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# Governing Extinction in the Era of Gene Editing

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# GOVERNING EXTINCTION IN THE ERA OF GENE EDITING\*

JONAS J. MONAST\*\*

*CRISPR-Cas9 genome-editing technology (“CRISPR”) offers a potential solution for some of the world’s critical conservation challenges. Scientists are harnessing CRISPR to expand genetic diversity of endangered species, control invasive species, or enhance species’ resiliency to a changing climate. Recreating extinct species is now realistic, as is engineering entirely new species. CRISPR also creates opportunities to address vector-borne infectious diseases such as malaria, dengue fever, and Zika using gene drive techniques that can spread genetic alterations through populations.*

*While CRISPR is a powerful tool to address public health and conservation goals, it could allow scientists to bypass long-standing value choices underlying national and international conservation efforts and foster permanent ecosystem impacts before public policy can react. This Article argues that, while current conservation laws do not directly address many of the specific questions that arise with CRISPR, the Endangered Species Act (“ESA”) establishes a framework that can, and should, guide the use of gene editing. The proposal calls for: (1) a presumption against the release of genetically modified organisms that could cause species extinction, (2) exemptions for specific public health and environmental goals, and (3) updates to the ESA to clarify oversight of gene editing.*

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## INTRODUCTION

The world is watching species go extinct in real time. The last male northern white rhino died in March 2018.<sup>1</sup> In September of the same year, scientists discovered a new threat to the critically endangered Asiatic lion: canine distemper carried by ticks.<sup>2</sup> Killer whales are at risk of extinction due to chemical pollution in oceans.<sup>3</sup> Invasive rodents threaten endangered island-dwelling bird species.<sup>4</sup>

1. Joshua Berlinger, *World's Last Northern White Rhino Dies*, CNN (Mar. 20, 2018, 12:41 PM), <https://www.cnn.com/2018/03/20/africa/last-male-white-rhino-dies-intl/index.html> [https://perma.cc/CPX8-9WMN]; Torill Kornfeldt, *Bring Back the Northern Rhino?*, SLATE (Nov. 15, 2018, 8:00 AM), <https://slate.com/technology/2018/11/reorigin-of-species-excerpt-cloning-northern-white-rhino-deextinction.html> [https://perma.cc/2HVV-UNHP] (“[N]o more northern white rhinos will be born by natural means.”).

2. Stuart Winter, *DEADLY Dog Diseases ‘Wiping OUT’ World’s Rarest Lions - 23 Dead in THREE WEEKS*, DAILY EXPRESS (Oct. 3, 2018, 15:00), <https://www.express.co.uk/news/nature/1026298/Lions-dying-deadly-pet-disease> [https://perma.cc/D7QC-CHT6].

3. “*A Population Marching Toward Extinction*”: *Missing Orca Feared Dead*, CBS NEWS (Sept. 14, 2018, 4:01 PM), <https://www.cbsnews.com/news/j50-missing-orca-declared-dead-a-population-marching-toward-extinction-2018-09-14/> [https://perma.cc/SA6E-592T].

4. Matt McGrath, *‘Super-Sized’ Mice Threaten Seabird Colonies with Extinction*, BBC NEWS (Oct. 22, 2018), <https://www.bbc.com/news/science-environment-45918770> [https://perma.cc/4THL-7B6F].

CRISPR-Cas9 genome-editing technology (“CRISPR”) offers a potential solution for some of these critical conservation challenges.<sup>5</sup> Scientists are harnessing CRISPR to expand genetic diversity of endangered species, control invasive species, and enhance species’ resiliency to a changing climate. Recreating extinct species is now realistic, as is engineering entirely new species.<sup>6</sup> CRISPR also creates opportunities to address vector-borne infectious diseases such as malaria, dengue fever, and Zika virus using gene drive techniques that can spread genetic alterations through populations.

These genetic interventions, however, could foster population collapse before triggering the Endangered Species Act (“ESA”)—the cornerstone of U.S. legal efforts to prevent extinction.<sup>7</sup> The statute presumes that extinction is gradual, permanent, and an outcome that humans should generally prevent.<sup>8</sup> Advances in biotechnology challenge each of these conclusions and could circumvent the ESA’s role in species conservation.<sup>9</sup> CRISPR, therefore, could allow scientists to bypass long-standing value choices underlying national and international conservation efforts and foster permanent ecosystem impacts before policymakers can react.

