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Editing Nature: Reconceptualizing Biotechnology Governance

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Abstract: CRISPR-Cas9 (CRISPR) and other advances in gene editing techniques are fostering a rapid evolution within the field of biotechnology. Scientists can now modify the DNA of living organisms with precision by removing undesirable traits or inserting desirable traits. The edits may impact a single organism or result in genetic alterations that are designed to pass on to offspring (referred to as "gene drives"), potentially altering or eradicating an entire species. Prior to the discovery of the CRISPR gene editing process, the state of the technology presented barriers to widespread and precise genetic engineering. CRISPR changes the equation. With fewer technological limits and the technical and economic accessibility of new gene editing techniques, society now must grapple with fundamental questions regarding the proper use of technologies that can reengineer organisms, species, and ecosystems. The existing approach to biotechnology governance is unprepared to address these new capabilities, in part because the technology has quickly surpassed the bounds once thought possible, and in part because the regulatory system is premised on a narrow set of considerations designed to foster advances in the field of biotechnology. This Article examines early regulatory oversight of advanced gene editing techniques and identifies important gaps in legal oversight of genetic engineering: a failure of existing laws to cover some CRISPR-edited organisms; narrow consideration of ecological impacts; regulators' inability to consider alternatives; and a failure to assess and respond to competing ideologies. This Article then argues for addressing those gaps by incorporating a natural resource management perspective into biotechnology governance. The article concludes by arguing that biotechnology governance should incorporate a natural resource management perspective. The scientific advances are new, but the challenges with balancing competing considerations

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regarding the use and alteration of natural resources are not. Although existing natural resource laws do not contemplate the ability to reorder ecosystems via gene editing, there is an established regulatory system designed to address risks of extinction, accommodate competing ideologies regarding resource use, and incorporate interests of future generations when considering irreversible decisions regarding natural resources—issues that are all implicated by gene editing.

> *[W]ith the newest and arguably most effective genetic engineering tool, CRISPR-Cas9 (CRISPR for short), the genome—an organism's entire DNA content, including all its genes—has become almost as editable as a simple piece of text. As long as the genetic code for a particular trait is known, scientists can use CRISPR to insert, edit, or delete the associated gene in virtually any living plant's or animal's genome.*[1]

> *Genetics has provided a paradigm for an entire new vision of human potential, and the potential of nature*.[2]

INTRODUCTION

In the summer of 2016, Florida residents faced warnings over the Zika virus, which is transmitted by mosquito bites and tied to birth defects such as microcephaly.[3] Pregnant women were advised to stay indoors, wear long sleeves and pants, apply bug spray, and sleep under bed nets to avoid Florida's ubiquitous mosquitoes.[4] To address this public health crisis, the United States Food and Drug Administration (FDA) approved a field test of genetically-modified mosquitoes to control the risk of Zika virus and dengue fever. If successful, the offspring of the modified mosquitoes would die before they could reproduce. To make the judgment about the mosquitoes, the FDA turned to existing biotechnology rules—a body of law that is not prepared for the latest developments in gene editing technologies.[5]

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[1] JENNIFER A. DOUDNA & SAMUEL H. STERNBERG, A CRACK IN CREATION: GENE EDITING AND THE UNTHINKABLE POWER TO CONTROL EVOLUTION, at xiii (2017).

[2] WORKING GRP. OF THE SOC'Y, RELIGION & TECH. PROJECT, ENGINEERING GENESIS: THE ETHICS OF GENETIC ENGINEERING IN NON-HUMAN SPECIES 258 (Donald Bruce & Ann Bruce eds., 2013) (1998).

[3] Sammy Mack, *Pregnant Women in Miami Take Extra Precautions Against Zika*, NAT'L PUB. RADIO (Aug. 17, 2016), http://www.npr.org/2016/08/17/490314048/pregnant-women-in-miami-take-extra-precautions-against-zika [https://perma.cc/W4VN-3XVQ]; *Questions About Zika,* CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/zika/about/questions.html [http://perma.cc/JG2F-CXR4].

[4] Mack, *supra* note 3.

[5] *See generally* FOOD & DRUG ADMIN., FINDING OF NO SIGNIFICANT IMPACT (FONSI) IN SUPPORT OF A PROPOSED FIELD TRIAL OF GENETICALLY ENGINEERED MALE *AEDES AEGYPTI* MOSQUITOES OF THE LINE OX513A IN KEY HAVEN, MONROE COUNTY, FLORIDA UNDER AN

The field trial was the first FDA-approved release of a genetically-modified insect and is an early example of a federal agency grappling with an emerging body of gene editing techniques and the modified organisms the techniques can produce.[6] The pace of these biotechnology advances is increasing dramatically thanks to a groundbreaking new development in gene editing known as "clustered, regularly interspaced, short palindromic repeats," or CRISPR-Cas 9 ("CRISPR").[7] CRISPR and other advances in genetic engineering give public and private actors the ability to edit the DNA of living organisms, including human beings, with precision.[8] Scientists may deploy CRISPR to remove undesirable traits or insert desirable traits. The edits may impact a single organism or result in genetic alterations designed to pass on to offspring (referred to as "gene drives"), potentially impacting an entire species.[9]

Public policy is only beginning to consider the broad implications of this new generation of genomic sciences.[10] Governance of CRISPR and other gene editing techniques relies on various existing laws which are designed to address previous methods of genetic engineering.[11] Safety and risk management are the dominant lenses through which regulators United States view questions regarding biotechnology research and commercialization—an approach that is incapable of addressing the fundamental ethical and moral issues raised by recent advances in gene editing technologies.[12]

INVESTIGATIONAL NEW ANIMAL DRUG EXEMPTION (Aug. 5, 2016) (relying in part on the Coordinated Framework for the Regulation of Biotechnology to make its determination).

[6] *Id.*

[7] Paul Enriquez, *CRISPR GMOs*, 18 N.C. J.L. & TECH. 432, 509−10 (2017). CRISPR technology varies from past methods of genetic engineering technology due to its ability to exactly target a specific DNA site by using the Cas9 protein which allows scientists to either delete or insert certain DNA at the targeted site. *Id.* The mosquitoes involved in the proposed Key Haven field trial were modified using a different method of genetic engineering. *See* FOOD & DRUG ADMIN., ENVIRONMENTAL ASSESSMENT FOR INVESTIGATIONAL USE OF AEDES AEGYPTI OX513A, at 16, 18, 21 (Aug. 5, 2016) [hereinafter FDA MOSQUITO ENVIRONMENTAL ASSESSMENT] (noting that Oxitec's mosquitoes include a "recombinant DNA (rDNA) construct").

[8] DOUDNA & STERNBERG, *supra* note 1, at xiii.

[9] Gregory E. Kaebnick et al., *Precaution and Governance of Emerging Technologies: Precaution Can Be Consistent with Support of Science*, 354 SCIENCE 710, 711 (2016).

[10] *See, e.g.*, Heidi Ledford, *Gene-Edited Cows, Rogue Clinics, Speedier Drug Approvals: The Challenges Facing Trump's FDA Chief*, 541 NATURE 146, 146–47 (2017) (identifying regulatory questions facing the Trump administration); Lars Noah, *Managing Biotechnology's (r)evolution: Has Guarded Enthusiasm Become Benign Neglect?,* 11 VA. J. L. & TECH., Spring 2006, at 8–9 (discussing early policy responses to biotechnology developments).

[11] *See, e.g.*, Gregory N. Mandel & Gary E. Marchant, *The Living Regulatory Challenges of Synthetic Biology*, 100 IOWA L. REV. 155, 173 (2014) (noting that synthetic biology will be subject to "existing environmental and human health protection statutes").

[12] NAT'L ACADS. OF SCIS., ENG'G, & MED., GENE DRIVES ON THE HORIZON: ADVANCING SCIENCE, NAVIGATING UNCERTAINTY, AND ALIGNING RESEARCH WITH PUBLIC VALUES 63–70

Policymakers' responses to the rapidly advancing field of gene editing technologies has the potential to fundamentally alter humans' relationship with the natural world.[13]

Early regulatory decisions regarding CRISPR and other advanced gene editing techniques reveal important gaps in legal oversight of genetic engineering. Some of these gaps—such as the limited consideration of ecological impacts, the lack of authority to compare gene editing with alternate approaches to achieve similar benefits, and the failure to address competing ideologies—existed prior to the advent of CRISPR but are exacerbated by the new techniques. Other gaps—primarily instances of gene-edited products escaping regulatory oversight altogether—raise important new questions for the role of public policy in shaping the evolution of emerging genomic sciences.[14]

This Article argues that gene editing should be viewed in the context of resource management.[15] Although CRISPR is new, many of the conflicts presented by the technology are not. Over the past century-and-a-half, a broad body of law has evolved to address conflicts regarding ownership of natural resources, acceptable uses for specific types of resources, environmental impacts of resource and ecosystem alterations, and the balance between resource use, conservation, and preservation. The nation's multifaceted approach to natural resource management reaches different conclusions regarding alteration, preservation, and use of specific resources, but collectively natural resource governance grapples with fundamental questions regarding humans' relationship with natural systems. To varying degrees, natural resource statutes require agencies to consider ecological impacts, economic interests, risk management, interests of future generations, and

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(2016) [hereinafter GENE DRIVES ON THE HORIZON]. The genetic engineering debate is not, and never has been, solely about concerns regarding safety and risk. Genetic engineering is controversial because it challenges existing norms about the proper use of technology and it raises vexing ethical and ecological concerns about safety, risk, irreversibility, and the disparity between those who may benefit and those who may be harmed. *Id.*; Kaebnick et al., *supra* note 9, at 711.

[13] *See, e.g.*, NUFFIELD COUNCIL ON BIOETHICS, GENOME EDITING: AN ETHICAL REVIEW—A SHORT GUIDE 4 (2016), http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review-short-guide.pdf [https://perma.cc/K7DP-RT9T] ("[G]enome editing could transform not only the field of biology, but the range of expectations and ambitions about human control over the biological world.").

[14] NAT'L ACADS. OF SCIS., ENG'G, & MED., PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY 67–70 (2017) [hereinafter PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY].

[15] *See infra* notes 225–304 and accompanying text. This is not to argue that a natural resource perspective should supplant other applicable bodies of law. Laws regarding public health, intellectual property, and protection of agricultural products all remain critical pieces of the biotechnology governance system. The central claim in this Article is that these existing laws leave out important considerations that are commonly addressed in the natural resources context.

evolving societal values.[16] Altering species and ecosystems via CRISPR raises the same suite of issues, yet there is little overlap between biotechnology governance and the broad body of natural resources law.[17]

Not only does the disconnect between biotechnology and natural resource governance create direct conflicts between policy goals, it also fails to incorporate the values-based considerations that underlie many of the natural resource statutes.[18] Natural resource management offers models for addressing the key regulatory gaps presented by gene editing techniques, as well as models for incorporating a broader set of considerations into the biotechnology governance framework.[19] A failure to incorporate this broader set of considerations leaves biotechnology governance unprepared to face the moral, legal, and ecological questions regarding proper use of a technology that can fundamentally alter living organisms and, by extension, ecosystems and economies. The paper focuses primarily on the governance of non-human applications, but draws lessons from the more restrictive, values-based regulatory standards applied to questions of human genome editing.

Although this Article calls for a conceptual shift toward a natural resource perspective, it does not advocate for a particular normative resolution of gene editing conflicts. Natural resource management is as much about balancing competing interests as it is about prioritizing a particular outcome (e.g., managing for conservation or preservation). Instead, the Article offers a new conceptual model for understanding gene editing's place within the values-based governance framework that already considers vexing topics such as irreversible changes to living organisms and ecosystems, interests of future generations, and conflicting viewpoints regarding resource extraction and preservation.

Part I of this Article introduces CRISPR and identifies governance challenges presented by new gene editing techniques.[20] Part II provides an overview of the existing approach to biotechnology governance in the United States.[21] Part III explores early examples of federal agencies applying this approach to organisms that are modified via gene editing techniques

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[16] *See infra* notes 47–99 and accompanying text.

[17] *See infra* notes 100–108 and accompanying text.

[18] *See* PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 69 box 3-1 (stating that "[v]alues are always embedded in risk analysis by the choices and interpretations of the people conducting them and the selection of risk-assessment endpoints of concern, methods, and questions").

[19] *See infra* notes 225–304 and accompanying text.

[20] *See infra* notes 25–46 and accompanying text.

[21] *See infra* notes 47–99 and accompanying text.

and identifies critical gaps in the regulatory system.[22] The focus on whether a product is altered in a manner that poses a risk to human health, plant and animal health, or ecosystems fails to address a broader range of ethical concerns and societal values that arise in the gene editing context. A prospective use may be deemed safe, yet it could still raise issues that extend beyond the realm of risk management or scientific expertise.

Part IV turns to natural resource law as a model for expanding the debate beyond a case by case risk management approach to an approach that addresses competing values regarding the use of gene editing and the ecological impacts of doing so.[23] It concludes by identifying strategies to incorporate a natural resource management approach into the current risk-based regulatory framework.[24] Together, these strategies offer an approach for balancing conflicting views of gene editing and establishing the equivalent of protected spaces in the genetic engineering context—circumstances where gene editing is prohibited or limited on a temporary or permanent basis.

I. NEW CHALLENGES FOR BIOTECHNOLOGY GOVERNANCE

CRISPR opens the door to a vast array of genetic alterations, allowing scientists to alter humans, plants, animals, and other living organisms by removing undesirable traits or inserting desirable ones.[25] These edits may apply to individual organisms through non-heritable edits.[26] The precision of CRISPR also significantly expands the ability to permanently alter or eradicate entire species though gene drives—edits to the germline (reproductive) cells that produce heritable traits.[27] Although only a handful of gene-edited organisms have been approved for release in the United States and the European Union, numerous releases are likely to occur in the near future.[28] CRISPR, therefore, presents one of many tests for the Anthropo-

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[22] *See infra* notes 100–224 and accompanying text.

[23] *See infra* notes 225–304 and accompanying text.

[24] *See infra* notes 225–304 and accompanying text.

[25] *See generally* Jennifer A. Doudna & Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 SCIENCE 1077 (2014); News Release, Nat'l Insts. of Heath, Researchers Identify Potential Alternative to CRISPR-Cas Genome Editing Tools, (Oct. 22, 2015), https://www.nih.gov/news-events/news-releases/researchers-identify-potential-alternative-crispr-cas-genome-editing-tools [https://perma.cc/C5AA-S4ZM].

[26] NAT'L ACADS. OF SCIS., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 3 (2017) [hereinafter HUMAN GENOME EDITING].

[27] GENE DRIVES ON THE HORIZON, *supra* note 12, at 156–57.

[28] *See* PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 41, 172 (explaining the scope of new biotechnology products not currently under U.S. regulatory power including, "[p]lants that glow, yogurts that harbor biosensors, pigs that develop twice as much muscle, and microbial communities that may protect honey bees from parasitic mites").

cene, in which technological advancements allow humans to fundamentally, and permanently, reshape and dominate natural systems.[29]

The new generation of gene editing techniques presents a complex mix of prospective benefits and complex ethical questions. Gene editing is both a miraculous scientific breakthrough with the potential to save or improve human and nonhuman lives and a pathway for creating designer babies and pets.[30] These techniques simultaneously offer a tool to permanently alter ecosystems by enhancing some species and driving others to extinction and create an emerging threat on the scale of weapons of mass destruction that humanity is not prepared to contain.[31] Casting the technology in the context

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[29] *See* Eric Biber, *Law in the Anthropocene Epoch*, 106 GEO. L.J. 1, 3, 6 (2017) (noting the Anthropocene Epoch is a proposed new "geological timeframe" denoted by the impact humans have had on Earth); R. Alta Charo & Henry T. Greely, *CRISPR Critters and CRISPR Cracks*, 15 AM. J. OF BIOETHICS 11, 15 (2015) (describing the Anthropocene Epoch as a proposed geologic division characterized by human modification of living things in the world).

[30] Antonio Regalado, *First Gene-Edited Dogs Reported in China*, MIT TECH. R. (Oct. 19, 2015), https://www.technologyreview.com/s/542616/first-gene-edited-dogs-reported-in-china/ [https://perma.cc/P8FA-3Y4S] [hereinafter Regalado, *First Gene Edited Dogs Reported in China*]; Antonio Regalado, *Engineering the Perfect Baby*, MIT TECH. R. (Mar. 5, 2015), https://www.technologyreview.com/s/535661/engineering-the-perfect-baby/ [https://perma.cc/J4UG-G7A7]; s*ee* Hong Ma et al., *Correction of a Pathogenic Gene Mutation in Human Embryos*, 548 NATURE 413, 413 (2017) (reporting on the first successful use of gene editing to repair a disease-causing genetic mutation); Gina Kolata, *Gene Editing Spurs Hope for Transplanting Pig Organs into Humans*, N.Y. TIMES (Aug. 10, 2017), https://www.nytimes.com/2017/08/10/health/gene-editing-pigs-organ-transplants.html [https://perma.cc/L3QF-DPVV] (noting the potential to use gene-editing to facilitate transplanting pig organs into humans).

[31] It is not uncommon for articles in scientific journals and popular press books, websites, and magazines to describe gene editing and genetic engineering as controlling or altering evolution or facilitating intentional extinction. *See*, *e.g.*, DOUDNA & STERNBERG, *supra* note 1, at xiii (describing capabilities of genomic editing technology); Statement for the Record to the Senate Armed Servs. Comm., Worldwide Threat Assessment of the US Intelligence Community, James R. Clapper (Feb. 9, 2016) (stating that "research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products"); *see also* Juan Enriquez & Steve Gullans, *With Gene Therapy We Could Direct Our Own Evolution*, DISCOVER (Mar. 9, 2015), http://blogs.discovermagazine.com/crux/2015/03/09/gene-therapy-direct-evolution/ [https://perma.cc/9ZZD-UUKX] (noting the potential for gene editing to allow selective evolution by choosing "desirable traits" and rejecting "negative traits"); Jens Hegg, *Is Intentional Extinction Ever the Right Thing?*, PLOS ECOLOGY COMMUNITY (July 1, 2016), http://blogs.plos.org/ecology/2016/07/01/is-intentional-extinction-ever-the-right-thing/ [https://perma.cc/EG2J-SD38] (considering the balance between extinction of one species for the benefit of another); Sean Illing, *Genetically-Engineered Humans Will Arrive Sooner Than You Think. And We're Not Ready*, VOX (Aug. 3, 2017), https://www.vox.com/conversations/2016/10/24/13357298/michael-bess-biotechnology-bio engineering-technology-revolution-science [https://perma.cc/7ZRH-WH5T] (interviewing historian Michael Bess about the implications of genetically-engineered humans); Antonio Regalado, *The Extinction Invention*, MIT TECH. R. (Apr. 13, 2016), https://www.technologyreview.com/s/601213/the-extinction-invention/ [https://perma.cc/P48C-HJKN] (identifying potential concerns associated with using gene drive to eliminate certain mosquito populations).

of designer babies, evolution and extinction, and global threats highlights the importance of updating the biotechnology regulatory framework to grapple with the critical value choices inherent in determining how to effectively govern this new form of genetic engineering with such broad applications and potentially profound and irreversible impacts. In the absence of technological restraints, effective regulatory standards will be critical to inform professional standards, ethics, and public policy guiding when professional and amateur scientists may alter individual organisms or entire ecosystems using precision gene editing procedures.[32]

Gene editing differs from previous genetic engineering techniques in significant respects. Unlike previous techniques, CRISPR can achieve genetic alterations by deleting a portion of an organism's existing DNA without inserting foreign DNA into the organism.[33] This distinction may allow CRISPR-edited organisms to avoid regulatory triggers that apply to organisms modified via earlier genetic engineering techniques.[34] CRISPR allows more precise genetic alterations than previous techniques, potentially mitigating concerns about unintended genetic changes resulting from the use of CRISPR. Perhaps the most important difference is CRISPR's relative simplicity and low cost. These factors have allowed the technique to spread quickly to laboratories across the globe, complicating governance efforts due to the large number of actors and international scope.[35]

For example, scientists are altering fruits and vegetables to increase shelf life in grocery stores. Work is underway to edit crops' drought tolerance and pest resistance to increase agricultural production.[36] Companies are experimenting with gene drive techniques to eradicate disease-carrying insects and insects that harm agricultural crops.[37] Laboratories in China and

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[32] The existence of conflicting views within the scientific community regarding human germline editing highlights the need for norms to guide both research and commercialization. Debates over proper types of research and commercial applications occur primarily within academic journals, often focusing on a single discipline. All the while, research and plans for commercialization continue.

