*, DAILY CALIFORNIAN (June 20, 2017), http://www.dailycal.org/2017/06/20/china-to-side-with-uc-on-crispr-patent/.

26. Paul A. Calvo, *March-In Rights and Compulsory License in the United States*, NAT'L L. REV. (Oct. 16, 2017), https://www.natlawreview.com/article/march-rights-and-compulsory-license-united-states.

27. 35 U.S.C. § 203(a).

28. Arti K. Rai & Robert Cook-Deegan, *Racing for Academic Glory and Patents: Lessons from CRISPR*, 358 SCI. 874 (2017).

29. Joseph Allen, *Another IP Professor Attack on Patenting*, IPWATCHDOG (Nov. 29, 2017), http://www.ipwatchdog.com/2017/11/29/another-ip-professor-attack-on-patenting/.

30. E-mail from Carrie D. Wolinetz, Acting Chief of Staff & Assoc. Dir. for Sci. Policy, Nat'l Insts. of Health, to James Love, Diane Singhroy & Andrew Goldman, Knowledge Ecology Int'l (June 21, 2017), https://www.keionline.org/23413/.

31. 64 Fed. Reg. 72,090, 72,095 (Dec. 23, 1999).

32. Lawrence A. Horn, *Amazing Gene-Editing Technology Needs a Pass on Patent Minefields*, MERCURY NEWS, Nov. 25, 2017, https://www.mercurynews.com/2017/11/25/opinion-amazing-gene-editing-technology-needs-a-pass-on-patent-minefields/.

33. Richard Lloyd, *First CRISPR Patent Pool Signs Up Key Patent Owner, but Significant Challenges Remain*, IAM (July 20, 2017), http://www.iam-media.com/Blog/Detail.aspx?g=09acb846-9af3-4d51-aee3-d6fa79351cfb.

34 Press Release, MPEG LA, MPEG LA Invites CRISPR-Cas9 Patents to be Pooled in a One-Stop License (Apr. 25, 2017), https://www.mpegla.com/Lists/MPEG%20LA%20News%20List/Attachments/103/CRISPRPatentCallPrsRls2017-04-25.pdf

35. Press Release, Broad Inst., Broad Institute of MIT and Harvard Joins Discussions to Create Worldwide CRISPR-Cas9 Licensing Pool (July 10, 2017), https://www.broadinstitute.org/news/broad-institute-mit-and-harvard-joins-discussions-create-worldwide-crispr-cas9-licensing-pool.

36. Letter from Ellen Law, Senior Advisor to the Dir., Broad Inst. of MIT & Harvard, to Lawrence A. Horn, President & CEO, MPEG LA LLC (June 28, 2017), https://www.broadinstitute.org/files/news/pdfs/MPEG-LA-Broad-joint-submission.pdf.

37. Peter Leung, *Patent Pool Seeks to Ease Gene-Editing Tech Licensing*, 17 BLOOMBERG BNA'S PAT. TRADEMARK & COPYRIGHT J., no. 147, Aug. 2, 2017.

38. Aggie Mika, *Flux and Uncertainty in the CRISPR Patent Landscape*, SCIENTIST (Oct. 1, 2017), https://www.the-scientist.com/?articles.view/articleNo/50441/title/Flux-and-Uncertainty-in-the-CRISPR-Patent-Landscape/.

39. Zachary Brennan, *Regulating CRISPR: FDA and Industry Offer Perspective*, REG. AFF. PROFS. SOC'Y (June 21, 2017), http://www.raps.org/Regulatory-Focus/News/2017/06/21/27951/Regulating-CRISPR-FDA-and-Industry-Offer-Perspective/.

40. *See* 42 U.S.C. § 262(i)(1).

41. *What Is Gene Therapy?*, FDA, http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm573960.htm (last updated Jan. 9, 2018).

42. Emily Mullin, *Biohackers Disregard FDA Warning on DIY Gene Therapy*, MIT TECH. REV. (Dec. 1, 2017), https://www.technologyreview.com/s/609568/biohackers-disregard-fda-warning-on-diy-gene-therapy/.

43. Stephanie M. Lee, *This Guy Says He's the First Person to Attempt Editing His DNA with CRISPR*, BUZZFEED (Oct. 14, 2017), https://www.buzzfeed.com/stephaniemlee/this-biohacker-wants-to-edit-his-own-dna.

44. *Information about Self-Administration of Gene Therapy*, FDA, https://www.fda.gov/biologics-bloodvaccines/cellulargenetherapyproducts/ucm586343.htm (last updated Nov. 21, 2017).