With CRISPR, the critical question is no longer whether humans can alter genes to eradicate some species and make others resilient to factors that may cause extinction. Instead, the questions are whether we should and, if so, under what circumstances. While the potential benefits are profound, CRISPR could also foment similarly profound, and potentially irreversible, negative impacts for the target species

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5. CRISPR, short for “clustered regularly interspaced short palindromic repeats,” utilizes engineered RNA and proteins to edit specific sections of DNA. *Questions and Answers about CRISPR*, BROAD INST., <https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/questions-and-answers-about-crispr> [<https://perma.cc/Q8XQ-5E9M>]. Scientists may use the process to remove targeted DNA or replace the original DNA with new DNA strands to create new traits. *Id.* For a more detailed description of CRISPR, see generally John M. Conley, *Introduction: A Lawyer’s Guide to CRISPR*, 97 N.C. L. REV. 1040 (2019).

6. Kevin M. Esvelt et al., *Emerging Technology: Concerning RNA-Guided Gene Drives for the Alteration of Wild Populations*, 3 ELIFE, no. e03401, July 17, 2014, at 1, 2 (“[S]everal published gene drive architectures could lead to extinction or other hazardous consequences if applied to sensitive species, demonstrating an urgent need for improved methods of controlling these elements.”); see also Amy Dockser Marcus, *Meet the Scientists Bringing Extinct Species Back From the Dead*, WALL ST. J. (Oct. 11, 2018, 6:27 PM), <https://www.wsj.com/articles/meet-the-scientists-bringing-extinct-species-back-from-the-dead-1539093600> [<https://perma.cc/B59C-V6AR> (dark archive)].

7. See Endangered Species Act of 1973, Pub. L. No. 93-205, 87 Stat. 884 (codified as amended at 16 U.S.C. §§ 1531–1544 (2012)).

8. See *infra* Section II.A.

9. See *infra* Section II.A.

and the broader ecosystems in which they exist.<sup>10</sup> Existing laws are not designed to grapple with these important value choices.

Gene editing raises many of the hallmark challenges with emerging technology governance.<sup>11</sup> These recent advances in biotechnology may fall outside the scope of existing regulatory schemes designed for earlier understandings of technologies. They may also require responses by multiple agencies operating under different bodies of law.<sup>12</sup> The pace of scientific developments is occurring much faster than traditional regulation can typically respond.<sup>13</sup> There are calls for flexibility and adaptability to allow the technologies to evolve.<sup>14</sup> Continued research is necessary to develop new, potentially beneficial uses for the technology, but the research also creates unknown risks. The technology is widely accessible, allowing individual research labs to create and release edited organisms with potentially wide-ranging impacts.<sup>15</sup> Nonbinding soft

10. Charleston Noble et al., *Current CRISPR Gene Drive Systems Are Likely to Be Highly Invasive in Wild Populations*, 7 ELIFE, no. e33423, June 19, 2018, at 1, 1.

11. COMM. ON GENE DRIVE RESEARCH IN NON-HUMAN ORGANISMS: RECOMMENDATIONS FOR RESPONSIBLE CONDUCT, NAT'L ACADS. OF SCI., ENG'G, & MED., GENE DRIVES ON THE HORIZON: ADVANCING SCIENCE, NAVIGATING UNCERTAINTY, AND ALIGNING RESEARCH WITH PUBLIC VALUES 149 (2016) [hereinafter GENE DRIVES ON THE HORIZON] (“[D]ifficult questions of [gene drive] governance [arise], e.g., who should make decisions, who should be consulted, who is accountable to whom, and how liability should be handled as a legal matter.”).

12. See, e.g., Igor Linkov et al., *Comparative, Collaborative, and Integrative Risk Governance for Emerging Technologies*, 38 ENV'T SYSTEMS & DECISIONS 170, 171 (2018) (“[A]n innovation often challenges several policy areas that are used to operating in silos, whereas innovation may require more flexible, adaptive, and integrated approaches.”); Gregory N. Mandel & Gary E. Marchant, *The Living Regulatory Challenges of Synthetic Biology*, 100 IOWA L. REV. 155, 162 (2014) (“Regulatory systems, almost always, are designed for technologies existing at the time of the regulatory systems’ formation and are based on the then-current understanding of that technology. Such systems often face difficulty and disruption when applied to newly emerging technologies.”).

13. Rachel Wynberg & Sarah A. Laird, *Fast Science and Sluggish Policy: The Herculean Task of Regulating Biodiscovery*, 36 TRENDS BIOTECHNOLOGY 1, 1 (2018). The Convention on Biological Diversity has only recently settled on a definition for synthetic biology and is still assessing how the convention applies to gene editing. Conference of the Parties to the Convention on Biological Diversity, *Synthetic Biology*, ¶ 4, CBD/COP/DEC/XIII/17 (Dec. 16, 2016), <https://www.cbd.int/doc/decisions/cop-13/cop-13-dec-17-en.pdf> [<https://perma.cc/TCL7-LGD4>] (defining synthetic biology as “a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems”).