[33] Enriquez, *supra* note 7, at 509–10.

[34] *Id.* at 512–13.

[35] *See* PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 41 (noting the large number of actors and products resulting from developments in biotechnology); Doudna & Charpentier, *supra* note 25, at 1077 (observing that many laboratories "around the world" are using new biotechnology to develop new applications). This paper does not tackle questions regarding international governance of CRISPR.

[36] GENE DRIVES ON THE HORIZON, *supra* note 12, at 4; PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 45–46.

[37] GENE DRIVES ON THE HORIZON, *supra* note 12, at 4, 26; PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 48–49.

the United States have utilized CRISPR to edit human embryos.[38] Other applications under development include hornless cows, customized dogs, and a reintroduced prehistoric wooly mammoth.[39] The list could go on. The genetically-engineered cat is out of the bag.

This is a critical time for reconsidering biotechnology governance. The current system of biotechnology governance in the United States is primarily designed to address risks to human health and agricultural products. Laws governing drugs and medical procedures for humans are generally far more restrictive than laws overseeing plant and animal products, particularly when those products are not intended for human consumption.[40] In in-

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[38] HUMAN GENOME EDITING, *supra* note 26, at 41; Steve Connor, *First Human Embryos Edited in U.S.*, MIT TECH R. (July 26, 2017), https://www.technologyreview.com/s/608350/first-human-embryos-edited-in-us/ [https://perma.cc/8ATA-EHQE].

[39] *See* Amy Maxmen, *Gene-Edited Animals Face US Regulatory Crackdown*, NATURE (Jan. 19, 2017), http://www.nature.com/news/gene-edited-animals-face-us-regulatory-crackdown-1.21331 [https://perma.cc/B3ZT-5CYW] (describing the creation of hornless dairy cattle "by inserting a gene from naturally hornless beef cattle into a breed of the same species that is used in milk production"); Regalado, *First Gene Edited Dogs Reported in China*, *supra* note 30 (reporting on the first gene-edited dogs); Simon Worrall, *We Could Resurrect the Woolly Mammoth. Here's How.*, NAT'L GEOGRAPHIC (July 9, 2017), https://news.nationalgeographic.com/2017/07/woolly-mammoths-extinction-cloning-genetics/ [https://perma.cc/3A5K-Y98R] (describing the project to use genetic editing to create a wooly mammoth).

[40] *See generally* Enriquez, *supra* note 7, at 499–500 (noting the limitation of the 2017 Update to Coordinated Framework that, "products posing little to no risk [to human health] ought not to be subject to onerous regulation"); Jennifer Kuzma & Lindsey Rawls, *Engineering the Wild: Gene Drives and Intergenerational Equity*, 56 JURIMETRICS J. 279, 293–94 (2016) (noting that the future consequences of gene drives are unknown and, therefore, could pose risks to future populations); Alison Peck, *Re-Framing Biotechnology Regulation*, 72 FOOD & DRUG L.J. 314, 317–23 (2017) (noting that new genetic engineering technology has surpassed the scope of the 2017 Update to Coordinated Framework's regulation). These articles complement a robust body of legal scholarship regarding governance of biotechnology and genetically-modified organisms (GMOs) generally. *See, e.g.*, Mary Jane Angelo, *Regulating Evolution for Sale: An Evolutionary Biology Model for Regulating the Unnatural Selection of Genetically Modified Organisms*, 42 WAKE FOREST L. REV. 93, 156–65 (2007) (proposing an evolutionary biology model for regulating GMOs); Carmen G. Gonzalez, *Genetically Modified Organisms and Justice: The International Environmental Justice Implications of Biotechnology*, 19 GEO. INT'L ENVTL. L. REV. 583 (2007) (examining the risks and benefits of GMOs for developing countries). Much of the CRISPR-focused legal scholarship that has been published to date focuses on patent and copyright issues. *See, e.g.*, Ian Ayres & Lisa Larrimore Ouellette, *A Market Test for Bayh-Dole Patents*, 102 CORNELL L. REV. 271, 278 (2017) (describing the dispute over patent rights for CRISPR); Deborah Ku, *The Patentability of the CRISPR-Cas9 Genome Editing Tool*, 16 CHI.-KENT J. INTELL. PROP. 408, 422–39 (2017) (discussing whether CRISPR technology is a patent-eligible subject matter); Robin Feldman, *The Crispr Revolution: What Editing Human DNA Reveals About the Patent System's DNA*, 64 UCLA L. REV. DISCOURSE 392, 404–10 (2016), https://www.uclalawreview.org/wp-content/uploads/2016/11/Feldman-D64-update.pdf [https://perma.cc/F82V-4TXT] (discussing the tension between the slow-moving U.S. patent system and the rapid innovation of CRISPR technology); Kristin Beale, Recent Development, *The Crispr Patent Battle: Who Will Be "Cut" Out of Patent Rights to One of the Greatest Scientific Discoveries of Our Generation?*, B.C. INTELL. PROP. & TECH. FORUM, Feb. 9, 2016, at 4–6, http://bciptf.org/wp-content/uploads/

stances not involving direct human applications, biotechnology governance is premised on the notion that genetically-engineered products are not inherently dangerous and do not require separate regulatory approaches.[41]

Although biotechnology has long faced opposition, the costs, technical limits, and barriers to entry associated with earlier genetic engineering techniques allowed decisionmakers to avoid grappling with many of the difficult decisions regarding appropriate and prohibited uses.[42] The range of potential uses of gene editing, the likely exponential increase in the number of edited organisms in the near future, and the increasing speed of further technological innovations will challenge the existing regulatory framework.[43]

Rapid advances in the field of gene editing are now forcing the unresolved issues, and in the process raising complex moral, ethical, and ecological questions.[44] For example, the same process for eradicating disease-carrying insects could also apply to insects that are considered nuisances to humans or animals but are not disease vectors. Should regulatory approaches differ depending on the type of gene editing applications, such as distinctions between those that address critical societal needs and those that allow discretionary alterations for mere convenience, comfort, cost reduction, or aesthetic preferences?[45] Furthermore, how will gene editing to eradicate

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2016/02/KBeale-CRISPR.pdf [https://perma.cc/R64A-TBML] (describing patent issues surrounding CRISPR).

[41] *See generally Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology*, Exec. Office of the President (Jan. 4, 2017) [hereinafter *2017 Update to Coordinated Framework*] (summarizing that governance decisions do not turn on the fact that scientists engineered the change, or the potential evolutionary impacts of the genetic changes).

[42] *See* GENE DRIVES ON THE HORIZON, *supra* note 12, at 64 (stating that "[g]enetic engineering sparked ethical debate as soon as it was imagined").

[43] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 27 (noting that "[i]ncreasing investment in the bioeconomy, complex societal challenges, the confluence of new technical drivers, and a proliferation of new actors are transforming both biotechnology products and the context in which the U.S. regulatory system operates"). Another recent National Academy report predicts calls for rapid release of gene-edited organisms to address, "crisis situations, before there is adequate knowledge of their ecological effects, and before mitigation plans for unintended consequences are in place." GENE DRIVES ON THE HORIZON, *supra* note 12, at 1; *see* Jay Bennett, *11 Crazy Gene-Hacking Things We Can Do with CRISPR*, POPULAR MECHANICS (Jan. 26, 2016), http://www.popularmechanics.com/science/a19067/11-crazy-things-we-can-do-with-crispr-cas9/ [https://perma.cc/Q9WH-SBBU] (listing potential uses for CRISPR); Kristopher Grunert, *Backyard Gene Editing Risks Creating a Monster*, NEW SCIENTIST (Mar. 15, 2017), https://www.newscientist.com/article/mg23331173-400-backyard-gene-editing-risks-creating-a-monster/ [https://perma.cc/9AYS-4VJ7] (noting the risks of unregulated use of CRISPR).

[44] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 27; Grunert, *supra* note 43; *see* GENE DRIVES ON THE HORIZON, *supra* note 12, at 1 (noting that "[g]enetic engineering sparked ethical debate as soon as it was imagined").

[45] *See* Bruce L. Webber et al., *Opinion: Is CRISPR-Based Gene Drive a Biocontrol Silver Bullet or Global Conservation Threat?*, 112 PROCEEDINGS OF THE NAT'L ACAD. OF SCIS. 10,565,

species interact with statutes regarding conservation and species preservation? Should public policy restrict gene editing if other conventional techniques are available to achieve the same result? Should policymakers consider new regulatory measures that account for a broader array of societal values implicated by gene editing techniques? Perhaps most fundamentally, who makes these decisions and to what degree do they need to engage affected stakeholders?

The widespread availability of the technology may create particular governance challenges, as numerous laboratories are able to experiment with engineering similar organisms, potentially resulting in multiple new species enhanced with different characteristics aimed at accomplishing different goals.[46] These new capabilities shine light on the direct role of human decision making in guiding the trajectory of species and ecosystems. The direct links to, and occasional conflicts with, existing environmental and natural resource regulatory schemes call for a more robust system of governance that oversees the use of CRISPR.

II. THE EXISTING BIOTECHNOLOGY GOVERNANCE FRAMEWORK

The existing system of biotechnology governance is unprepared to adequately answer the questions posed by gene editing, in part because the technology has quickly surpassed the bounds once thought possible, and in part because the regulatory system is premised on a narrow set of considerations designed to foster advances in the field of biotechnology while managing prospective risks. Early regulatory responses to proposals for releasing genetically-engineered organisms indicate how the current biotechnology governance system will apply to the upcoming wave of gene editing applications. This section provides an overview of the existing framework for biotechnology governance in the United States, analyzes case studies applying this framework to the recent advancements in genetic engineering, and identifies regulatory gaps exposed by these case studies.[47]

The Reagan Administration established the Coordinated Framework for Regulation of Biotechnology ("Coordinated Framework") in 1986 to clarify agency roles under existing law, streamline agency collaboration,

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10,565 (Aug. 25, 2015) (stating that "[t]he question is no longer whether we can control invasive species using gene drive, but whether we should").

[46] *See* David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCIENCE 36, 36 (Apr. 3, 2015) (stating that "[t]he simplicity of the CRISPR-Cas9 system allows any researcher with knowledge of molecular biology to modify genomes, making feasible experiments that were previously difficult or impossible to conduct").

[47] *See infra* notes 48–99 and accompanying text.

and avoid overlapping regulations.[48] Two key decisions provide the foundation for the Coordinated Framework. First, the Reagan Administration prioritized safety and risk, primarily to human health and agriculture, when evaluating the use of genetic engineering.[49] Second, government officials concluded that biotechnology is not "inherently risky," and thus opted to evaluate the safety and risk of individual genetically-altered products on a case-by-case basis.[50] Governance decisions do not turn on the fact that scientists engineered the change, or the potential evolutionary impacts of the genetic changes.[51] These conclusions supported reliance on existing law to oversee biotechnology products.[52] The Coordinated Framework continues to define the United States approach to biotechnology governance. The decision to prioritize risk management over other concerns and the focus on products (in other words, the organism and any risks it may pose) rather than the fact that the organism was genetically-modified remain sources of conflict in debates regarding genetic engineering.[53]

The Obama Administration's 2017 Update to the Coordinated Framework reiterates the view that the product-specific, risk-based approach adequately addresses both health and environmental risks of biotechnology products.[54] Rather than suggesting revisions to the regulatory system, the update focuses on increasing transparency, clarifying agency authority, and reducing regulatory hurdles.[55] The update "describes the types of biotechnology product areas regulated by the various components within each primary regulatory agency (*i.e.*, EPA, FDA, or USDA)" and outlines each agency's responsibility when a particular type of product falls within the scope of

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[48] *See generally* Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302 (June 26, 1986) [hereinafter Coordinated Framework].

[49] *See, e.g.*, *id.* at 23,303 (requiring that regulatory reviews deem a new product to be safe before it can be commercialized).

[50] NAT'L RESEARCH COUNCIL, GENETICALLY MODIFIED PEST-PROTECTED PLANTS: SCIENCE AND REGULATION 25 (2000) [hereinafter GM PEST-PROTECTED PLANTS]. For example, the FDA considers development of new plant varieties as a "continuum" that includes selective breeding and genetic engineering. Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22, 984, 22,985–86 (May 29, 1991). The obligation to ensure that new food products are safe applies anywhere along that continuum. *Id.* at 22,985.

[51] 57 Fed. Reg. at 22,985–86.

[52] *See* Coordinated Framework, *supra* note 48, at 23,303 (stating that existing laws are sufficient to regulate most new biotechnology).

[53] Jennifer Kuzma et al., *Evaluating Oversight Systems for Emerging Technologies: A Case Study of Genetically Engineered Organisms*, 37 J.L. MED. & ETHICS 546, 549 (2009); *see* GENE DRIVES ON THE HORIZON, *supra* note 12, at 1 (noting that "[g]enetic engineering sparked ethical debate as soon as it was imagined"); Grunert, *supra* note 43 (noting the risks of unregulated use of CRISPR).

[54] *2017 Update to Coordinated Framework*, *supra* note 41, at 5.

[55] *Id.* at 2, 5.

more than one agency.[56] The update also clarifies the timeline of review to minimize delays and support innovation, by "discuss[ing] provisions for future review of the Coordinated Framework."[57]

The 2017 Update to the Coordinated Framework includes hypothetical biotechnology products to demonstrate how the regulatory system might apply.[58] Notably, the hypotheticals do not specify examples of products developed via gene editing technologies despite the growing prevalence of CRISPR during the 18-month process of producing the update.[59] The hypotheticals also fail to provide clear guidance regarding when a product triggers collaboration among the three agencies, or which agency takes the lead in initiating the collaborations.[60]

The National Strategy for Modernizing the Regulatory System for Biotechnology Products ("National Strategy"), released in 2016, complements the update to the Coordinated Framework by "develop[ing] a long-term strategy to ensure that the Federal regulatory system is equipped to efficiently assess the risks, if any, of the future products of biotechnology."[61] Like the 2017 Update to the Coordinated Framework, the National Strategy does not specifically address new risks raised by CRISPR and other recent advancements in biotechnology.[62] Instead, the report identifies general options for future actions ranging from holding stakeholder meetings to "explor[ing] mechanisms to enhance coordination" among the agencies.[63]

The FDA, Department of Agriculture (USDA), and Environmental Protection Agency (EPA) have primary responsibility for biotechnology governance, applying existing statutes to perform product-specific risk-based assessments. Whether a genetically-engineered product falls within an agency's respective jurisdiction depends on the type of organism, how the genetic modification occurred and the intended uses of the modified product. The FDA considers whether a genetically-altered plant, animal, or other organism poses a health risk to humans or animals. The FDA also oversees gene therapy and human genome editing, applying higher levels of

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[56] *Id.* at 2. When necessary, the agencies are to form ad hoc working groups potentially including members outside the three agencies for additional expertise. *Id.* at 36. The update provides examples to provide specific, non-binding mechanisms to guide agency collaboration. *Id.* at 37–38.

[57] *Id.* at 2.

[58] *Id.* at 39–51.

[59] The Executive Office of the President launched the update process on July 2, 2015. *Id.* at 1.

[60] *Id.* at 36, 39.

[61] NAT'L SCI. & TECH. COUNCIL, NATIONAL STRATEGY FOR MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS 4 (Sept. 2016), https://www.epa.gov/sites/production/files/2016-12/documents/biotech_national_strategy_final.pdf [https://perma.cc/YM79-7GQT].

[62] *See generally id.*

[63] *Id.* at 12, 19.

scrutiny to gene editing intended for direct human applications.[64] The USDA focuses on potential harm to agricultural plants and animals. The EPA regulates new genetically-engineered products if they meet the definition of a pesticide or produce "new chemical substances" that are not otherwise regulated by the FDA or USDA. The following subsections provide an overview of each agency's role in biotechnology governance and recent developments to address advances in gene editing.

A. FDA Oversight

The FDA oversees three primary categories of genetically-engineered products: (1) human drugs and medical products, (2) animal drugs, and (3) foods derived from plants.[65] The applicable laws generally require premarket approval of drugs, biological products, medical devices, food additives, and dietary supplements.[66]

Consistent with the Coordinated Framework's focus on the characteristics of a product rather than the biotechnology process used to develop the product, the FDA evaluates the safety and effectiveness of covered products regardless of the technique used to produce the products.[67] Recognizing

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[64] There is a ban on federal funding for human genome editing. Consolidated Appropriations Act of 2016, Pub. L. No. 114−113, 129 Stat. 2242, 749 (adopted Dec. 18, 2015) (banning federal funding of "research in which a human embryo is intentionally created or modified to include a heritable genetic modification"); Francis S. Collins, Dir. of Nat'l Insts. of Health, *Statement on NIH Funding of Research Using Gene-Editing Technologies in Human Embryos*, NAT'L INSTS. OF 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/3B3B-34G2].

[65] The Federal Food, Drug, and Cosmetic Act focuses on food safety and the safety and effectiveness of human and animal drugs. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. § 301 (2018)); *2017 Update to Coordinated Framework*, *supra* note 41, at 9 tbl.1. The Public Health Service Act governs the safety of biological products developed for "the prevention, treatment, or cure of diseases or injuries of man," including but not limited to viruses, vaccines, and blood. Public Health Service Act, Pub. L. No. 78-410, 58 Stat. 682 (1944) (codified as amended at 42 U.S.C. § 262 (2018)). The FDA may also regulate biotechnology products involving cosmetics, foods and food additives, dietary supplements, tobacco products, new animal drugs, and drugs and devices. *What Does FDA Regulate?*, FOOD & DRUG ADMIN. https://www.fda.gov/aboutfda/transparency/basics/ucm194879.htm [https://perma.cc/F8T4-AKDY]. The FDA also addresses other angles of biotechnology—for example, valid nutritional and health claims. *See, e.g.*, 21 U.S.C §§ 301, 341, 348, 350–364, 387a (2018) (stating the FDA's authority to regulate various biotechnology products).

[66] Food additives do not require pre-market approval if they are classified as "generally recognized as safe" for their intended uses. 21 U.S.C. § 321(s).

[67] For example, the FDA's method to evaluate "foods derived from new plant varieties, includ[es] those developed by recombinant DNA (rDNA) techniques." Robert M. Califf & Ritu Nalubola, *FDA's Science-based Approach to Genome Edited Products*, FDA VOICE (Jan. 18, 2017), https://blogs.fda.gov/fdavoice/index.php/2017/01/fdas-science-based-approach-to-genome-edited-products/ [https://perma.cc/PE6V-L67Q]. The FDA's regulation of biological products includes products produced via gene editing. *Id.*

uncertainties regarding approval of biotechnology products, the agency established a voluntary pre-market consultation process for foods derived from genetically-engineered products.[68] The FDA has yet to complete a consultation for foods derived from a plant produced from gene editing.[69]

Of the three agencies with primary oversight of biotechnology products, the FDA has been the most active in updating regulations to address advances in gene editing.[70] The agency released two draft guidance documents in early 2017 aimed at updating its approach to genetically-engineered animals and mosquito-related products, and requested comments regarding regulation of gene editing in plants.[71] As discussed below, these steps would expand the definition of "animal drug" to subject gene editing of animals to additional regulatory review.[72]

B. USDA Oversight

The USDA's role in biotechnology governance is rooted in its authority to control animal and plant pests pursuant to the Animal Health Protection Act ("AHPA") and Plant Protection Act ("PPA").[73] The AHPA requires the USDA to prohibit or restrict the importation into the United States and transportation across state lines of any pests or disease-causing organisms in

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[68] *Consultation Procedures Under FDA's 1992 Statement of Policy—Foods Derived from New Plant Varieties*, FOOD & DRUG ADMIN. (revised Oct. 1997), https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096126.htm [https://perma.cc/CF47-CAUA] [hereinafter *1992 Consultation Procedures*]; *see Biotechnology Consultations on Food from GE Plant Varieties*, FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/scripts/fdcc/?set=Biocon [https://perma.cc/5JBZ-NXFM] (listing records of biotechnology consultations that used the FDA's 1992 consultation procedures).

[69] *See 1992 Consultation Procedures*, *supra* note 68 (detailing the process that developers of biotechnology products may use to consult with the FDA prior to market release).

[70] *Q&A on FDA Regulation of Intentionally Altered Genomic DNA in Animals*, FOOD & DRUG ADMIN., https://www.fda.gov/animalveterinary/developmentapprovalprocess/geneticengineering/geneticallyengineeredanimals/ucm113605.htm [https://perma.cc/HRD4-YRB2].

[71] *See generally* FOOD & DRUG ADMIN., CLARIFICATION OF FDA AND EPA JURISDICTION OVER MOSQUITO-RELATED PRODUCTS: GUIDANCE FOR INDUSTRY (Oct. 2017), https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM533600.pdf [https://perma.cc/D6EA-CVQH] [hereinafter FDA MOSQUITO DRAFT GUIDANCE]; FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: REGULATION OF INTENTIONALLY ALTERED GENOMIC DNA IN ANIMALS, DRAFT GUIDANCE (Jan. 2017), https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf [https://perma.cc/C6H4-MFSU] [hereinafter FDA GE ANIMALS DRAFT GUIDANCE]; *FDA Requests Comments on Documents Related to Certain Biotechnology and Mosquito-related Products*, FOOD & DRUG ADMIN., https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm536949.htm [https://perma.cc/PB48-YKG7].

[72] FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 4–7.

[73] Plant Protection Act, 7 U.S.C. §§ 7701–7786 (2018); Animal Health Protection Act, 7 U.S.C. §§ 8301–8322 (2018).

livestock populations, including animals that may present a risk of transmitting such pests or diseases.[74] The agency conducts an animal health risk assessment to determine if genetically-engineered animals present a risk to livestock health.[75] If so, the genetically-engineered organism is subject to import or transport restrictions.[76] Genetically-engineered insects may also fall under AHPA provisions if there is a risk they could spread livestock diseases.[77] The PPA requires the USDA to control plant pests and noxious weeds.[78] Importantly for gene editing governance, PPA regulations presume that genetically-engineered organisms include foreign DNA—a characteristic of earlier genetic engineering techniques.[79] Other genetically-engineered organisms may also be subject to regulation if they are unclassified under the PPA, the classification is unknown, or they "contain[] such an organism, or any other organism or product altered or produced through genetic engineering which the [USDA] Administrator, determines is a plant pest or has reason to believe is a plant pest."[80] If a genetically-engineered organism is subject to PPA regulations, the USDA requires notification prior to the importation, interstate transport, or release of a covered plant pest or noxious weed.[81] Entities may petition for an exemption by demonstrating that the product is not a plant pest.[82]

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[74] 7 U.S.C. §§ 8303, 8305.

[75] *See id.* § 8303.

[76] *Id.*; 7 C.F.R. § 340.0 (2018).

[77] 7 U.S.C. § 8302 (13).

[78] 7 U.S.C. § 7701 (2018). Statutory definitions of "plant pest" and "noxious weed" are quite broad. *See id.* §§ 7702 (10) (defining a "noxious weed" as "any plant or plant product that can directly or indirectly injure or cause damage to crops (including nursery stock or plant products), livestock, poultry, or other interests of agriculture, irrigation, navigation, the natural resources of the United States, the public health, or the environment"), 7702 (14) (defining "plant pest" as "any living state of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product: (A) a protozoan; (B) a nonhuman animal; (C) a parasitic plant; (D) a bacterium; (E) a fungus; (F) a virus or viroid; (G) an infectious agent or other pathogen; (H) any article similar to or allied with any of the articles specified in the preceding subparagraphs").

[79] *See* 7 C.F.R. § 340.1 (defining a "regulated article" as "[a]ny organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belongs to any genera or taxa designated in § 340.2 and meets the definition of plant pest").

[80] *Id.*

[81] *Id.* § 340.0.

[82] Importation, Interstate Movement, and Environmental Release of Certain Genetically Engineered Organisms, 82 Fed. Reg. 7008, 7016 (Jan. 19, 2017) [hereinafter Import and Release of GE Organisms].

In January 2017, the USDA proposed new PPA regulations to adapt to advances in the field of biotechnology.[83] If approved, this would be the first comprehensive revision of the regulations since they were established in 1987.[84] Under the proposed rule, the USDA would make an initial determination whether a genetically-engineered organism poses a plant pest or noxious weed risk rather than impose permitting requirements and allow entities to petition for exemptions.[85] The proposal maintains the focus on genetically-engineered products rather than the process; therefore, only those products that pose a plant risk or noxious weed risk would be subject to regulation.[86]

C. EPA Oversight

The EPA's role in biotechnology governance focuses primarily on pesticides and toxic materials. The Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") requires the agency to regulate "the distribution, sale, or use in any State of any pesticide that is not registered . . . ."[87] Pesticides include "any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, . . . [or] intended for use as a plant regulator, defoliant, or desiccant, [or] nitrogen stabilizer . . . ."[88] The EPA must determine that the pesticide in question presents no "unreasonable adverse effects on the environment" prior to its sale or distribution.[89]

The Federal Food, Drug, and Cosmetic Act ("FDCA") tasks the EPA with establishing the amount of pesticide chemical residues that may be present in food and to "determine[] that there is a reasonable certainty that

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[83] *See generally* APHIS, QUESTIONS & ANSWERS: APHIS REQUESTS PUBLIC INPUT ON NEXT STEPS TOWARDS REVISION OF ITS BIOTECHNOLOGY REGULATIONS (Jan. 2017), https://www.aphis.usda.gov/biotechnology/downloads/340/q&a_biotech-reg-revisions.pdf [https://perma.cc/RTH8-K7CA] [hereinafter APHIS Q&A].

[84] *Id.* In 2008, APHIS proposed a multi-tiered permit system and a significant expansion of agency regulatory authority revisions. Import and Release of GE Organisms, *supra* note 82, at 7011. The proposed revisions were rejected due to a lack of detail regarding which organisms would fall under regulatory control. *Id.* The failure of that proposal informed the revisions included in the current proposal. *Id.* at 7011–12.

[85] APHIS Q&A, *supra* note 83.

[86] *Id.*

[87] Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. § 136a (2018).

[88] *Id.* § 136(u).

[89] *Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Federal Facilities*, ENVTL. PROT. AGENCY, https://www.epa.gov/enforcement/federal-insecticide-fungicide-and-rodenticide-act-fifra-and-federal-facilities#Summary [https://perma.cc/TX56-9QRK]. Unreasonable adverse effects may include: (1) products that cause unreasonable risk to humans or the environment and (2) "a human dietary risk from residues that result from the use of a pesticide in or on any food inconsistent with the standard under section 346a of title 21." 7 U.S.C. § 136(bb).

no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."[90] The tolerance levels set by the EPA apply to both domestic and imported foods.[91] The EPA has the ability to alter either the tolerance or tolerance exemption levels, and the FDA must follow the levels set by the EPA.[92]

The EPA also regulates certain biotechnology products pursuant to the Toxic Substances Control Act ("TSCA").[93] For example, the TSCA applies to plant-incorporated protectants ("PIPs"), genetically-modified microbial pesticides, herbicide tolerant crops, and intergeneric microorganisms.[94] Although some plants naturally produce defenses against pests, these TSCA-regulated organisms are modified to "express[] pesticidal properties by producing a bacterial protein that will protect the plants from specific insects."[95] In the case of herbicide-tolerant crops, the EPA regulates the herbicide even though the plant falls under USDA jurisdiction and the FDA is responsible for regulating the food produced from the plant.[96] The EPA sets the tolerance levels for the herbicide, ensuring that the levels comply with the legal limits of pesticide residue.[97]

Although the 2016 amendments to TSCA do not specifically pertain to biotechnology, the law requires alterations in the review process that require "an affirmative finding on the safety of new chemical substances . . . before they are allowed into the marketplace."[98] This finding includes populations

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[90] 21 U.S.C. § 346a(b)(2)(A)(ii) (2018).

[91] ENVTL. PROT. AGENCY, *Chapter 11—Tolerance Petitions*, *in* PESTICIDE REGISTRATION MANUAL, https://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-11-tolerance-petitions#main-content [https://perma.cc/H4QM-5YLU].

[92] 21 U.S.C. § 346a.

[93] Toxic Substances Control Act, 15 U.S.C. §§ 2601–2629 (2018). The TSCA aims to "[p]revent the manufacture, processing, distribution in commerce, use, or disposal of chemical substances, or any combination of such activities with such substances, from presenting an unreasonable risk to potentially exposed or susceptible population, without consideration of costs or other non-risk factors." *2017 Update to Coordinated Framework*, *supra* note 41, at 9.

[94] *2017 Update to Coordinated Framework*, *supra* note 41, at 13. Intergeneric organisms are "[m]icroorganisms formed by the deliberate combination of genetic material from organisms classified in different taxonomic genera, including microorganisms constructed with synthetic genes not identical to DNA that would be derived from the same genus as the recipient . . . ." *Id.*

[95] *EPA's Regulation of Biotechnology for Use in Pest Management*, ENVTL. PROT. AGENCY, https://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/epas-regulation-biotechnology-use-pest-management [https://perma.cc/RLS6-MHJP].

[96] *Id.*

[97] *Id.*

[98] *2017 Update to Coordinated Framework, supra* note 41, at 14; *Regulatory Determinations Made Under Section 5 of the Toxic Substances Control Act (TSCA)*, ENVTL. PROT. AGENCY, https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/regulatory-determinations-made-under [https://perma.cc/N23K-5NP5].

that may be affected other than the one intended.[99] Unlike the FDA and USDA, the EPA has not proposed any updates to its biotechnology regulatory framework to address new gene editing technologies.

III. GAPS IN GENE EDITING GOVERNANCE

A 2017 National Academy of Sciences study, produced at the request of the White House Office of Science and Technology, considered the future of biotechnology as part of the process for updating the Coordinated Framework.[100] The study identified additional regulatory gaps and resource needs.[101] For example, the report concludes that the FDA, the USDA, and the EPA "lack the expertise and resources to effectively address the rise in biotechnology products."[102] The report recommends a single entry point for categories of genetically-engineered products to better streamline and identify circumstances that require more complex risk assessments.[103] Additionally, the report raises concerns regarding new types of biotechnology products not previously encountered, such as toys or pets, and suggests that newer products require a completely new approach to risk analysis because they will be so different from those that currently exist.[104] The study also notes that "[existing] statutes may not empower regulators to require product developers to share in the burden of generating information about product safety . . . ."[105]

These issues remain unaddressed. For example, the FDA's draft guidance concerning genetically-engineered mosquitoes seeks to clarify the circumstances under which the FDA or EPA would act as the lead agency in the future. The guidance proposes that the FDA would oversee "products that limit disease transmission or modify mosquitoes in non-lethal ways."[106] The FDA argues that products engineered to reduce the size of a mosquito population should be considered pesticides rather than a new animal drug,

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[99] *See 2017 Update to Coordinated Framework, supra* note 41, at 13 (noting the consideration of "potentially exposed or susceptible population[s]").

[100] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 67–70.

[101] *Id.* at 98–102.

[102] *2017 Update to Coordinated Framework*, *supra* note 41, at 5–6.

[103] *Id.* at 9−10.

[104] *Id.* at 11.

[105] *Id.* at 173.

[106] Jack Karsten & Darrell M. West, *New Biotech Regulations Require Balance of Safety and Innovation*, BROOKINGS: TECHTANK (Mar. 3, 2017), https://www.brookings.edu/blog/techtank/2017/03/03/new-biotech-regulations-require-balance-of-safety-and-innovation/ [https://perma.cc/M6PA-RWAV]; *see* FDA MOSQUITO DRAFT GUIDANCE, *supra* note 71, at 5 (differentiating between FDA regulation of new animal drugs and EPA regulation of pesticide products).

thereby falling under the EPA's jurisdiction pursuant to the FIFRA.[107] Although the goal of the document is to separate unnecessary overlap between the EPA and the FDA, it identifies some situations when the FDA may consult with the EPA.[108] As of the publication of this Article, the EPA has not weighed in on the question. Unless the proposed guidance receives final approval, releases of gene-edited insects and animals will continue to fall within the FDA's jurisdiction if the modified organism could directly impact human health.

Early examples of agencies applying existing law to gene-edited organisms expose four additional regulatory gaps that extend beyond those identified by the National Academy report. The first, a gap in regulatory oversight, is exposed by the recent advances in gene editing. The remaining three—minimal consideration of ecological impacts, regulators' inability to consider alternatives, and a failure to assess and respond to competing ideologies—have been evident for quite some time but are exacerbated by the accessibility and far-reaching impacts of CRISPR. These gaps demonstrate that the deficiencies in biotechnology governance require more than additional resources, expertise, and coordination. Instead, addressing these issues requires rethinking the nation's approach to biotechnology governance and the goals and values that guide agencies as they evaluate the next wave of genetically-modified organisms.

A. Regulatory Oversight

Despite recent efforts to update and enhance the coordination among the relevant agencies, some gene-edited products fall outside the scope of existing regulation.[109] Deleting an organism's own genes, rather than inserting foreign DNA, may alter the species and potentially its ecosystem, but it may not increase the direct risks the organism poses to human or animal health.[110] Choosing not to regulate certain products may be appropriate. As

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[107] FDA MOSQUITO DRAFT GUIDANCE, *supra* note 71, at 5–6; *see* Karsten & West, *supra* note 106 (noting a proposal that would give the EPA authority over genetically-engineered products that limit or eliminate mosquitos and the FDA authority over products that inhibit mosquito-borne diseases or alter mosquitoes without complete elimination).

[108] FDA MOSQUITO DRAFT GUIDANCE, *supra* note 71, at 6.

[109] FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 6, 8–9; Maxmen, *supra* note 39; *see* Jennifer Kuzma, *Reboot the Debate on Genetic Engineering*, 531 NATURE 165, 166 (2016), (noting that approximately twenty genetically-engineered plants have escaped USDA regulatory review since 2011).

[110] *See* Import and Release of GE Organisms, *supra* note 82, at 7015−16 (stating that new genetic-engineering techniques that delete an organism's own genes simply speed up results of ordinary breeding, and therefore the risk is comparable to ordinary breeding, thus finding no inherent increased risks).

it stands, however, that choice occurs by default because drafters of existing laws and regulations did not imagine the new options for editing genes—hardly an appropriate rationale for declining to govern a new technology with potentially profound cultural, economic, and ecological implications.

1. Mushrooms and Corn

In April 2016, the USDA determined that a CRISPR-edited white button mushroom modified to reduce browning and a variety of waxy corn that increases the starch content in the kernels are not subject to review by the agency. These were the USDA's first considerations of agricultural products edited via CRISPR.[111] In both cases, the USDA's Animal and Plant Health Inspection Service ("APHIS") concluded that there is "no reason to believe" that CRISPR-edited white button mushrooms or waxy corn are plant pests as defined by the PPA.[112] Neither product triggered EPA regulation because they did not produce pesticides or toxic materials.[113] The FDA did not have jurisdiction over the crop itself, but can oversee the product at a later date if the developer decides to bring the mushroom to market.[114]

The gene-edited white button mushroom and waxy corn join a growing number of genetically-engineered agricultural products considered non-regulated articles under the USDA regulations, highlighting how recent technologies are beginning to fall outside the scope of the USDA's product-

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[111] Letter from Michael J. Firko, Deputy Director, APHIS, to Dr. Daria H. Schmidt (Apr. 18, 2016), https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-352-01_air_response_signed.pdf [https://perma.cc/4ALR-WMKQ] [hereinafter USDA Waxy Corn Letter]; Letter from Michael J. Firko, Deputy Director, APHIS, to Dr. Yinong Yang (Apr. 13, 2016), (https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-321-01_air_response_signed.pdf [https://perma.cc/D2PX-XLH9] [hereinafter USDA White Button Mushroom Letter]; *see* Emily Waltz, *CRISPR-Edited Crops Free to Enter Market, Skip Regulation*, 34 NATURE BIOTECHNOLOGY 582, 582 (2016) (stating that "[t]he first CRISPR-edited crops presented to the US regulatory system can be cultivated and sold without oversight by the [USDA]"). The USDA subsequently announced that it would not regulate gene-edited crops "that could otherwise have been developed through traditional breeding techniques as long as they are developed without the use of a plant pest as the donor or vector and they are not themselves plant pests." *Details on USDA Plant Breeding Innovations*, U.S. DEP'T AGRIC. (June 14, 2018), https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/brs-news-and-information/2018_brs_news/pbi-details [https://perma.cc/CT5W-QDHV].

[112] USDA Waxy Corn Letter, *supra* note 111, at 2; USDA White Button Mushroom Letter, *supra* note 111, at 2; *cf.* Plant Protection Act, 7 U.S.C. § 7702 (14) (2018) (defining plant pests).

[113] *See* USDA Waxy Corn Letter, *supra* note 111, at 2 (noting that the engineered corn is not subject to regulation under 7 C.F.R. § 340); USDA White Button Mushroom Letter, *supra* note 111, at 2 (noting that the engineered mushroom is not subject to regulation under 7 C.F.R. § 340).

[114] *See* 21 U.S.C. §§ 342(a)(1), 348 (2018) (stating that substances that are not added to food are not considered "adulterated" if they are not harmful to health and, therefore, not subject to FDA regulation).

based regulations.[115] APHIS's reasoning regarding CRISPR could lead to a growing class of genetically-engineered food products that falls outside USDA jurisdiction.[116]

2. The Hornless Cow

A gene-edited hornless cow may provide the next test of the biotechnology governance system. The genetic modification to create hornless dairy cows, which the developers promote as improving animal welfare and farmer safety, inserts a gene from an existing breed of hornless beef cattle into a breed of dairy cattle.[117] Recombinetics, Inc., the firm seeking to market the hornless cows, bases its arguments on a selective breeding analogy for gene editing.[118] Proponents of this viewpoint argue that editing an organism's genetic code by removing or altering specific strands of DNA is simply speeding up the selective breeding process farmers have used for thousands of years; in other words, there is nothing harmful about the process.[119] Furthermore, because selective breeding is perfectly legal, new techniques that achieve the same result should be legal as well.

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[115] Emily Waltz, *Gene-Edited CRISPR Mushroom Escapes US Regulation*, 532 NATURE 293, 293 (2016). For example, the USDA approved a genetically-engineered potato that reduces browning and bruising. Determination of Nonregulated Status of Genetically Engineered Potato, 80 Fed. Reg. 53,101, 53,101 (Sept. 2, 2015). Unlike traditional genetically-modified crops, however, this technique only contains a trace of foreign DNA—a key trigger for USDA regulation. DEP'T OF AGRIC., NATIONAL ENVIRONMENTAL POLICY ACT DECISION AND FINDING OF NO SIGNIFICANT IMPACT: X17 AND Y9 POTATOES WITH LATE BLIGHT RESISTANCE, LOW ACRYLAMIDE POTENTIAL, LOWERED REDUCED SUGARS, AND REDUCED BLACK SPOT (16-064-01p), at 5 (Oct. 28, 2016). The agency has also approved an apple designed to resist browning using a similar technique. Preliminary Determination for an Extension of a Determination of Nonregulated Status for Non-Browning Artic Apple Event NF872 Apple, 81 Fed. Reg. 53,396, 53,396 (Aug. 12, 2016).

[116] *See* USDA Waxy Corn Letter, *supra* note 111, at 2 (stating that "given the speed, ease, and wide use of CRISPR gene-editing, many other crops are sure to follow [the CRISPR-edited waxy corn]"); Melody M. Bomgardner, *CRISPR: A New Toolbox for Better Crops*, 95 CHEM. & ENG'G NEWS 30, 30–34 (2017) (noting that "questions persist" regarding regulation and that the USDA commented that "it does not have the authority to regulate" plants that do not contain certain gene-edited plants that "do not contain foreign genes").

[117] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 45; DEP'T OF AGRICULTURE RESEARCH, EDUC., & INFO. SYS., IMPROVEMENT OF DIARY ANIMAL WELL-BEING BY GENETIC DEHORNING, https://portal.nifa.usda.gov/web/crisprojectpages/1005738-improvement-of-diary-animal-well-being-by-genetic-dehorning.html [https://perma.cc/2XL2-YSSY] [hereinafter DAIRY ANIMAL WELL-BEING]. The dehorning method utilizes a gene editing technique referred to as "transcription activator-like effector nucleases" rather than CRISPR. DAIRY ANIMAL WELL-BEING, *supra.*

[118] DAIRY ANIMAL WELL-BEING, *supra* note 117.

[119] *See, e.g.*, Luisa Bortesi & Rainer Fischer, *The CRISPR/Cas9 System for Plant Genome Editing and Beyond*, 33 BIOTECHNOLOGY ADVANCES 41, 48–49 (2015) (noting that genome editing both speeds up and increases the efficiency of "conventional breeding"); Harry Pettit, *Genetically-Modified Cows Without Horns Are Created to Make the Countryside Safer*, DAILY MAIL (Feb. 20,

The selective breeding narrative argues for little or no additional regulation due to the genetic similarities between a product edited using CRISPR and a product developed over multiple generations using conventional breeding techniques. It also situates CRISPR within a context familiar and nonthreatening. This lens calls into question the justifications for regulating a CRISPR-edited organism, as well as the notion of what it means to label a product as "natural."[120] If CRISPR is analogous to selective breeding or natural selection, it follows that gene-edited organisms are no less natural than their counterparts that could foster similar genetic changes through conventional reproduction.

The selective breeding analogy calls for limited oversight, even in circumstances where genetic alteration could foster irreversible impacts to species and the environment. Adopting this perspective would likely lead to the development of edited organisms that extend well beyond those necessary to protect vexing health and ecological issues. It is easy to imagine, for example, the multibillion-dollar pest control industry deploying gene editing to eradicate insects that are nuisances but do not pose threats to human health or agricultural products.

The argument has its limitations, as there are important differences between CRISPR and selective breeding. Selective breeding takes time and allows ecosystems and systems of governance to adjust. Gene editing speeds the process, allowing it to outpace traditional regulatory responses. Gene editing also allows a relatively small number of scientists to guide how evolution occurs. Furthermore, genetic modifications may produce different results than conventional breeding.[121]

The FDA proposed a different tack that, if implemented, could provide a model for stretching existing statutory language to address advances in biotechnology. In January 2017, immediately prior to the end of the Obama presidency, the FDA released new draft guidance that would apply to Recombinetics's hornless cows.[122] The proposal expands the definition of "new

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2017), http://www.dailymail.co.uk/sciencetech/article-4242148/Genetically-modified-hornless-cows-developed-scientists.html [https://perma.cc/6E43-THJF] (noting that developers of a gene-edited hornless dairy cow "compare their genetic modification methods to that of selective breeding").

[120] *See generally* William Cronon, *The Trouble with Wilderness; or, Getting Back to the Wrong Nature*, *in* UNCOMMON GROUND: RETHINKING THE HUMAN PLACE IN NATURE 69, 69–90 (William Cronon ed. 1995) (explaining how the terms "wilderness" and "nature" originated and why their current meanings may lead to misconceptions for environmentalists).

[121] *See* Gregory N. Mandel, *Gaps, Inexperience, Inconsistencies, and Overlaps: Crisis in the Regulation of Genetically Modified Plants and Animals*, 45 WM. & MARY L. REV. 2167, 2234 (2004) ("[G]enetic modification may cause different effects than those caused by conventional breeding.").

[122] FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 6–8; Maxmen, *supra* note 39.

animal drug" under the FDCA to include "animals with intentionally altered genomic DNA developed through use of genome editing technologies, as well as techniques such as rDNA in genetic engineering."[123] The FDA justifies the expanded definition because genetic engineering alters the "structure or function of the animal."[124] The guidance applies to non-heritable gene edits, but is primarily aimed at addressing heritable (germline) edits.[125] The regulatory change would subject both the animal initially altered ("the founder animal") and the "entire subsequent lineage of animals that contains the genomic alteration" to the FDCA's pre-market approval requirements—a process some stakeholders argue would discourage beneficial uses of gene editing due to the length of the FDA's review.[126]

This draft guidance signals a partial departure from the presumption that biotechnology is not inherently risky. Although it maintains the risk-based, case-by-case assessment of new products, the expanded definition of animal drug would establish a rebuttable presumption that genetically-modified animals are subject to FDA regulation. This issue remains unsettled, however. Because gene editing does not insert foreign DNA into animals, the FDA requested public comment regarding the risks associated with technologies such as CRISPR to determine whether they should be subject to the expanded animal drug definition.[127]

Relying on the natural selection analogy, Recombinetics contends that the FDA should consider the hornless cows as "generally recognized as safe" and therefore allow marketing without FDA approval.[128] Recombinetics executives believe that the USDA's reasoning in the CRISPR mushroom and waxy corn cases should apply in this case as well, arguing that the cows should not face FDA review simply because an edited gene was "intention-

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[123] *Animals with Intentionally Altered Genomic DNA*, FOOD & DRUG ADMIN., https://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/default.htm [https://perma.cc/79VZ-C5ST].

[124] FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 7. The animal itself is not considered the drug. Rather the genetically-engineered animals are regulated as containing "new animal drugs." *Id.*

[125] *Id.* at 4 (stating that "[a]lthough much of this guidance will be relevant to non-heritable intentionally altered genomic DNA, this guidance primarily addresses heritable intentionally altered genomic DNA").

[126] *Id.* at 3. The proposed guidance document identifies seven elements required for the approval process of "new animal drugs": (i) product definition, (ii) molecular characterization of the intentional alteration, (iii) molecular characterization of the lineage animal, (iv) phenotypic characterization of the animal, (v) durability assessment and plan, (vi) environmental and food safety, and (vii) claim validation. *Id.* at 22–27.

[127] *Id.* at 14.

[128] Maxmen, *supra* note 39. According to Recombinetics, gene editing provides "a simple, direct, rapid solution" to the animal welfare concerns regarding dehorning. DAIRY ANIMAL WELL-BEING, *supra* note 117.

ally put it into the cows' DNA."[129] The FDA has not made a final determination regarding the hornless cow or the draft guidance. The outcomes of both will be important indications of how the current legal system will respond to the evolving field of gene editing.

B. Ecological Impacts

A second gap in the biotechnology governance framework is the lack of a comprehensive system for evaluating the ecological impacts of gene-edited organisms. As the USDA notes, a rigid distinction between products that are plant pests and those that are not fails to sufficiently identify all of the plant risks that the products present to other plants or plant products.[130]

Rather than directly address the scope of ecological considerations that should inform regulators as they consider approval of genetically-modified organisms, the FDA and USDA rely primarily on the National Environmental Policy Act ("NEPA") to assess environmental impacts.[131] NEPA serves an important function by requiring entities to collect data, evaluate potential environmental impacts, and provide the public with an opportunity to submit comments prior to issuing a final decision.[132] NEPA does not, however, mandate any specific action after evaluating environmental impacts, thus failing to provide any guidance regarding the types of environmental risks that are acceptable.[133] Nor do existing statutes applicable in the biotechnology context address broader ecological impacts. USDA regulations, for example, fail to address questions regarding the release of genetically-modified organisms ("GMOs") intended to minimize the potential for environmental risk that may occur after the release of genetically-engineered products.[134]

The following subsections use two recent examples of NEPA review prior to the release of genetically-modified insects to demonstrate how the law applies in the biotechnology context and explore the limitations of reliance on NEPA as the primary means of considering the ecological impacts of gene-edited organisms.

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[129] Maxmen, *supra* note 39.

[130] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 96, 98.

[131] National Environmental Policy Act, 42 U.S.C. § 4332(C) (2018); *see 2017 Update to Coordinated Framework*, *supra* note 41, at 21−22 (stating that both the USDA and FDA still comply with NEPA requirements when they are applicable).

[132] *2017 Update to Coordinated Framework*, *supra* note 41, at 22−23; *see* Victor B. Flatt, *The "Worst Case" May Be the Best: Rethinking NEPA Law to Avoid Future Environmental Disasters*, 6 ENVT'L & ENERGY L. & POL'Y J. 25, 32–36 (2011) (describing the requirements of an environmental impact study under NEPA).

[133] 42 U.S.C. § 4332(C).

[134] Angelo, *supra* note 40, at 136–37.

1. Mosquitoes and Moths

In August 2016, the FDA approved a proposed field test of genetically-modified *Aedes aegypti* mosquitoes on the island of Key Haven, Florida—the first modified animal approved for release by the FDA.[135] Oxitec, the sponsor of the proposed field trial, used recombinant DNA to alter genes of male mosquitoes to prevent their offspring from reaching maturity (referred to as a "self-limiting" gene).[136] Although the proposed trial utilizes transgenic modifications (inserting foreign DNA into the male mosquitoes) rather than gene editing via CRISPR, the FDA's approach to the proposed trial will likely apply to any future proposals to release organisms modified via gene editing techniques.[137]

In addition to the FDA's approval, the Florida Keys Mosquito Control District allowed local residents to vote on a nonbinding resolution regarding approval of the proposed trial, offering one ballot referendum for residents living in the area where the mosquitoes would be released and another referendum for all residents of the surrounding county.[138] Voters split on the issue when it was added to a ballot referendum.[139] Residents living in the area where the mosquitoes were to be released voted against the trial, whereas residents in the surrounding county approved the referendum.[140] Oxitec executives subsequently announced the company would work with the FDA to identify an alternate release site.[141]

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[135] Susan Milius, *FDA OKs First GM Mosquito Trial in U.S. but Hurdles Remain*, SCI. NEWS (Aug. 5, 2016), https://www.sciencenews.org/article/fda-oks-first-gm-mosquito-trial-us-hurdles-remain [https://perma.cc/LC47-JS2Z].

[136] FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 16, 18, 21; *see Friendly Mosquitoes*, OXITEC, https://www.oxitec.com/friendly-mosquitoes/ [https://perma.cc/TUD3-H6ZT] (describing Oxitec's proposed trial).

[137] *See* FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 16 (noting that Oxitec's mosquitoes include a "recombinant DNA (rDNA) construct").

[138] *GMO Mosquito Plan Headed for Residents' Vote in Florida Keys*, ASSOCIATED PRESS (Apr. 20, 2016), https://apnews.com/cbc584373614495c9df8703a61c6b6ac [https://perma.cc/97R3-YHHB] [hereinafter *GMO Mosquito Plan Vote*]; Ike Swetlitz, *Genetically Modified Mosquitoes Are One Step Closer to Being Released in Florida*, STAT (Aug. 5, 2016), https://www.statnews.com/2016/08/05/mosquitoes-genetically-modified-florida-zika/ [https://perma.cc/VT6W-2VEN].

[139] Andrew Joseph, *Florida Keys Voters Split on Genetically Modified Mosquito Trial*, STAT (Nov. 8, 2016), https://www.statnews.com/2016/11/08/florida-keys-voters-split-on-genetically-modified-mosquitoes/ [https://perma.cc/YBF8-JGP2].

[140] *Id.*

[141] Marley Walker, *Florida Votes to Release Millions of Zika-Fighting Mosquitos*, WIRED (Nov. 10, 2016), https://www.wired.com/2016/11/florida-votes-release-millions-zika-fighting-mosquitos/ [https://perma.cc/W9ZZ-TTAT].

Prior to approving the field test, the FDA conducted an environmental assessment ("EA") pursuant to its obligations under NEPA.[142] The scope of the EA was limited to the potential impact of the limited field trial. A broader release, or a release in different locations, may require additional EAs and potentially more in-depth Environmental Impact Assessments.[143]

The FDA considered a series of risk-based questions to evaluate the potential adverse effects on humans, animals, and the environment.[144] The EA identified forty-three endangered species in the area of the proposed field trial; however, it found no overlap between the identified endangered species and the area of the field test.[145] The EA further identified two wildlife refuge sites nearby but found that target mosquitoes were "rarely" located in those areas.[146] The FDA determined that the release of the gene-edited mosquito would not affect the refuges or the endangered species as the isolated site allows for no habitat overlap among the species.[147] Additionally, the FDA concluded that ingesting the altered mosquito would not pose a health risk to animals because the genetic modification does not create toxins.[148]

The FDA also analyzed the impacts of the mosquitoes escaping either en route to the field site or at the actual field site, finding only a low risk for human health and the environment.[149] Expanding the scope of the potential risks, the FDA examined the effects on the environment of the United States as a whole.[150] Again, the EA found that "release, survival, establishment,

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[142] 42 U.S.C. § 4332; FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 19.

[143] *See FDA Releases Final Environmental Assessment for Genetically Engineered Mosquito*, FOOD & DRUG ADMIN. (Aug. 5, 2016), https://www.fda.gov/animalveterinary/newsevents/cvmupdates/ucm490246.htm [https://perma.cc/6RAB-CHA4] (stating that "FDA's finalization of the EA and FONSI does not mean that Oxitec's GE mosquitoes are approved for commercial use").

[144] FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 17. The questions included:

> [T]he likelihood of inadvertent release[,] . . . the likelihood of establishment of [the modified] mosquitoes at the proposed trial site[,] . . . the likelihood of dispersal of [the] mosquitoes and their progeny from the proposed trial site[,] . . . the likelihood that the rDNA construct could be transferred to humans or other organisms[,] . . . the likelihood that release of [the modified] mosquitoes would have of adverse effects on non-target species at the proposed site[,] . . . the likelihood [of] adverse effects on humans or other animals[,] . . . [and] the likely consequences to, or effects on the environment of the United States . . . .

Id. at 16–17.

[145] *Id.* at 45–46, 91.

[146] *Id.* at 46–48.

[147] *Id.* at 48.

[148] *Id*.

[149] *Id.* at 75 tbl.6.

[150] *Id.* at 99–103.

and spread" of the modified mosquito would not have adverse effects on either the environment, human health, or non-target animal health.[151]

The FDA determined that a full environmental impact statement was unnecessary due to three key findings. First, approximately 95% of the modified mosquitoes' offspring would perish before reproducing, thus providing a biological containment mechanism for the proposed trial.[152] Second, the island location provided "geophysical containment."[153] Third, the EA compared the field test to the risks associated with a "no action" alternative of continued reliance on integrated mosquito management practices involving aerial larvicide application from an airplane.[154]

Oxitec has also received approval for a field test of genetically-modified diamondback moths, insects that feed on kale, broccoli, brussels sprouts, and other crops, causing an estimated global loss of $5 billion annually.[155] The gene modification is similar to that used to develop the modified *Aedes aegypti* mosquito, whereby the female offspring of a genetically-modified moth die before they are able to reproduce.[156] The moth is classified as a "pest" under the PPA and therefore subject to USDA jurisdiction.[157] The moth does not fall within the jurisdiction of the FDA or EPA because it does not yield food for human or livestock consumption and does not contain plant-incorporated protectants or require the use of other pesticides that are not already in use for other non-gene-edited moths.[158] The modified moth could potentially fall within the FDA's proposed guidance regarding genetically-engineered animals.[159]

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[151] *Id.* at 103.

[152] *Id.* at 17−18.

[153] *Id.* at 17.

[154] *Id.* at 20–21. Even with additional unpredictable adulticide methods, the effectiveness rate of controlling the specific disease carrying mosquito is only around 50% not including the mosquitoes developing a potential resistance. *Id.*

[155] DEP'T OF AGRIC., PROPOSAL TO PERMIT THE FIELD RELEASE OF GENETICALLY-ENGINEERED DIAMONDBACK MOTH IN NEW YORK: ENVIRONMENTAL ASSESSMENT 1, 10, 62 (Dec. 2016), https://www.aphis.usda.gov/brs/aphisdocs/16_076101r_pea.pdf [https://perma.cc/JW2F-BGH3] [hereinafter DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT]. The field trial took place on a ten-acre plot of the Cornell University New York State Agricultural Experiment Station in Geneva, New York, and lasted approximately one month. *Id.* at 1, 59.

[156] Availability of a Final Environmental Assessment and Finding of No Significant Impact for the Field Release of Genetically-Engineered Diamondback Moths, 82 Fed. Reg. 31,548, 31,548 (July 7, 2017).

[157] DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 155, at 2−3, 6−8.

[158] *Id.* at 7–8.

[159] *See* FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 6–8 (noting that the FDA has authority over "new animal drugs" defined in the FDCA as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals," and "articles (other than food) intended to affect the structure or any function of the boy of man or other animals").

The USDA completed an EA that compared the current strategy of controlling moth populations via pesticides to risks associated with the proposed field trial of the genetically-modified moth.[160] The EA revealed no cumulative environmental impacts resulting from approval of the field release and concluded that the field release would not impact threatened or endangered species.[161] On the contrary, the USDA determined that approving the genetically-modified moth may lead to environmental benefits by reducing the amount of insecticides applied during the growing season.[162] Harm to species that prey on the moths was unlikely because the moth population would otherwise be controlled with pesticides and the preying species consume other insects.[163] Additionally, the introduced traits were not likely allergenic or toxic to those consuming the genetically-modified moths.[164] The USDA identified the potential risk of DNA transfer from the gene-edited moths to individual soil microflora, but concluded the transfer was unlikely.[165] Overall, the EA revealed that permitting the field trial simply continues the approaches already in place in the agroecosystem limiting biodiversity and thus concluded that the impact of the field trial on the physical environment (including soil, water, air quality, and climate change) was comparable to impacts of conventional pesticide use via the no action alternative.[166]

The EA also assessed the current health hazards to both the general public and farmworkers.[167] The USDA distinguished between the two groups because the proximity of the farmworkers to the moth raises their exposure risks compared to the general public, including risks associated with conventional pesticides as well as any risks associated with the genetically-modified moths.[168] For example, there is a potential risk that farmworkers may develop allergic responses as a result of the moths' hair and scales.[169] The USDA found little variance from current exposure to non-gene-edited moths, however.[170] Unlike the proposed Key Haven mosquito

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[160] DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 155, at 1–6.
[161] *Id.* at 62.
[162] *Id.* at 58.
[163] *Id.* at 57–58.
[164] *Id.* at 57.
[165] *Id.* at 44–45.
[166] *Id.* at 32–33, 44, 58.
[167] *Id.* at 59–61.
[168] *Id.* at 59–60.
[169] *Id.* at 61.
[170] *Id.*

trial, there was no public referendum, although the USDA accepted public comments on the EA.[171]

2. Limitations of NEPA

The direct connection between natural resource management, environmental protection, and governance of genetic engineering is irrefutable. Altering genomes alters organisms and, in the case of gene drives, potentially the genetic makeup of future generations. The impacts may also extend far beyond the target organisms. Gene edits may allow some species to outcompete others, allow them to move to new habitats and thus affect a new group of species, or potentially make some resources more valuable for human consumption and thus more subject to extraction. In the context of gene editing technologies that could eradicate species and permanently alter others, reliance on a procedural statute—NEPA—to inform decisions about environmental risk is insufficient.[172] Although NEPA may identify the important issues, it does not offer guidance to resolve the issues or require the agencies considering release of gene-edited organisms to address the concerns.

The prospect of engineering extinction or de-extinction (using gene editing to recreate extinct species) via CRISPR is an acute example of the interplay between natural resource statutes and gene editing that requires more than NEPA review. Although protection against invasive species is an important aspect of resource management, statutes generally aim to prevent, rather than facilitate, extinction.[173] The Endangered Species Act ("ESA") and Marine Mammal Protection Act ("MMPA") prohibit a wide range of activities that could harm or kill threatened or endangered species.[174] The

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[171] *Id.* at 8–9.

[172] *See, e.g.*, Strycker's Bay Neighborhood Council, Inc. v. Karlen, 444 U.S. 223, 227 (1980) (stating that "once an agency has made a decision subject to NEPA's procedural requirements, the only role for a court is to insure that the agency has considered the environmental consequences"); Vt. Yankee Nuclear Power Corp. v. Nat. Res. Def. Council, Inc., 435 U.S. 519, 558 (1978) (finding that NEPA is "essentially procedural"); Philip Michael Ferester, *Revitalizing the National Environmental Policy Act: Substantive Law Adaptations from NEPA's Progeny*, 16 HARV. ENVTL. L. REV. 207, 217 (1992) (stating that "[f]earing extensive judicial intervention in administrative decision making under NEPA, the Court began limiting the effect of the various circuit court decisions that seemed to allow such intervention").

[173] *See, e.g.*, *Invasive Species*, ILL. DEP'T OF NAT. RES., https://www.dnr.illinois.gov/conservation/IWAP/Pages/InvasiveSpecies.aspx [https://perma.cc/9CYM-NQCQ] (stating that "[i]nvasive species pose one of the greatest threats to Illinois' natural areas, native communities, and natural resources").

[174] *See, e.g.*, Marine Mammal Protection Act of 1972, 16 U.S.C. §§ 1361−1421h (2018) (prohibiting the "taking" of marine mammals, defined as "to harass, hunt, capture, or kill, or attempt to harass, hunt, capture, or kill any marine mammal"); Endangered Species Act of 1973, 16 U.S.C.

Pelly Amendment and Packwood-Magnuson Amendment seek to enforce international whaling restrictions.[175] Other statutes seek to restrict international trade in threatened or endangered species and support conservation measures in countries of origin.[176] These statutes are explicitly values-based, dedicating tax dollars to preserve some of the world's most vulnerable species, restricting economic activity, and, in the case of the ESA, implementing federal restrictions on private land use to protect habitat of covered species.[177] These restrictions are not based solely on anthropocentric goals or on ecosystem health. The statutes aim to protect individual members of a threatened or endangered species, and protections are based on scientific assessments rather than consideration of the value to humans or economic impacts.[178]

Extinction is generally a slow process. This is a key presumption of the ESA, allowing government scientists time to identify potentially vulnerable species and complete studies assessing their status and threats to their viability.[179] The United States Fish & Wildlife Service must complete the pro-

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§ 1538 (2018) (prohibiting the import, export, and taking of any endangered species of fish or wildlife).

[175] Packwood-Magnuson Amendment, Pub. L. No. 96-61, 93 Stat. 407 (1979) (codified as amended at 16 U.S.C. § 1821(e)(2) (2018)) (imposing a reduction of not less than fifty percent in the fishing rights of any foreign country that violates international whaling laws in U.S. waters); Pelly Amendment, Pub. L. No. 92-219, 85 Stat. 786 (1971) (codified as amended at 22 U.S.C. § 1978 (2018)) (allowing the president to restrict fish imports from nations that violate international whale conservation standards).

[176] *See, e.g.*, Lacey Act Amendments of 1981, 16 U.S.C. §§ 3371−3378 (2018) (prohibiting interstate and international trafficking in exotic animals); African Elephant Conservation Act, 16 U.S.C. § 4203 (2018) (stating that the Act seeks to aid in the "conservation and protection of the African elephant by supporting the conservation programs of African countries");Wild Bird Conservation Act, 16 U.S.C. §§ 4901−4916 (2018) (restricting international trade of exotic birds and encouraging conservation programs in countries of origin); Rhinoceros and Tiger Conservation Act, 16 U.S.C. § 5302 (2018) (stating the Act's purpose is "[t]o assist in the conservation of rhinoceros and tigers by supporting the conservation programs of nations whose activities directly or indirectly affect rhinoceros and tiger populations").

[177] *See, e.g.*, Bruce Babbitt, *Between the Flood and the Rainbow: Our Covenant to Protect the Whole of Creation*, 2 ANIMAL L. 1, 1 (1996) (discussing "the moral, ethical, and religious values underlying the Endangered Species Act").

[178] *See* 16 U.S.C. §§ 1533(b) (stating that the secretary determines whether a species is endangered or threatened based on "scientific and commercial data"); 4211(d)(1) (providing protections for the African elephant through research, conservation and management programs, and development of scientific information); 5304(d)(3) (allowing projects to assist conservation efforts and development of scientific information for the protection of rhinoceros or tigers).

[179] *Endangered Species: Listing and Critical Habitat: Overview*, U.S. FISH & WILDLIFE SERV., https://www.fws.gov/endangered/what-we-do/listing-overview.html [https://perma.cc/4XY9-Y53G]. The MMPA protects marine mammals by default but provides for limited exceptions. *NOAA Fisheries, Laws & Policies: Marine Mammal Protection Act*, NAT'L OCEANIC & ATMOSPHERIC ADMIN., http://www.nmfs.noaa.gov/pr/laws/mmpa/ [https://perma.cc/CC48-FQ6W].

cess and list a species as either endangered or threatened before ESA protections apply.[180]

Using gene drives to prevent reproduction could foster population collapses at such a rapid pace that the Fish & Wildlife Service could not complete the listing process.[181] Furthermore, even if regulators were able to complete an expedited listing process, the gene drive could still result in eventual extinction. A gene drive proliferating through a population would not trigger ESA or MMPA restrictions if there is no additional prohibited act to the listed species. In other words, the "harm" to the species caused by the gene drive could occur prior to listing, and thus fall outside the scope of the ESA.

De-extinction may challenge natural resource statutes from a different angle, calling into question core tenets of laws and treaties aimed at protecting threatened and endangered species.[182] Is the goal merely existence of the species, or does the ability to engage in de-extinction also require habitat rehabilitation?[183] In the event a single member of an extinct species is recreated, it would be endangered by definition (but not subject to ESA protections prior to listing the species as threatened or endangered).[184] Would reintroducing additional members of the species be necessary to ensure the survival of the species, or would it be acceptable to mate with existing species, maintain the recreated organism in captivity, or release the organism in areas that are similar to its original habitat? The ESA and the suite of laws applying to genetically-engineered organisms do not contemplate these issues, and at best NEPA only requires that the agencies give them due consideration.

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[180] 16 U.S.C. § 1538(a) (2018).

[181] Charleston Noble et al., *Current CRISPR Gene Drive Systems Are Likely to Be Highly Invasive in Wild Populations*, 7 eLife e33423 (2018), https://elifesciences.org/articles/33423 [https://perma.cc/4RTX-2X7N] ("Our models show that although resistance prevents spread to fixation in large populations, even the least effective drive systems reported to date are likely to be highly invasive. Releasing a small number of organisms will often cause invasion of the local population, followed by invasion of additional populations connected by very low rates of gene flow.").

[182] *See* Gregory E. Kaebnick & Bruce Jennings, *De-extinction and Conservation*, 47 HASTINGS CTR. REP. S2, S2 (July–Aug. 2017) (discussing the ethical considerations presented by de-extinction).

[183] *See* Alejandro E. Camacho, *Going the Way of the Dodo: De-Extinction, Dualisms, and Reframing Conservation*, 92 WASH. U. L. REV. 849, 856–57 (2015) (noting that the placement of a de-extinct species into its prior habitat could have ecological benefits).

[184] 16 U.S.C. § 1538(a).

C. Agencies' Authority to Consider Alternatives

Avoidance of regulatory coverage and the lack of substantive ecological considerations are not the only gaps in biotechnology oversight presented by CRISPR. In many circumstances, existing laws also limit the factors that government officials may consider when determining whether to approve a genetically-engineered product. Where officials do have authority to look beyond the product-specific risk assessment, there is a lack of policy guidance to inform how they should wield that authority. For example, the current governance framework, including the 2017 Update to the Coordinated Framework, does not consider whether there are circumstances when a genetic modification may be safe but offer no benefit beyond those achievable via alternate, equally safe means.[185] Gene editing may also play an important role in modifying species to help them adapt to the changing climate and related issues such as the spread of diseases.[186] Releasing genetically-modified organisms when equally effective alternatives exist, or when the gene modification is not aimed at addressing a critical health or environmental concern, may be another matter.[187]

Opponents of the Key Haven field test pointed to the ability to achieve a similar result using conventional bacteria rather than genetically-engineered organisms, suggesting opposition to genetically-modified organisms rather than eradicating the species by interfering with the reproduction cycle.[188] The FDA's basis for approval, however, did not rest on the severe health impacts of the mosquito-borne diseases, the potential benefits of reduced pesticide use, or the fact that the *Aedes aegypti* mosquito is not native

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[185] *2017 Update to Coordinated Framework*, *supra* note 41.

[186] *See, e.g.*, Chase Purdy, *A Global Chocolate Crisis Looms, but Scientists Believe They Can Genetically Engineer a Fix*, QUARTZ (Jan 3, 2018), https://qz.com/1170536/crispr-gene-edited-cacao-plants-could-save-the-chocolate-industry-from-climate-change/ [https://perma.cc/PL4Q-T3NN] (explaining that gene editing is helping develop cocoa plants less vulnerable to diseases resulting from a changing climate in areas where the plant is primarily grown).

[187] Research suggests that public perceptions of gene editing differ depending on the specific applications. *See, e.g.*, Dietram A. Scheufele et al., *U.S. Attitudes on Human Genome Editing*, 357 SCI. 553, 553–54 (2017) (detailing greater public acceptance of gene editing for therapeutic purposes and lower acceptance for enhancement purposes).

[188] *See* Susan Milius, *In Florida, They're Fighting Mosquitoes by Meddling with Their Sex Lives*, SCI. NEWS (May 8, 2017), https://www.sciencenews.org/article/florida-theyre-fighting-mosquitoes-meddling-their-sex-lives [https://perma.cc/A9GS-NH2F] (describing a 2017 alternate field trial in Key Haven involving mosquitoes infected with existing—i.e., not genetically-modified—*Wolbachia* bacteria). Notably, because the *Wolbachia* bacteria is not genetically-modified, the release falls under EPA rather than FDA jurisdiction even though it, like Oxitec's modified mosquito, aims to significantly reduce the *Aedes aegypti* population by preventing male mosquitoes from reproducing. News Release, Envtl. Prot. Agency, EPA Grants Extension of Experimental Use Permit for 'Wolbachia Mosquito' (Sept. 21, 2016), https://www.epa.gov/pesticides/epa-grants-extension-experimental-use-permit-wolbachia-mosquito [https://perma.cc/62NM-X44P].

to the Florida Keys. The focus was on the safety of the trial, not the relative benefits of the genetically-modified mosquito in the event the trial is ultimately successful.[189] The Coordinated Framework does not identify circumstances for proper and improper release of genetically-engineered organisms, provided they satisfy the lead agency's risk-based assessment.

The argument here is not that gene editing should not proceed if other options exist. Some of these potential changes undoubtedly offer societal benefits. It is important, however, to recognize that the legal system is not designed to distinguish between gene editing applications that address critical societal needs versus those that are cosmetic, duplicative of equally effective options, or address social needs but raise the prospect of harmful impacts beyond the scope of an agency's current jurisdiction.

D. Consideration of Competing Ideologies

A fourth gap points to a more fundamental challenge for biotechnology governance: although the existing regulatory framework may consider near-term anticipated risks presented by evolving gene editing technologies, it fails to address the broader range of societal interests and values inherent in the biotechnology debate.[190] Value choices are embedded in every aspect of biotechnology governance.[191] Research and risk assessments may answer a threshold question regarding safety, but are not dispositive on their own. Data suggesting the likelihood of significant harm to humans or the ecosystem would create a powerful presumption against release. The reverse is not necessarily true. Scientific consensus regarding safety and anticipated benefits of a new genetically-engineered organism may be persuasive but may also fail to consider additional concerns regarding the modified organism or the rationales for utilizing genetic modifications.

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[189] *See* FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 16–19 (providing overview and discussing the goals of the assessment).

[190] This gap is not unique to the field of gene editing. *See* Gary E. Marchant et al., *What Does the History of Technology Regulation Teach Us About Nano Oversight?*, 37 J.L. MED. & ETHICS 724, 727 (2009) (stating that "[e]xisting regulatory frameworks often exclude consideration of social and moral concerns, ruling them outside the bounds of the jurisdiction of regulatory agencies or reviewing courts").

[191] *See* GENE DRIVES ON THE HORIZON, *supra* note 12, at 5 (stating that "[q]uestions about gene drives rest on values at every step, from whether, why, and how research should be conducted to whether and where a gene-drive modified organism should be released into the environment"); PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 69 box 3-1 (stating that "[v]alues are always embedded in risk analysis by the choices and interpretations of the people conducting them and the selection of risk-assessment endpoints of concern, methods, and questions"); Kuzma, *supra* note 109, at 167 ("[I]t is impossible to be completely 'science based' in a regulatory system. Value judgements are embedded in all risk and safety assessments.").

The decision to prioritize development of biotechnology products through a product-based regulatory system is itself a value choice. The focus on risk as a primary criterion for governance is another implicit value choice and raises numerous follow-up questions.[192] Determining who is at risk, what risks are considered, and what is an unacceptable risk requires tradeoffs.[193] Furthermore, policymakers implementing the risk-based approach must decide whether to discount future risks, how much weight, if any, to grant to ecological risks and risks to non-human organisms, and how certain must a risk be to influence a regulatory decision.[194] Value choices also arise when considering whether to draw distinctions between germline and somatic alterations, therapeutic versus enhancement purposes, and human versus non-human applications.[195]

Defining safety and risk as the primary (or sole) criteria for evaluating a biotechnology application results in a one-dimensional debate. GMO advocates frequently point to the high level of market penetration of agricultural GMO seeds and the lack of evidence of safety issues as an open and shut case regarding the value and safety of genetic engineering.[196] The result is a consistent dismissal of concerns about existing GMO products and, by extension, advances in genetic engineering generally.[197] Health concerns regarding genetically-modified agricultural products have proven unfounded, and proponents of minimal regulatory limitations on biotechnology de-

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[192] Samuel J. Rascoff & Richard L. Revesz, *The Biases of Risk Tradeoff Analysis: Towards Parity in Environmental and Health-and-Safety Regulation*, 69 U. CHI. L. REV. 1763, 1765 (2002).

[193] *Id.*

[194] *See, e.g.*, David Winickoff et al., *Adjudicating the GM Food Wars: Science, Risk, and Democracy in World Trade Law*, 30 YALE J. INT'L L. 81, 94 (2005) (discussing the ways that risk identification and framing impact risk analysis, including "by dictating how different types and sources of scientific uncertainty will be integrated into the risk-identification and risk-evaluation process"); *see also* NAT'L RES. COUNCIL, UNDERSTANDING RISK: INFORMING DECISIONS IN A DEMOCRATIC SOCIETY 103 (Paul C. Stern & Harvey V. Fineberg eds., 1996) (stating that "[t]echniques that aim to simplify risk necessarily embed value choices, some of them highly contentious").

[195] *See, e.g.*, Kelly E. Ormond et al., *Human Germline Genome Editing*, 101 AM. J. HUM. GENETICS 167, 169 (2017) (differentiating between germline editing and somatic gene editing and both methods' impact on CRISPR-Cas9).

[196] *See, e.g.*, Jon Entine, *Will Biotechnology Regulations Squelch Next Food and Farming Innovation?*, GENETIC LITERACY PROJECT 1, 2 (2017) (arguing that advancements in recent genetic engineering technology support changing of old, "overly-restrictive" regulations that do not account for a "clear consensus on [genetic engineering] safety"); *Commonly Asked Questions About the Food Safety of GMOs*, MONSANTO (Apr. 6, 2017), https://monsanto.com/company/commitments/safety/statements/are-gmos-safe/ [https://perma.cc/88PZ-B88B] (citing the prevalence of genetically-modified organisms and benefits associated with their use).

[197] *See* Entine, *supra* note 196 (noting that the regulations of genetically engineered products are out of date and stifle innovation).

velopments point to these results as evidence that future gene editing of seeds and livestock is also likely to be safe.[198]

To dismiss these concerns with a response about a product's safety misses the point. The range of issues leading to concern with, or opposition to, genetic engineering is broad. If the debate were truly one dimensional, reliance on data demonstrating a lack of negative health or ecological impacts caused by existing GMO products would presumably be persuasive. The fact that opposition continues, even among scientists involved in biotechnology research, demonstrates that concerns extend beyond safety and risk.[199] The debate about GMOs is as much about values as it is about science.[200] Although some opposition to GMOs is about health concerns, and those holding those concerns may continue to maintain their beliefs despite any amount of evidence to the contrary, policymakers should also understand ongoing references to health concerns as rooted in a deeper set of values-based concerns.

Stakeholder perspectives regarding biotechnology governance take many forms. For many scientists in the public and private sectors, there is a moral imperative to pursue advances in the field of genetics.[201] If scientists

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[198] *See* NAT'L ACADS. OF SCIS., ENG'G, & MED., GENETICALLY-ENGINEERED CROPS: EXPERIENCES AND PROSPECTS 225 (2016) (finding that GE foods pose no higher human health risks than non-GE food, based upon extensive data and tests conducted); *see also* Enriquez, *supra* note 7, at 514−15 (explaining that despite the unknowns of future biotechnology, decades of scientific research indicate that the health risks associated with both recombinant and non-recombinant GM crops are similar, and thus a strictly "risk-based approach" supports deregulation of future biotechnology products); Alessandro Nicolia et al., *An Overview of the Last 10 Years of Genetically Engineered Crop Safety Research*, 34 CRITICAL REVS. IN BIOTECHNOLOGY 77, 84–85 (2013) (finding that research over the past ten years has yet to directly link health risk to GM crops).

[199] GENE DRIVES ON THE HORIZON, *supra* note 12, at 65 (noting "the possibility that some ways of using genetic technologies conflict with underlying moral norms that are implicit in how human beings understand the world, including their own nature and relationship to the rest of the world"); *see* Emily Marden, *Risk and Regulation: U.S. Regulatory Policy on Genetically Modified Food and Agriculture*, 44 B.C. L. REV. 733, 743 (2003) (highlighting that the debate surrounding GMOs ranges from economic concerns, to health concerns, to agriculture and more).

[200] *See* GENE DRIVES ON THE HORIZON, *supra* note 12, at 65 (stating that "[q]uestions about gene drives rest on values at every step, from whether, why, and how research should be conducted to whether and where a gene-drive modified organism should be released into the environment"); *see also* Keith Kloor, *Food Evolution Is Scientifically Accurate. Too Bad It Won't Convince Anyone*, SLATE (June 23, 2017), http://www.slate.com/articles/health_and_science/science/2017/06/food_evolution_is_correct_on_gmos_and_unconvincing.html [https://perma.cc/L3H6-8RH9] (noting that individuals' values or beliefs regarding GMOs often outweigh scientific evidence of GMO safety).

[201] *See* Kuzma, *supra* note 109, at 166 (quoting plant scientist Ingo Potrykus stating that "it would be a 'crime against humanity' not to change from 'regulating a technology on ideological terms' to 'science-based regulation, guided by considerations of the risks and benefits of the trait'"); *see also* George Church, *Encourage the Innovators*, 528 NATURE S7, S7 (2015) ("[T]he concept of a ban on germline editing does not make sense. . . . Banning human-germline editing

have the ability to address severe health problems, it becomes a moral choice whether to do so.[202] These biotechnology proponents argue that restrictions on gene editing research could deny society numerous promising benefits: elimination of vector-borne diseases such as the Zika virus and malaria, diseases such as sickle cell anemia and cystic fibrosis caused by genetic defects, and potentially a range of other lethal and debilitating viruses and diseases, including HIV.[203] Increased food production and decreased use of pesticides are other commonly cited benefits.[204] Some opponents of restrictions on gene editing and other biotechnologies also point to the competitive disadvantages if the United States maintains its ban on human hereditary modifications even though other countries permit it.[205] The moral imperative ideology is not solely about human health benefits. Restrictions on gene editing could also prevent developments that could help conserve threatened and endangered species by inserting traits that make them more resilient to changing environmental conditions or potentially bringing species back from extinction.[206]

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could put a damper on the best medical research and instead drive the practice underground to black markets and uncontrolled medical tourism . . . ."); Julian Savulescu et al., *The Moral Imperative to Continue Gene Editing Research on Human Embryos*, 6 PROTEIN & CELL 476, 476 (2015) (stating that "[t]o intentionally refrain from engaging in life-saving research is to be morally responsible for the foreseeable, avoidable deaths of those who could have benefitted") (citing PETER SINGER, PRACTICAL ETHICS 208–09, 226–28 (2d ed. 1993)); William J. Clinton, President of the United States, Remarks on Presenting the National Medals of Science and Technology (Mar. 14, 2000) (transcript available at http://www.presidency.ucsb.edu/ws/index.php?pid=58246 [https://perma.cc/RE6L-CYDS]) ("Perhaps no science today is more compelling than the effort to decipher the human genome, a string of three billion letters that make up our genes . . . . This will be the scientific breakthrough of the century, perhaps of all time").

[202] Kevin M. Esvelt, *The Morality of Nature*, SCULPTING NATURE, http://www.sculptingevolution.org/blog/themoralityofnature [https://perma.cc/6686-Y58Q].

[203] Marcy E. Gallo & John F. Sargent, Jr., *CRISPR: A Revolutionary Tool for Editing the Code of Life?*, CONG. RES. SERV. INSIGHT 1, 2 (2016); *see* Doudna & Charpentier, *supra* note 25, at 1077 (stating that "[CRISPR's] application in genome-wide studies will enable large-scale screening for drug targets and other phenotypes and will facilitate the generation of engineered animal models that will benefit pharmacological studies and the understanding of human diseases").

[204] *See, e.g.*, Thomas O. McGarity, *Seeds of Distrust: Federal Regulation of Genetically Modified Foods*, 35 U. MICH. J.L. REFORM 403, 408−15 (2002) (discussing "potential benefits of genetically modified foods").

[205] *See, e.g.*, I. Glenn Cohen & Eli Y. Adashi, *The FDA Is Prohibited from Going Germline*, 353 SCI. 545, 545−46 (2016) (noting the ban includes prohibitions on genetic modifications that could prevent "rare incurable Mendelian disorders . . .[,] secure 'savior siblings' through editing of the genome of a human embryo when in vitro fertilization fails to secure tissue-matched embryos for intrauterine transfer[, and] mitochondrial DNA diseases by mitochondrial replacement").

[206] GENE DRIVES ON THE HORIZON, *supra* note 12, at 5–6. Efforts to reverse extinction could prove ineffective unless the underlying causes of the extinction, such as habitat loss, are also addressed. *Id.* at 37–38; *see* Patrick Parenteau, *Rearranging the Deck Chairs: Endangered Species*

Ongoing advocacy for risk-based governance presents a second viewpoint: faith in expert management to identify, evaluate, and manage risks associated with the rapidly developing field of genetic engineering.[207] Science-based risk governance is a dominant theme for emerging technologies generally, as it provides a pathway to allow continued technological development even when risks are unknown and potentially catastrophic.[208] Proponents of expert risk management recognize that there may be potential downsides to a technology, but generally have faith that the risks are manageable if the proper oversight mechanisms are in place. Trust the experts, these proponents argue, as they understand the technology and have the means to control its impacts.[209] Although there is general support for risk-based governance, viewpoints regarding the proper application of risk management are not uniform. There is an ongoing debate among scientists and other experts regarding the appropriate level of risk tolerance and the role of the precautionary principle.[210] These debates are important and may impact future governance choices, but they generally accept risk-based governance as the appropriate starting point.

The first two viewpoints drive the dominant approach under U.S. law and are reflected in the prioritization of risk management in recent reports on gene editing by the National Academies.[211] As discussed in Part II, the original 1986 Coordinated Framework and the 2017 Update to the Coordinated Framework conclude that continued advances in biotechnology are desirable, that genetic engineering processes are not inherently risky, and that it is possible to manage risks presented by specific genetically-engineered products using the same regulatory mechanisms that apply to conventional products.[212]

Act Reforms in an Era of Mass Extinction, 22 WM. & MARY ENVTL. L. & POL'Y REV. 227, 233 (1998) (identifying habitat loss as the primary factor driving mass extinction).

[207] This viewpoint is similar to the reliance on technocratic federal resource managers that emerged in the early 1900s. Jedediah Purdy, *American Natures: The Shape of Conflict in Environmental Law*, 36 HARV. ENVTL. L. REV. 169, 173−74, 208 (2012).

[208] *See* Kuzma, *supra* note 109, at 166 (describing the United States' risk-based regulation of genetically-engineered products and processes).

[209] *See, e.g.*, Webber et al., *supra* note 45, at 10,565 (stating that "[r]esearchers, policymakers, and resource managers must carefully weigh the risks of implementation that could threaten rather than assist a given ecosystem").

[210] Kaebnick et al., *supra* note 9, at 710.

[211] *See* GENE DRIVES ON THE HORIZON, *supra* note 12, at 22, 117–18 (listing numerous factors to consider in an ecological risk assessment of gene edited products); HUMAN GENOME EDITING, *supra* note 26, at 59 (listing factors such as promoting well-being, responsible science, respect for persons, and fairness as key components of gene editing oversight).

[212] *See 2017 Update to Coordinated Framework*, *supra* note 41, at 1 (explaining that the Coordinated Framework "effectively protects health and the environment," and the update serves to prevent unnecessary barriers to developments in biotechnology innovation); *see also* 1986 Coor-

Other perspectives in the gene editing debate extend beyond disagreements regarding scientific expertise and risk management.[213] Ecological concerns, for example, frequently arise in the biotechnology context.[214] One category of ecological concerns represent a subset of risk-based governance, focusing on concerns regarding impacts on other species, uncertain environmental impacts, and irreversible, and potentially unintended, ecological changes.[215] Other ecological concerns extend beyond risk and merge into a form of romanticism.[216] Some opponents to genetically-modified organisms evoke arguments similar to those used to promote wilderness preservation—an appeal for sacred space unaltered (at least by deliberate means) by humans.[217] Not only could gene editing alter the ecological balance, but it could also fundamentally alter humans' relationship with nature

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dinated Framework, *supra* note 48, at 23,303 (explaining that a working committee found that current laws adequately addressed both traditional and new biotechnology techniques).

[213] *See, e.g.*, JOHN H. EVANS, PLAYING GOD?: HUMAN GENETIC ENGINEERING AND THE RATIONALIZATION OF PUBLIC BIOETHICAL DEBATE 11–44 (2002) (analyzing how scientific expertise came to dominate the debate regarding human genetic engineering); Celia Deane-Drummond et al., *Genetically Modified Theology: The Religious Dimensions of Public Concerns About Agricultural Biotechnology*, 14 STUDIES IN CHRISTIAN ETHICS 23, 23 (2001) (arguing that opposition to GMOs is better understood "at the level of ontology and theology rather than simply as concerns about physical risk and health"); Jennifer Kuzma & John C. Besley, *Ethics of Risk Analysis and Regulatory Review: From Bio- to Nanotechnology*, 2 NANOETHICS 149, 159 (2008) (noting that principles such as "integrity, justice, non-maleficence, and autonomy" affect public perceptions of a new technology and "cannot be separated from beneficence, and risk analyses, and regulatory review").

[214] As with many other issues, there is wide divergence among environmental groups regarding biotechnology. *See, e.g.*, *Advocacy Groups Call for Halt to Open Air Field Trials of Genetically Engineered Moths*, CTR. FOR FOOD SAFETY (Nov. 10, 2015), http://www.centerforfoodsafety.org/press-releases/4118/advocacy-groups-call-for-halt-to-open-air-field-trials-of-genetically-engineered-moths# [https://perma.cc/G8ZP-F5EB] (describing advocacy groups' attempts to prevent the genetically-engineered moth trials and release due to safety concerns); *Our Position on Biotechnology*, ENVTL. DEF. FUND, https://www.edf.org/our-position-biotechnology [https://perma.cc/26F2-TBJV] (stating that the organization "will support or oppose specific biotechnology products or processes based on transparent assessments of their health, environmental, social, and economic risks and benefits"); News Release, Friends of the Earth, USDA Proposal for Biotech Regulations Falls Short (Jan. 19, 2017), http://www.foe.org/news/news-releases/2017-01-usda-proposal-for-biotech-regulations-falls-short [https://perma.cc/A7DK-RBZB] (stating that "consumers don't want a bunch of new unregulated GMO foods secretly flooding onto the market. All GMOs—including those made with CRISPR, synthetic biology or other new genetic engineering techniques—must be regulated, safety assessed and labeled so that consumers can choose for themselves what they are eating and feeding their families").

[215] *See* GENE DRIVES ON THE HORIZON, *supra* note 12, at 37 (discussing potential impacts on non-target species); Angelo, *supra* note 40, at 103 (noting the environmental and ecological risks posed by genetically-modified organisms).

[216] Purdy, *supra* note 207, at 211.

[217] *See* MARY SHELLEY, FRANKENSTEIN; OR, THE MODERN PROMETHEUS 40, 43–44 (1823) (detailing the scientist's turmoil in creating a "life"); Enriquez, *supra* note 7, at 438–39 (noting gene editing opponents view that the process is "unnatural" and "wrong").

by eroding societal norms regarding the use of technology to alter species and ecosystems.[218]

Other stakeholders express a general discomfort with "playing God" through genetic engineering.[219] This viewpoint arises most commonly in the context of direct human applications.[220] Limitations on human embryo editing are partly justified under a risk-based ideology—there is too much we do not know and too much harm could occur, especially in the context of germline edits that may persist through future generations.[221] The existing ban on federal funding for human embryo editing, and recommendations for stricter oversight for human embryo editing in the event it is allowed,

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[218] Charo & Greely, *supra* note 29, at 15; *see* Heidi Ledford, *The Landscape for Human Genome Editing: A View of International Regulations Suggests Where in the World a CRISPR Baby Could Be Born*, 526 NATURE 310, 310 (2015) ("Fears loom that if genome editing becomes acceptable in the clinic to stave off disease, it will inevitably come to be used to introduce, enhance or eliminate traits for non-medical reasons."). Nature is not a discreet, static, or easily identified state. *See* William Cronon, *Introduction: In Search of Nature*, *in* UNCOMMON GROUND, RETHINKING THE HUMAN PLACE IN NATURE 23, 34−52 (William Cronon ed. 1995) (describing the difficulty society has faced over time in defining and understanding nature). References to nature and wilderness do, however, suggest that they are areas beyond the realm of human development. For example, the Wilderness Act, states that:

> In order to assure that an increasing population, accompanied by expanding settlement and growing mechanization, does not occupy and modify all areas within the United States and its possessions, leaving no lands designated for preservation and protection in their natural condition, it is hereby declared to be the policy of the Congress to secure for the American people of present and future generations the benefits of an enduring resource of wilderness.

16 U.S.C. § 1131(a) (2018).

[219] *See, e.g.*, GENE DRIVES ON THE HORIZON, *supra* note 12, at 64–65 (identifying and discussing moral concerns surrounding genetic engineering and referencing *Splicing Life: The Social and Ethical Issues of Genetic Engineering with Human Beings*, a "seminal report" issued by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in 1982); Johnjoe McFadden, *Genetic Editing Is Like Playing God—And What's Wrong with That?*, THE GUARDIAN (Feb. 2, 2016), https://www.theguardian.com/commentisfree/2016/feb/02/genetic-editing-playing-god-children-british-scientists-embryos-dna-diseases [https://perma.cc/XMS9-BXY9] ("The opponents are right. We are indeed playing God with our genes. But it is a good thing because God, nature or whatever we want to call the agencies that have made us, often get it wrong and it's up to us to correct those mistakes.").

[220] *Gene Editing: A CBC Interview of Margaret Somerville and Julian Savulescu*, PRACTICAL ETHICS (Dec. 7, 2015), http://blog.practicalethics.ox.ac.uk/2015/12/gene-editing-a-cbc-interview-of-margaret-somerville-and-julian-savulescu/ [https://perma.cc/99M6-V7VC] (noting that until 2015 "there was almost universal agreement . . . that humans have a right to come into existence with their own unique genetic heritage and other humans have no right to alter them, to design them").

[221] *See, e.g.*, Eileen M. Kane*, Human Genome Editing: An Evolving Regulatory Climate,* 57 JURIMETRICS J. 301, 315−18 (2017) (discussing arguments for banning human germline editing); Collins, *supra* note 64 (noting "serious and unquantifiable safety issues, ethical issues presented by altering the germline in a way that affects the next generation without their consent, and a current lack of compelling medical applications justifying the use of CRISPR/Cas9 in embryos").

demonstrate that editing the germline of a human embryo raises concerns that extend beyond risk management.[222]

Concerns regarding human rights, environmental justice, distributional impacts, intergeneration equity, consumer choice, and animal rights reflect additional perspectives regarding biotechnology governance.[223] Those who may not advocate for a ban on GMOs but still call for labeling represent an additional perspective in the biotechnology debate—consumer choice. Labeling and other transparency measures allow stakeholders to use purchasing power to determine whether to support an approach to agriculture or medicine, to reject uses that are counter to their understandings of the proper role of humans in the ecosystem, to support smaller industry players who may not have the resources to license an emerging technology or navigate the regulatory system, or simply to avoid products that they consider distasteful.[224]

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[222] *See, e.g.*, HUMAN GENOME EDITING, *supra* note 26, at 5–6 (advocating limiting human trials to only "to the most compelling circumstances, [to] subject [them] to a comprehensive oversight framework that would protect the research subjects and their descendants, and [to institute] sufficient safeguards . . . to protect against inappropriate expansion to uses that are less compelling or less well understood"); Collins, *supra* note 64 (referring to "strong arguments against engaging in [human germline editing] . . . includ[ing] the serious and unquantifiable safety issues, ethical issues presented by altering the germline in a way that affects the next generation without their consent, and a current lack of compelling medical applications justifying the use of CRISPR/Cas9 in embryos").

[223] *See, e.g.*, MICHAEL BESS, OUR GRANDCHILDREN REDESIGNED: LIFE IN THE BIOENGINEERED SOCIETY OF THE NEAR FUTURE 87–89 (2015) (identifying unequal access to genetic enhancements as potentially creating a new, permanent type of caste system); BERNARD E. ROLLIN, THE FRANKENSTEIN SYNDROME: ETHICAL AND SOCIAL ISSUES IN THE GENETIC ENGINEERING OF ANIMALS 18–21 (1995) (stating that science and genetic engineering inherently require value judgments); Kuzma & Rawls, *supra* note 40, at 281 ("Humanity's ability to alter populations within ecosystems through genetic engineering raises issues associated with biodiversity and conservation that, in turn, may affect the abilities of current and future generations to use and enjoy the benefits of the natural world."); *see also* Jonathan H. Adler, *Compelled Commercial Speech and the Consumer "Right to Know,"* 58 ARIZ. L. REV. 421, 458–59 (2016) (stating that "[m]any policymakers and activist organizations argue that consumers have a right to know whether food products contain, or were manufactured with, ingredients that were produced with these modern genetic engineering techniques"); Carmen G. Gonzalez, *Genetically Modified Organisms and Justice: The International Environmental Justice Implications of Biotechnology*, 19 GEO. INT'L ENVTL. L. REV. 583, 604–05 (2007) (describing the "environmental justice" perspective that the import of genetically-modified products into developing countries risks an increase in socioeconomic inequality); UNESCO, UNIVERSAL DECLARATION ON THE HUMAN GENOME AND HUMAN RIGHTS art. 11 (1997) (calling for a ban on "[p]ractices which are contrary to human dignity, such as reproductive cloning of human beings" and calling for international cooperation "to ensure that the principles set out in this Declaration are respected").

[224] Cass R. Sunstein, *On Mandatory Labeling, with Special Reference to Genetically Modified Foods*, 165 U. PA. L. REV. 1043, 1077 (2017) (citing Sydney E. Scott et al., *Evidence for Absolute Moral Opposition to Genetically Modified Food in the United States*, 11 PERSP. ON PSYCHOL. SCI. 316, 317 (2016)); *see* Peck, *supra* note 40, at 316 (noting complaints by "small private and public

The perspectives described above are not necessarily mutually exclusive of one another. A stakeholder may hold numerous viewpoints at once, such as a general apprehension about decentralized decision making regarding the use of gene drives, appreciation that certain genetic engineering applications may foster greater environmental benefits, and a belief that scientists should continue to pursue gene therapies to address severe genetic disorders, provided appropriate ethical and risk management protections are in place. The key takeaway for biotechnology governance is not that policy should prioritize one viewpoint over others, but rather that the current debate reflects these competing viewpoints and that existing regulatory schemes offer models for accommodating multiple perspectives.

IV. INCORPORATING A NATURAL RESOURCES FRAMEWORK INTO BIOTECHNOLOGY GOVERNANCE

The scientific advances allowing gene editing are new, but the challenges with balancing competing considerations regarding the use and alteration of natural resources are not.[225] Focusing on threshold questions regarding values, irreversibility, and the public good, the debate over gene editing governance reflects longstanding debates over natural resource management. The nation's strategies for balancing conservation, preservation, and numerous other uses of federal lands, wildlife, plants, water, and minerals have dealt with similar issues for well over a century.[226] Gene editing adds a new, albeit complex, dimension to these existing debates by expanding the tools available to alter public and private resources.

Natural resource management offers a new conceptual model for biotechnology governance that moves beyond a risk-based, case by case approach. Incorporating a natural resource management perspective into biotechnology governance would provide a frame of reference for considering gene editing and its implications through the lens of public and private re-

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laboratories" that the current biotechnology regulatory system "is so difficult to navigate that many are discouraged from pursuing biotechnology research"); Jacob S. Sherkow, *How Much Is a CRISPR Patent License Worth?,* FORBES (Feb. 21, 2017), https://www.forbes.com/sites/jacobsherkow/2017/02/21/how-much-is-a-crispr-patent-license-worth/#7fe3b6e56b77 [https://perma.cc/7YBX-ZBCW] (analyzing the likely value of an exclusive CRISPR patent).

[225] Purdy, *supra* note 207, at 186–89; *see* RODERICK FRAZIER NASH, WILDERNESS AND THE AMERICAN MIND 23–43 (4th ed. 2001) (detailing the efforts by early American settlers to use natural resources and hold dominion over the land rather than preserve its natural state).

[226] *See* Purdy, *supra* note 207, at 199–203 (noting the rise of the Sierra Club in 1892 and its publication of material describing natural landscapes). United States laws addressing natural resource management are as old as the country itself, but the contemporary conflicts regarding use, conservation, and preservation emerged in the late 1800s as the federal government shifted away from its previous policy of transferring federal lands to the states. *Id.* at 199–200, 205–06.

sources for which there are conflicting perspectives regarding appropriate uses and preservation. Although existing laws do not contemplate the ability to reorder ecosystems via gene editing, there is an established regulatory system designed to address risks of extinction, accommodate competing ideologies regarding resource use, and incorporate interests of future generations when considering irreversible decisions regarding natural resources—all issues that are implicated by gene editing.[227]

Federal lands policies, for example, have evolved to manage conflicting interests and values, identifying appropriate uses and allocating resources.[228] As Professor Jedediah Purdy notes, federal resource policies now reflect a combination of ideologies that emerged at different times in U.S. history.[229] Together, these policies simultaneously view the public good as utilizing resources to promote the country's economic growth, rely on technocratic management to balance competing resource uses, prioritize conservation, recreation, and preservation of the nation's lands, and recognize the complex interactions necessary to maintain a healthy ecosystem.[230]

At times, natural resource statutes include precommitments to refrain from certain uses due to the characteristics of the resource(for example, national monuments and national parks), concerns regarding irreversible impacts (for example, protecting endangered species), or prioritizing nonuse values over other potential uses (for example, wilderness areas). National Wilderness Areas, National Parks, National Forests, National Monuments, and National Recreation Areas each have distinct statutory and regulatory criteria for designation, access, and resource use based on the characteristics

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[227] *See, e.g.*, Amy Joi O'Donoghue, *State Wildlife Board Opposes Bears Ears Monument in Letter to Feds*, KSL.COM (Aug. 16, 2016), https://www.ksl.com/?sid=41096372&nid=148 [https://perma.cc/7NR2-99HZ] (discussing opposition to the Bears Ears National Monument due to the "area's importance to wildlife and wildlife-based recreation"). Designated wilderness areas, national monuments, and national wildlife refuges each represent a precommitment to restrict resource extraction despite the potential for local and state economic benefits from other uses. *Id.*

[228] *See, e.g.*, JAMES RASBAND ET AL., NATURAL RESOURCES LAW AND POLICY 45 (3d ed. 2016) (stating that "competition over scarce natural resources inevitably causes a clash of competing interests"); Jan G. Laitos & Thomas A. Carr, *The Transformation on Public Lands*, 26 ECOLOGY L.Q. 140, 144 (1999) (noting the tension between preservation and recreation); Jan G. Laitos & Rachael B. Gamble, *The Problem with Wilderness*, 32 HARV. ENVTL. L. REV. 503, 505 (2008) (describing the rise of recreation and conservation goals, and the conflicts among these uses and different uses of undeveloped lands); J.B. Ruhl & Robert L. Fischman, *Adaptive Management in the Courts*, 95 MINN. L. REV. 424, 436 (2010) (stating that "natural resource law is as much the management of conflict as it is the management of public lands, waters, or species"); Walter Rusinek, *Balancing Competing Interests: A Natural Resources Law Primer*, ARIZ. ATT'Y, Mar. 1995, at 24–29 (describing the tension and balance in natural resources law between use and preservation of natural resources).

[229] Purdy, *supra* note 207, at 173−74.

[230] *See id.* at 173–74, 208 (detailing the impacts of federal resource policies).

of the lands and resources contained therein.[231] For example, the Federal Land Policy and Management Act of 1976 instructs the Bureau of Land Management to balance "recreation, range, timber, minerals, watershed, wildlife and fish resources" as well as "natural scenic, scientific and historical values."[232] The management practices must ensure "sustained yield" and protect current and future use.[233] The Organic Act of 1916 requires the Park Service to achieve the conflicting goals of conserving "the scenery, natural and historic objects, and wild life" while also allowing for recreation, and leaving the resources "unimpaired for the enjoyment of future generations."[234] In other circumstances, Congress specifies how to resolve competing uses at the outset, such as the Wilderness Act prohibiting commercial enterprises, permanent roads, motorized vehicles, and manmade structures, while permitting continued livestock grazing.[235]

Federal land management also generally requires consideration of ecological impacts. In some instances, these considerations take the form of balancing ecological impacts with other statutory goals, such as multiple use.[236] In other instances, ecological considerations take priority. Specifying the relative importance of ecological impacts provides important guidance to regulators and, similar to requirements to consider the interests of future generations, outlines substantive requirements that may be subject to judicial review. These requirements operate in conjunction with NEPA's procedural mandate to evaluate actions that may have significant environmental impacts.[237]

Strategies for resolving natural resource conflicts are far from perfect. Intense disputes persist regarding species preservation, land preservation, and access to resources.[238] Taken as a whole, however, the system of natural

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[231] Wilderness Act, Pub. L. No. 88-577, 78 Stat. 890 (1964) (codified as amended at 16 U.S.C. § 1131 (2018)); Organic Act of 1916, Pub. L. No. 64-235, 39 Stat. 535 (1916) (codified as amended at 54 U.S.C. § 100101 (2018)); National Forest Management Act of 1976, Pub. L. No. 94-588, 90 Stat. 2949 (1976) (codified as amended at 16 U.S.C. § 1600 (2018)); Antiquities Act, Pub. L. No. 59-209, 34 Stat. 225 (1906) (codified as amended at 16 U.S.C. § 431 (2018)). This is far from a complete list. Federal agencies may have multiple land classifications under their jurisdiction. *See, e.g.*, Garett R. Rose, *"Reservations of Like Character"—The Origins and Benefits of the National Park System's Classification Hierarchy*, 121 PENN ST. L. REV. 355, 362–71 (2016) (identifying land classifications under National Park Service jurisdiction).

[232] 43 U.S.C. § 1702(c) (2018).

[233] *Id.* §§ 1701(a)(2), 1702(h).

[234] 54 U.S.C. § 100101(a) (2018).

[235] 16 U.S.C. §§ 1133(c), (d)(4).

[236] *See, e.g.*, *id.* § 1611(a) ("[A]ny such planned departure must be consistent with the multiple-use management objectives of the land management plan").

[237] 42 U.S.C. § 4332(C) (2018).

[238] *See, e.g.*, Kirk Siegler, *With National Monuments Under Review, Bears Ears Is Focus of Fierce Debate*, NAT'L PUB. RADIO (May 5, 2017), https://www.npr.org/2017/05/05/526860725/

resource governance requires consideration of the tradeoffs associated with altering natural systems and balancing competing values. The range of natural resource statutes thus provides models for considering categories of gene editing applications in terms of their economic, ecological, and cultural impacts, including risks, benefits, and values-based considerations that extend beyond the risk-benefit framework.

Explicitly incorporating additional criteria to biotechnology governance would allow policy discussions to move beyond the product versus process focus. Instead, the focus would shift from product to potential for natural resource impacts. This change would allow a multifaceted regulatory approach that is better prepared to consider the range of complex ecological and distributional impacts that will likely arise due to gene editing. Considering the values implicated by the prospect of altering organisms or eradicating species properly situates concerns about safety and risk within the broader context of ideologies underlying the biotechnology debate.

Few may question the benefits of eradicating a non-native species of mosquito to prevent spreading the Zika virus, a virus that can cause severe birth defects, including microcephaly, when passed from pregnant women to embryos, or dengue fever, "a leading cause of illness and death in the tropics and subtropics" for which there is no vaccine to prevent infection, if the eradication method does not harm humans or the environment.[239] That acceptance may not extend to other uses that do not address such pressing health concerns.

Requiring government officials to consider additional criteria would likely face opposition. Such a shift would incorporate the narrative of engineering evolution and extinction as a starting point, potentially leading to more stringent regulatory oversight in some circumstances. Proponents of minimal oversight of gene-edited organisms may worry that such a shift would result in unnecessary regulation and permitting delays, thus stifling innovation, restricting competitiveness of U.S. biotechnology firms, and delaying or denying benefits to society.

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with-national-monuments-under-review-bears-ears-is-focus-of-fierce-debate [https://perma.cc/4SLV-QE6K] (describing tension over the designation of monuments and use of federal lands in Utah); *see also* Jan G. Laitos, *The Multiple to Dominant Use Paradigm Shift in Natural Resources Management*, 24 J. LAND, RES., & ENVTL. L. 221, 227 (2004) (analyzing conflicts among recreational users of federal lands).

[239] *Dengue*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/dengue/index.html [https://perma.cc/VXS7-E4Z5]. The *Aedes aegypti* mosquito, the mosquito strain targeted in the proposed Key Haven trial, is "the most important transmitter or vector of dengue viruses" in the Western Hemisphere. *Dengue: Frequently Asked Questions: What Is Dengue?*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/dengue/faqfacts/index.html [https://perma.cc/TT72-GVXF]; Questions About Zika, *supra* note 3.

Broad-based opposition to the notion of additional regulatory oversight is misplaced. First, delays and restrictions are an acceptable outcome if they result in a more effective regulatory approach for an emerging technology that could simultaneously offer dramatic benefits and risks. Furthermore, requiring federal agencies to consider criteria like the interests of future generations does not mandate a uniform approach for all gene editing applications nor a particular outcome. It is possible, for example, to realize health benefits of gene therapies, eradicate certain disease-carrying insects, and allow the sale of certain ecologically benign agricultural products without accepting a laissez-faire approach to gene editing. It is also possible to maintain different restrictions for research and deployment phases of gene editing, and to implement an adaptive approach to resource decisions that allows regulatory limits to shift as new information becomes available.[240] Where timeliness is crucial, such as preventing the rapid spread of a highly contagious disease, regulations could allow for expedited review or provide exemptions. As it stands, the limited regulatory inquiries required by existing law foreclose many of these considerations.

This section identifies three general strategies that may serve as a starting point for amending biotechnology governance to incorporate lessons of effective natural resource management: balancing competing values; providing mechanisms for participatory governance; and implementing conservation strategies. Taken together or individually, these measures provide a foundation for a more robust regulatory scheme to address the fundamental questions presented by rapid advancements in biotechnology. Federal agencies could implement some of the ideas presented in this section via administrative action. The FDA proposal to expand the definition of animal drug demonstrates that interpretation of statutory language may change as technologies evolve.[241] Agencies could also increase opportunities for public engagement under current statutory authority. Other ideas described below would require legislative action, such as explicitly incorporating impacts on future generations as part of an approval process or distinguishing between gene editing that addresses acute health concerns versus those that offer benefits of convenience or aesthetics. The discussion introduces options to facilitate a broader approach to biotechnology governance but does not go into detail regarding implementation.

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[240] *See* Ruhl & Fischman, *supra* note 228, at 436–43 (detailing adaptive management practices for natural resources).

[241] *See* FDA GE ANIMALS DRAFT GUIDANCE, *supra* note 71, at 6–7 (noting each specific DNA or genomic alteration is a "new animal drug" subject to regulation).

A. Explicit Identification of Values-Based Considerations

As the natural resource statutes described above demonstrate, Congress can define, and federal agencies can address, broad, values-based language that recognizes multiple interests involved in decisions regarding resource management. The statutes may grant wide discretion to agencies making resource decisions.[242] Specifying governance criteria in a statute, even if by broad language, however, requires agencies to give them due consideration and explain their rationales.[243] In the process, the specified criteria may also incorporate, and potentially solidify, cultural norms.[244]

The debate over human genome alterations is the most prevalent example of explicit values-based limitations on gene editing and other biotechnology applications. [245] Gene therapies for medical purposes, including those utilizing gene editing techniques, face a higher level of regulatory scrutiny by the FDA than genetic alterations applied to animals, plants, and insects. Gene therapies are also subject to oversight by the National Institute of Health's Recombinant DNA Advisory Committee ("RAC"), institutional review boards, and biosafety committees.[246] A 1996 budget amendment, referred to as the Dickey-Wicker amendment, prohibits federal funding for research on human embryos or for research that results in the destruction of human embryos.[247] National Institute of Health Guidelines prohibit the RAC from "entertain[ing] proposals for germ line alteration[]."[248] The RAC

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[242] *See* S. Utah Wilderness All. v. Dabney, 222 F.3d 819, 826 (10th Cir. 2000) (interpreting the phrase "unimpaired for the enjoyment of future generations" in the Organic Act).

[243] *See id.* at 829 (remanding to determine whether the National Park Service's interpretation of "unimpaired for the enjoyment of future generations" was reasonable).

[244] *See* John D. Leshy, *Legal Wilderness: Its Past and Some Speculations on Its Future*, 44 ENVTL. L. 549, 551, 622 (2014) (noting the symbiotic relationship between legal and cultural perceptions of natural resource preservation).

[245] *See* Collins, *supra* note 64 (explaining "[t]he concept of altering the human germline in embryos for clinical purposes has been debated over many years from many different perspectives, and has been viewed almost universally as a line that should not be crossed" and discussing arguments against human genome editing, including "the serious and unquantifiable safety issues, ethical issues presented by altering the germline in a way that affects the next generation without their consent, and a current lack of compelling medical applications justifying the use of CRISPR/Cas9 in embryos"); *see also* GENE DRIVES ON THE HORIZON, *supra* note 12, at 60 (stating that "[t]he most prominent moral questions about genetic engineering have always been about its prospective benefits and harms to human beings").

[246] NAT'L ACADS. OF SCIS., ENG'G, & MED., OVERSIGHT AND REVIEW OF CLINICAL GENE TRANSFER PROTOCOLS: ASSESSING THE ROLE OF THE RECOMBINANT DNA ADVISORY COMMITTEE 77 (2014).

[247] Balanced Budget Downpayment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

[248] NAT'L INSTS. OF HEALTH, NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT ON SYNTHETIC NUCLEIC ACID MOLECULES 100 (Apr. 2016), https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf [https://perma.cc/HGC2-URYL].

reviews and monitors protocols for experimental gene therapy clinical trials and provides a venue for public comment and review.[249] Other gene therapy oversight bodies do not involve the general public.

Like other areas of biotechnology, gene therapy research is advancing quickly. The FDA approved a gene therapy for the first time in August 2017.[250] An FDA advisory committee recommended approval of a second gene therapy one month later.[251] The National Institute of Health prohibits federal funding for human germline modifications, but the use of CRISPR for non-inheritable treatments is underway.[252] The RAC recently approved a protocol for the first clinical trial of a CRISPR gene therapy in humans.[253] The trial, involving CRISPR edits of human T-cells, is privately funded and not aimed at germline modifications.[254] In August 2017, another group of scientists announced the successful editing of a human embryos to address a genetic blood disorder—the first successful human germline editing involving U.S. scientists.[255]

The National Academies of Sciences, Engineering, and Medicine have responded to these rapid developments with numerous reports on genetic engineering, including a 2017 report focused directly on human germline editing.[256] The report concludes that if human germline editing were to occur, "it would be essential to limit these trials only to the most compelling cir-

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[249] *Id*. at 23, 31, 37.

[250] Press Release, Food & Drug Admin., FDA Approval Brings First Gene Therapy to the United States (Aug. 30, 2017), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm [https://perma.cc/AF23-SVFV].

[251] Laurie McGinley, *Novel Cancer Treatment Wins Endorsement of FDA Advisers*, WASH. POST (July 12, 2017), https://www.washingtonpost.com/news/to-your-health/wp/2017/07/12/novel-cancer-treatment-wins-endorsement-of-fda-advisers/ [https://perma.cc/SY8J-L36M].

[252] NIH GUIDELINES, *supra* note 248, at 100.

[253] Collins, *supra* note 64; Dep't of Health & Human Servs., Recombinant DNA Advisory Committee, Minutes of Meeting, 14–15, 26 (June 21–22, 2016) (minutes available at https://osp.od.nih.gov/wp-content/uploads/2017/02/Minutes_RAC_Jun2016_508_0.pdf [https://perma.cc/FM3N-SLEC]).

[254] Sara Reardon, *First CRISPR Clinical Trial Gets Green Light From US Panel*, NATURE (June 22, 2016), http://www.nature.com/news/first-crispr-clinical-trial-gets-green-light-from-us-panel-1.20137 [https://perma.cc/C4NL-W2WD].

[255] Ma et al., *supra* note 30; Pam Belluck, *In Breakthrough, Scientists Edit a Dangerous Mutation from Genes in Human Embryos*, N.Y. TIMES (Aug. 2, 2017), https://www.nytimes.com/2017/08/02/science/gene-editing-human-embryos.html [https://perma.cc/62G5-UCWU].

[256] *See generally* NAT'L ACADS. OF SCIS., ENG'G, & MED., GENETICALLY ENGINEERED ORGANISMS, WILDLIFE, AND HABITAT: A WORKSHOP SUMMARY (2008); NAT. RESEARCH COUNCIL COMM. ON IDENTIFYING AND ASSESSING UNINTENDED EFFECTS OF GENETICALLY ENGINEERED FOODS ON HUMAN HEALTH, SAFETY OF GENETICALLY ENGINEERED FOODS: APPROACHES TO ASSESSING UNINTENDED HEALTH EFFECTS (2004); HUMAN GENOME EDITING, *supra* note 26; GENE DRIVES ON THE HORIZON, *supra* note 12; GENETICALLY-ENGINEERED CROPS, *supra* note 198; GM PEST-PROTECTED PLANTS, *supra* note 50.

cumstances, to subject them to a comprehensive oversight framework that would protect the research subjects and their descendants, and to institute safeguards against inappropriate expansion into uses that are less compelling or well understood."[257] The National Academies' proposed regulatory framework includes the following elements:

> (i) absence of reasonable alternatives; (ii) restriction to preventing a serious disease or condition; (iii) restriction to editing genes that have been convincingly demonstrated to cause or to strongly predispose to the disease or condition; (iv) restriction to converting such genes to versions that are prevalent in the population and are known to be associated with ordinary health with little or no evidence of adverse effects; availability of credible pre-clinical and/or clinical data on risks and potential health benefits of the procedures; (v) ongoing, rigorous oversight during clinical trials of the effects of the procedure on the health and safety of the research participants; (vi) comprehensive plans for long-term, multigenerational follow-up that still respect personal autonomy; (vii) maximum transparency consistent with patient privacy; (viii) continued reassessment of both health and societal benefits and risks, with broad ongoing participation and input by the public; and (ix) reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition.[258]

The report recognizes that these criteria are open for interpretation.[259] The authors also note the difficulty inherent in defining concepts such as "enhancement," "reasonable alternative," and "serious disease condition."[260]

The same suggested criteria for strict oversight of human germline editing could apply to non-human gene editing applications currently underway. This is not to suggest that concerns regarding human and non-human genetic modifications are on par with one another. Implementation may differ depending on the human or non-human uses, but the National Academies' recommendations for allowing human gene editing while addressing moral and ethical concerns are applicable in both contexts. For example,

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[257] HUMAN GENOME EDITING, *supra* note 26, at 7.

[258] *Id.* at 7–8.

[259] *Id*. at 8 (noting that stakeholders could view the criteria as (1) effectively "promoting well-being within a framework of due care and responsible science," (2) providing a framework "strict enough to prevent the harms" or (3) satisfying opponents of gene editing because the criteria are "so strict that they would have the effect of preventing all clinical trials involving germline genome editing").

[260] *Id.* at 8–9.

biotechnology policy could limit the use of gene editing to purposes where there is a convincing public benefit. Laws could require credible data on the risks and potential benefits of releasing genetically-modified organisms. Approval could be coupled with requirements to engage in ongoing, rigorous oversight of the modified organisms and their ecosystem impacts. Release could also be conditioned on the availability of effective safeguards to prevent unanticipated impacts.[261] Regulators could require comprehensive plans for long-term studies in a manner accessible to government agencies and the general public. Companies releasing genetically-modified organisms could be subject to continued reassessment of the benefits and risks to public health and the environment, with ongoing participation and input by the public. Laws could create a presumption against genetic alterations to animals, plants, or other organisms when other reasonable alternatives exist.[262] Approval could also require demonstrations of reliable oversight mechanisms to ensure the genetically-modified organisms are released and managed in the approved manner.

Even maintaining the current focus on human and agriculture impacts, biotechnology governance is too limited to protect those interests in the new CRISPR era. Gene editing may permanently impact ecosystems in a manner that affects public health (for example, creating ecosystem changes that increase the risk of other disease vectors) or alters flora or fauna in a manner that impacts local resource-dependent industries (for example, creating tree or animal species that out-compete indigenous varieties).[263] There is a long history of seemingly benign ecosystem changes producing unforeseen impacts. The increasing prevalence of ticks due to a lack of natural predators for their hosts, the introduction of kudzu to manage erosion, and the loss of topsoil and increased flooding due to deforestation are but a few notable examples.[264]

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[261] Kevin M. Esvelt, *An Analysis of Gene Drive Risks and Safeguards*, SCULPTING NATURE, http://www.sculptingevolution.org/genedrives/safeguards [https://perma.cc/8GEX-5KBF].

[262] Doug Gurian-Sherman, *Genetically Engineered Crops in the Real World—Bt Corn, Insecticide Use, and Honey Bees*, UNION OF CONCERNED SCIENTISTS (Jan. 10, 2012), https://blog.ucsusa.org/doug-gurian-sherman/genetically-engineered-crops-in-the-real-world-bt-corn-insecticide-use-and-honeybees-2?_ga=2.4208688.243407572.1534856677-940336054.1534856677 [https://perma.cc/L76L-9Z8U] (identifying crop breeding and changes to farm management as alternatives to genetically-engineered crop).

[263] *See, e.g.*, Kenneth A. Oye et al., *Regulating Gene Drives*, 345 SCIENCE 626, 627 (2014) (noting the potential for gene drives to produce "unintended ecological side effects").

[264] *See, e.g.*, Derek H Alderman & Donna G'Segner Alderman, *Kudzu: A Tale of Two Vines*, 7 SOUTHERN CULTURES 49, 52 (2001) (stating that kudzu went from being a "highly valued resource to lowly pest"); Corey J. A. Bradshaw et al., *Global Evidence That Deforestation Amplifies Flood Risk and Severity in the Developing World*, 13 GLOBAL CHANGE BIOLOGY 2379, 2380–81 (2007) (describing evidence that deforestation directly impacts flooding); Sean M. Moore et al.,

Implementation could vary depending on the organisms involved, the circumstances motivating the proposal to use genetic engineering, and the types of risks and uncertainties presented by the genetic engineering and non-genetic engineering alternatives. In some cases, the requirement to pursue alternatives prior to deploying genetic engineering could allow exceptions if the gene editing option is found to be safe and superior to conventional options. In other cases, where risks are high or core values are implicated, the requirement could be more restrictive.[265] The approach could also distinguish between laboratory experimentation and deployment of gene-edited products, allowing research and testing to continue.

Policymakers could look to federal lands statutes such as the National Park Organic Act, the Federal Land Policy and Management Act, and the National Forest Management Act as models for incorporating additional values-based considerations into the biotechnology statutory framework.[266] For example, just as current federal land management decisions impact the interests of future generations, future generations also have an interest in how biotechnology impacts humans and ecosystems. Explicit consideration of these interests as a part of biotechnology oversight would provide important symbolic and substantive (in other words, judicially reviewable) criteria to guide decision making.[267] Updates to the biotechnology governance framework could also incorporate substantive requirements to evaluate potential ecological impacts of gene editing applications that expand beyond the procedural requirements of NEPA.[268]

Applying this inquiry in the context of genetically-modified mosquitoes, regulators would consider the societal benefit of releasing the modified organism and arguments regarding the availability of effective alternatives. Genetic modifications to eradicate the Zika virus may be approved, but modifications to eradicate or control non-disease carrying insects may not. The inquiry could also distinguish between the types of diseases a mosquito species may carry, weigh those risks with the risks to other species in the ecosystem, and require ongoing public engagement and risk assessment. The process could also allow for expedited review in circumstances such as

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Predators Indirectly Control Vector-Borne Disease: Linking Predator-Prey and Host-Pathogen Models, 7 J. OF ROYAL SOC'Y: INTERFACE 161, 161 (2010) (noting the relationships between disease carrying vectors and their ecological communities).

[265] This discussion is intentionally general and identifies possible governance strategies that could place limits on gene editing rather than propose specific approaches.

[266] 16 U.S.C. § 1600 (2018); 43 U.S.C. § 1702(c) (2018); 54 U.S.C. § 100101 (2018).

[267] *See* 54 U.S.C. § 100101(a) (requiring that resources be left "unimpaired for the enjoyment of future generations").

[268] *See* 42 U.S.C. § 4332(C) (2018) (listing NEPA's procedural mandate to evaluate actions that may have significant environmental impacts).

the Zika virus. The environmental assessment for the Key Haven field trial already includes many of these elements.[269] The natural resource management framework could shift the inquiry from procedural review of risks to substantive instructions to the regulators assessing the risks. Decisions could then be judicially reviewable, increasing societal oversight for deployment of genetic sciences.

The hornless cow may or may not receive regulatory approval under the proposed framework.[270] If the justification for approving the modified dairy cow is increasing safety for cows and farmers, the inquiry would assess what causes the risk. One obvious alternative to modifying the DNA of dairy cattle is to require greater space for the cattle. That outcome may raise costs, which would force agencies to weigh economic interests against the implications of gene editing. To the extent an agency is prioritizing one criterion over another—for example, short-term economic gains over long-term moral or ecological concerns regarding gene editing—the process should be explicit and transparent. The natural resource framework for gene editing could require it.

This approach has multiple benefits for effective biotechnology governance. It may avoid risks by limiting the number of discretionary releases of gene-edited products. It may reduce opposition to biotechnology where there is a more robust regulatory system that identifies benefits and risks and provides for stakeholder engagement. It may provide a market signal that guides biotechnology investment toward the most beneficial uses, as well as enhance support for gene editing when it is the only viable option. Consideration of value choices may also refine the use of precautionary principles when determining how to proceed with a biotechnology product.[271]

There are also potential downsides, such as impacts on investment, slower timelines for product development, and potentially allowing companies engaged in gene editing in countries with less oversight to achieve a competitive advantage over U.S. firms.[272] Government officials incorporating the natural resource framework into biotechnology governance would need to consider these concerns. The multi-faceted approach to natural re-

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[269] FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 7, at 17.

[270] *See* DAIRY ANIMAL WELL-BEING, *supra* note 117 (detailing Recombinetics Inc.'s proposal to genetically-engineer hornless cows).

[271] Kaebnick et al., *supra* note 9, at 710–11 (noting that precaution requires consideration of questions regarding harms, benefits, distributional impacts, and governance regarding new biotechnology products).

[272] *See id.* at 710 (noting various risks relating to use of gene drives).

source management demonstrates that it is possible to tailor government oversight to specific resources, locations, and values.

Creating a common set of criteria based on a combination of risk-assessment and non-risk values would be an important step in breaking down the process-versus-product distinction.[273] If the inquiry determines that a type of gene editing does not pass threshold questions of acceptability, it may be unnecessary to proceed to risk analysis. This stage may identify applications subject to the highest level of restrictions—equivalent to wilderness areas or national monuments.[274] In the genome context, these "protected spaces" may include categories of gene editing such as editing for aesthetic enhancements or deploying gene drives to eradicate non-harmful insects, plants, or animals.

B. Participatory Governance

Many natural resource management regimes rely on varying degrees of public engagement to inform the decision-making process, going beyond formal notice-and-comment requirements.[275] These strategies include engaging individual actors affected by natural resource statutes, creating local advisory committees, and soliciting input when developing plans for parks or forests.[276] These efforts contribute to more informed management strate-

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[273] *See* Rascoff & Revesz, *supra* note 192 (noting the tradeoffs required to determine the party at risk, what the risks are, and what risks are unacceptable).

[274] *See* 16 U.S.C. §§ 1131−1136 (creating a national wilderness preservation system); Mark Squillace et al., *Presidents Lack the Authority to Abolish or Diminish National Monuments*, 103 VA. L. REV. ONLINE 55, 55–56 (2017), http://www.virginialawreview.org/sites/virginialawreview.org/files/Hecht%20PDF.pdf [https://perma.cc/DW4K-YQFA] (noting that only Congress has the authority to get rid of national monuments).

[275] *See, e.g.*, Mark Squillace, *Embracing a Civic Republican Tradition in Natural Resources Decision-Making*, *in* THE EVOLUTION OF NATURAL RESOURCES LAW AND POLICY 195, 209−18 (Lawrence J. MacDonnell & Sarah F. Bates eds., 2010) (detailing various public engagement efforts including formal and informal hearings, town hall meetings, open houses, workshops and consensus-based processes, and personal meetings). Some federal natural resource statutes require agencies to work with local authorities when developing management plans. *See, e.g.*, 16 U.S.C. §§ 1600–1687 (2018) (detailing the National Forest Management Act and the ability of local authorities to participate in program development); 43 U.S.C. §§ 1701−1787 (2018) (detailing the Federal Land Policy and Management Act and the ability of local authorities to participate in program development).

[276] An example of engaging individual actors affected by natural resources is through a Habitat Conservation Plan under the ESA. *See* Endangered Species Act of 1973, 16 U.S.C. § 1539 (2018) (detailing the process to implement a Habitat Conservation Plan); Alejandro E. Camacho, *Can Regulation Evolve? Lessons from a Study in Maladaptive Management*, 55 UCLA L. REV. 293, 298 (2007) (referring to the Habitat Conservation Plan as "one of the earliest experiments in regulatory innovation").

gies. They may also reduce controversies by allowing affected citizens to participate in the decision-making process.[277]

Stakeholder engagement is a particular challenge in the biotechnology context.[278] Reports and scholarly articles discussing developments in genetic engineering frequently call for more robust public engagement and education, but neglect to specify how to accomplish those goals.[279] Although there are mechanisms for public participation in the biotechnology regulatory system, they often occur within the existing risk-based framework and do not accommodate the range of competing interests discussed above.[280] Creating a broader governance framework that expands beyond risk-based considerations could allow decisionmakers to implement engagement strategies tailored to the different types of gene editing applications. In the absence of an expanded framework, engagement is limited primarily to whether stakeholders accept data regarding the safety of a genetically-engineered product.[281]

More robust government-led engagement efforts could contribute by expanding opportunities for stakeholders to comment on appropriate uses of gene editing and available alternatives, including non-risk-based arguments

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[277] *See, e.g.*, Robert L. Fischman, *What Is Natural Resources Law?,* 78 U. COLO. L. REV. 717, 734–36 (2007) (discussing how "place-based collaboration" aids in reaching a decision that caters to the needs of a given area, and thus is generally more favorable to "command-and-control" regulations); Sheila Foster*, Environmental Justice in an Era of Devolved Collaboration*, 26 HARV. ENVTL. L. REV. 459, 474 (2002) ("In bringing together traditional adversaries (e.g., landowners, resource extractors, environmentalists, and federal agencies) to seek solutions of mutual benefit, these ad hoc collaborative partnerships strive to elevate the pursuit of practical, multi-stakeholder plans above the conflict, delays, and administrative red tape so characteristic of mandated planning processes and regulatory programs.").

[278] Kuzma & Besley, *supra* note 213, at 149.

[279] *See, e.g.*, HUMAN GENOME EDITING, *supra* note 26, at 9 ("Precisely because of the difficulty of evaluating the benefit of an enhancement to an individual given the large role of subjective factors, public discussion is needed to inform the regulatory risk/benefit analyses that underlie decisions to permit research or approve marketing. Public discussion also is needed to explore social impacts, both real and anticipated, as governance policy for such applications is developed."); NUFFIELD COUNCIL ON BIOETHICS, PUBLIC DIALOGUE ON GENOME EDITING: WHY? WHEN? WHO? 1, 4 (May 2016), http://nuffieldbioethics.org/wp-content/uploads/Public-Dialogue-on-Genome-Editing-workshop-report.pdf [https://perma.cc/54B9-Q8E4] [hereinafter PUBLIC DIALOGUE ON GENOME EDITING] ("In papers in major scientific journals and statements from high-level meetings and conferences, the voices of researchers, funders, and others have joined together in calling for early and open engagement about genome editing with policy makers and the wider public.").

[280] *See* HUMAN GENOME EDITING, *supra* note 26, at 9–10 (describing the mechanisms for public participation in the gene-editing debate); Marchant et al., *supra* note 190, at 727 (stating that "[e]xisting regulatory frameworks often exclude consideration of social and moral concerns, ruling them outside the bounds of the jurisdiction of regulatory agencies or reviewing courts"); *see also supra* note 185–224 and accompanying text (identifying and discussing the competing interests at stake).

[281] *See 2017 Update to Coordinated Framework*, *supra* note 41, at 7–8 (describing the risk-based approach to regulating genetically-engineered products).

for restricting certain types of gene editing. Similar to the federal lands context, these engagement strategies may differ depending on the resources, and the cultural and ecological implications.[282]

Professor Kevin Esvelt and his colleagues offer a promising example of engaging local communities where gene-edited organisms may be released.[283] Prior to conducting an experiment to control Lyme disease by releasing white-footed mice whose DNA was altered to make the organisms "immune to the bacteria that cause Lyme and other tick-borne diseases," Esvelt focused on educating local communities about the risks and benefits, promised to make information gained through the experiment publicly-available rather than treat it as proprietary, and committed to forgoing the experiment if local residents opposed the process.[284] This effort empowers local residents to participate in decisions regarding the release of genetically-altered organisms and provides information so that each resident can develop an informed opinion.

Referendum-based measures could also help identify values-based considerations and provide mechanisms for stakeholder engagement. Public referendums, such as those conducted prior to the Key Haven trial of genetically-modified mosquitoes, allow affected populations to express their opinions regarding the release of genetically-modified organisms or other uses of biotechnology techniques.[285] Product labeling may facilitate another a type of referendum on biotechnology, allowing consumers to "vote with their checkbooks" by deciding whether to support genetic engineering through the purchase of engineered products.[286] Product labeling has been a source of controversy since GMO products first started entering the marketplace.[287] Pursuant to the Coordinated Framework's focus on products rather than process, the FDA determined that the use of genetic engineering to produce a product is not a "material fact" subject to disclosure require-

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[282] *See* Purdy, *supra* note 207, at 173−74 (describing four historical stages of American interaction with nature arising from shifting cultures and values).

[283] Michael Specter, *Rewriting the Code of Life,* NEW YORKER, Jan. 2, 2017, https://www.newyorker.com/magazine/2017/01/02/rewriting-the-code-of-life [https://perma.cc/7NHV-AYUQ].

[284] *Id.*

[285] S*ee* Joseph, *supra* note 139 (noting that nearly two-thirds of Key Haven residents voted to opposed the GM mosquito trial and residents in the surrounding county approved it); *GMO Mosquito Plan Vote*, *supra* note 138 (describing the process of the non-binding referendum for Kay Haven residents).

[286] *See generally* Sunstein, *supra* note 224 (summarizing the debate regarding labeling of genetically-modified products).

[287] *See* Nan Feng, *The Recent Enactment of National Mandatory GMO Labeling Law: Superior to a Voluntary Labeling Scheme but Unlikely to End the Labeling Controversy*, 40 SEATTLE U. L. REV. 821, 827–31 (2017) (describing the national and state level debates regarding labeling of GMO products).

ments.[288] Labeling of GMO products will soon become more common. In 2016, Congress amended the Agricultural Marketing Act to require labeling of genetically-modified food products.[289] It is not clear whether the new law will cover "foods that are the product of genetic deletions."[290]

Labeling allows consumers to choose whether to purchase genetically-modified products. Opponents of mandatory labeling argue that it may suggest that the GMO products are unsafe, again restricting the debate to concerns about risk and safety and denying, or dismissing, that concerns may reflect a larger set of values regarding the appropriate uses of biotechnology.[291] Labeling currently exists for premium products and products where consumers may be particularly concerned about health risks.[292] Mandatory labeling for biotechnology products could send an important market signal regarding public acceptance of genetic engineering, likely a reason that producers of genetically-modified products often oppose labeling requirements.

Elevating the role of referendum-based governance could also have the positive effect of creating incentives for more effective public education and engagement.[293] Allowing affected populations to determine whether products or techniques are permitted accepts that approval or rejection may occur for a variety of reasons, some of which are fact-based and some of which are based on values, fears, or misinformation.[294] Increasing reliance on referendums or labeling risks turning engagement efforts into public relations battles among interest groups, potentially undermining, rather than facilitating, efforts to provide objective information. It could result in delaying or preventing release, perhaps an acceptable outcome for emerging technologies with the potential for irreversible negative impacts. It could also identify the areas where the public is most willing to accept gene edit-

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[288] *2017 Update to Coordinated Framework*, *supra* note 41; *see* Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(n) (2018) (noting that the extent that labeling does not disclose material facts should be considered to determine if labeling is misleading).

[289] National Bioengineered Food Disclosure Standard, Pub. L. No. 114-216, 130 Stat. 834, 835, 838 (July 29, 2016) (codified at 7 U.S.C. §§ 1639–1639j).

[290] PREPARING FOR THE FUTURE PRODUCTS OF BIOTECHNOLOGY, *supra* note 14, at 81.

[291] *See* Feng, *supra* note 287, at 827 (describing opponents of labeling laws view that these laws could "demonize GM foods" and inhibit innovation).

[292] *See* Sunstein, *supra* note 224, at 1052–53 (noting the potential impact that "non-GM" labeling has on consumer perception of risk).

[293] *See* Kaebnick et al., *supra* note 9, at 711 ("Any proposed release requires engagement with relevant publics, fostering attention to the values questions, broadening control over decisions beyond the community of scientists and engineers, creating an additional layer of review, and improving scientists' understanding of potential outcomes.").

[294] *See* Sunstein, *supra* note 224, at 1051–55 (detailing market variables that inhibit acceptance of GM products such as consumer demand, incomplete information, and producer behavior in labeling); PUBLIC DIALOGUE ON GENOME EDITING, *supra* note 279, at 9 (noting the risks of early dialogue regarding gene editing).

ing. Both outcomes would inform governance measures as the science of gene editing evolves and potential uses expand.

C. Conservation Measures

Preservation, conservation, and concerns about irreversibility are recurring themes in natural resource management. Extracting resources, particularly non-renewable resources, foreclose the option to utilize the resources at a later date when supplies may be limited, prices may increase, or shifts in public opinion would result in different choices.[295] Extracting renewable resources may present similar issues, depending on the time required to replenish the resource or the potential for extraction to alter irreversibly the local ecosystem (for example, deforestation resulting in loss of top soil).

Resource economists have developed numerous strategies to quantify the value of different resource uses and gauge public opinions regarding natural resource extraction.[296] Consideration of use and non-use values, as well as "option value," comparing impacts of near-term actions against the value of preserving choices in the future, are explicitly incorporated into resource decision making.[297] In particular, option value could provide a useful analytical framework for evaluating arguments for early uses of CRISPR versus uses that could lead to irreversible impacts on biodiversity, or do not justify release based on current circumstances because they do not offer sufficient societal benefits or present unacceptable risks.[298] This approach would limit the near-term uses of CRISPR, but preserve options to utilize gene editing in the future if more information is available regarding benefits and risks or if societal perspectives on gene editing shift.

Prohibiting the use of gene editing in some contexts would not necessarily be permanent, but initial decisions to delay actions could preserve

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[295] Michael A. Livermore, *Patience Is an Economic Virtue: Real Options, Natural Resources, and Offshore Oil*, 84 U. COLO. L. REV. 581, 589 (2013).

[296] *See* Catherine M.H. Keske, *How to Value Environmental and Non-Market Goods: A Guide for Legal Professionals*, 39 DENV. J. INT'L L. & POL'Y 423, 423–28 (2011) (detailing the method to value environmental resources through valuation of both "use and non-use values").

[297] *See, e.g.*, Ohio v. U.S. Dep't of the Interior, 880 F.2d 432, 464 (D.C. Cir. 1989) (requiring the Department of Interior to consider non-consumptive values in natural resource damage assessment regulations because market valuation alone "will necessarily be incomplete"); Livermore, *supra* note 295, at 589–90 (defining "real option value" as the value of "information about the benefits and costs of a project" that has been obtained through delayed decisions).

[298] *See* Sunstein, *supra* note 224, at 1088 n.189 (citing Anthony C. Fisher, *Uncertainty, Irreversibility, and the Timing of Climate Policy* 9 (Oct. 2001), http://stephenschneider.stanford.edu/Publications/PDF_Papers/timingFfisher.pdf [https://perma.cc/B49V-L97M] (describing potential risk and unforeseeable consequences of GMO and the "option value" of slow decision making).

options in the event gene editing proves riskier than initially thought, unnecessary due to development of other options, or undesirable due to evolving social norms. Decisions regarding management, use, and preservation may change as societal values evolve. For example, the National Park Service and the Bureau of Land Management have the discretion to change uses for areas that they respectively manage, provided the decisions satisfy judicial review pursuant to their respective authorizing statutes and the Administration Procedure Act.[299] Congress designates national wilderness areas and may reverse those decisions.[300] Questions regarding the ability of the executive branch to reverse national monument designations have resurfaced under the Trump Administration, but it remains indisputable that Congress could reverse a monument designation.[301]

Although these designations may not be permanent, they create a presumption of conservation or preservation in certain circumstances, as well as a specified process for altering the management approaches.[302] Congress could similarly reverse agency decisions in the biotechnology context and could also specify the circumstances under which agencies can (or should) alter regulatory restrictions.

Gene editing governance could also establish the equivalent of protected spaces in the genetic engineering context—circumstances where gene editing is prohibited or limited on a temporary or permanent basis. Additional preservation measures may focus on preserving DNA, maintaining species, and ecosystems. For example, seed banks and storage facilities for the DNA of endangered species (gene banks) could contribute to preservation measures in an era of expanding uses to biotechnology to alter species and ecosystems. These strategies are already utilized to preserve DNA for a variety of reasons, including research, resilience of food supplies, and maintaining genetic diversity.[303] Preserving unaltered genetic material could po-

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[299] *See* 43 U.S.C. § 1702(c) (2018) (requiring the balance of "recreation, range, timber, minerals, watershed, wildlife and fish resources" as well as "natural scenic, scientific and historical values"); 54 U.S.C. § 100101 (2018) (authorizing the Secretary to regulate the National Park System to "conserve the scenery, natural and historic objects, and wild life" and to enable the preservation of those for the "enjoyment of future generations").

[300] 43 U.S.C. § 1782(b).

[301] *See* Squillace, *supra* note 274 (noting that only Congress has the authority to get rid of national monuments).

[302] For example, the National Forest Management Act specifies aspects of National Forest management plans, including requirements for public participation. 16 U.S.C. § 1604 (2018).

[303] *See* Victoria Russo, *Five Global Seed Banks That Are Protecting Biodiversity*, WORLDWATCH INST. BLOG (Oct. 12, 2013), http://blogs.worldwatch.org/five-global-seed-banks-that-are-protecting-biodiversity/ [https://perma.cc/MJN5-3KRA] (describing conservation and education efforts at major seed banks); Oliver A. Ryder et al., *DNA Banks for Endangered Animal Species*,

tentially help mitigate unanticipated impacts of biotechnology products, serving as an emergency backstop.[304]

CONCLUSION

Advances in genetic engineering such as CRISPR give public and private actors the ability to edit the DNA of living organisms, including human beings, with precision. Biotechnology governance in the United States is not equipped to address the new generation of gene editing techniques. As technological limits fall, policy choices will determine whether and how to deploy gene editing techniques.

To the parties conducting gene editing experiments, the companies seeking to commercialize a genetically-engineered organism, or a regulator operating under the current legal regime, questions regarding the appropriate uses of gene editing techniques may appear as isolated issues that turn on whether a proposed use presents specific, known risks. Considering the questions through the narrow lens of a single application of gene editing misses the full scope of the issues, however. These questions are about more than risk management.

Moving beyond the product versus process distinction to more effectively balance competing interests requires a different conceptualization of the genome, one that recognizes the range of conflicts inherent in the biotechnology debate. Here, the nation's natural resource policies provide important lessons for implementing a heterogenous approach to resource exploitation and conservation, accommodating conflicting views, and creating a corollary to protected areas by prohibiting or limiting certain biotechnology applications. Decisionmakers should look to these laws as models for modernizing the system of biotechnology governance to consider a wider scope of interests, concerns, and values.

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288 SCI. 275, 275–77 (2000) (arguing for the implementation of DNA banks as a critical step to preserve endangered animal species).

[304] Phillip A. Morin et al., *Preservation of DNA from Endangered Species*, 289 SCI. 725, 725–27 (2000).