14. See, e.g., Linkov et al., *supra* note 12, at 171.

15. See, e.g., Brooke Borel & Quanta, *When Evolution Fights Back Against Genetic Engineering*, ATLANTIC (Sept. 12, 2016), <https://www.theatlantic.com/science/archive/2016/09/gene-drives/499574/> [<https://perma.cc/7J8T-KCYS>] (noting that scientists can now “order the essential biological tools on the internet and build a working gene drive in mere

law measures, such as professional standards and codes of conduct, will play important roles in overseeing research and development of CRISPR-edited organisms. Gene editing implicates diverse and deep-seated values, but engaging a broad range of stakeholders is difficult. Developers seek rapid regulatory approval for releasing new genetically engineered (“GE”) organisms.

Experts continue to debate the proper role of risk as the primary governance criteria, the role of the precautionary principle, and the ethics of intentional eradication of certain species while engaging in de-extinction for others.<sup>16</sup> This Article argues that, while current conservation laws do not directly address many of the specific questions that arise with CRISPR, the ESA framework can, and should, guide the use of gene editing.<sup>17</sup> The ESA affirms the intrinsic value of species conservation, prohibits harming or killing members of protected species, and provides regulatory tools to help species and their habitats recover.<sup>18</sup> Using the ESA as a model for CRISPR governance would not require a blanket prohibition on the use of gene editing when extinction is a possible outcome. There are compelling public health and ecological arguments for using the technique. For example, the ESA exempts pest insects and invasive species,<sup>19</sup> and an ESA-based framework for biotechnology governance could allow exemptions to achieve public health and conservation goals.

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weeks”); Antonio Regalado, *The Extinction Invention*, MIT TECH. REV. (Apr. 13, 2016), <https://www.technologyreview.com/s/601213/the-extinction-invention/> [<https://perma.cc/5AAQ-5SJ8>] (“[W]ith CRISPR, even a two-person team could, in theory, change an entire species.”).

16. See, e.g., GENE DRIVES ON THE HORIZON, *supra* note 11, at 10, 78 (“There is insufficient evidence available at this time to support the release of gene-drive modified organisms into the environment.”); Austin Burt et al., *Open Letter: Research on Gene Drive Technology Can Benefit Conservation and Public Health*, OUTREACH NETWORK FOR GENE DRIVE RES. (Nov. 14, 2018), <https://genedrivenetwork.org/open-letter> [<https://perma.cc/9L85-6WQ7>] (opposing a proposed ban on gene drive research); Richard Conniff, *Should Genetic Engineering Be Used as a Tool for Conservation?*, YALE ENV'T 360 (July 20, 2017), <https://e360.yale.edu/features/should-new-genetic-engineering-be-used-as-a-conservation-tool> [<https://perma.cc/L339-FB55>] (noting concerns about using gene editing for conservation).

17. This Article focuses on domestic biotechnology governance, but it is important to note that critical gaps also exist at the international level. Laboratories across the globe are utilizing the technology and gene-editing developments made in one country that may affect many other countries. See generally Noble et al., *supra* note 10 (describing such developments).

18. See *infra* Section II.A.

19. See *infra* note 76 and accompanying text.

The Article proceeds in three parts. Part I presents three general categories for understanding the interaction between gene editing and species viability: population management, conservation, and broader ecosystem impacts. Part II provides an overview of the key U.S. governance tools that apply to gene editing: the ESA, the Coordinated Framework for Regulation of Biotechnology Governance (“Coordinated Framework”), and nonregulatory measures that guide research and development. Part III proposes steps to incorporate an ESA-based framework into U.S. biotechnology governance. The framework would restrict some uses of gene editing, but it does not stifle continued research, and it targets gene-editing efforts on the most critical public health challenges.

### I. GENE EDITING AND SPECIES VIABILITY

The recent advances in gene-editing techniques allow scientists to create new organisms, modify existing organisms, and eradicate unwanted species. Research is underway to apply these techniques to eliminate disease vectors, control invasive species, expand the genetic pools for endangered species, help species migrate, and recreate extinct species. The range of potential uses for gene editing highlights the governance challenges, as each potential use of gene-editing techniques raises distinct legal, ecological, and ethical issues. This part identifies three broad categories where gene editing and species viability intersect: reducing populations via gene editing, utilizing gene editing as a tool for conservation, and fostering broad ecosystem impacts.

#### A. *Population Management*

According to the World Health Organization, there were approximately 219 million malaria cases and 435,000 malaria deaths in 2017.<sup>20</sup> Dengue fever is a threat for almost half of the world’s population, and “[s]evere dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries.”<sup>21</sup> The same mosquito that transmits dengue can also

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20. *Malaria: Key Facts*, WORLD HEALTH ORG. (Nov. 19, 2018), <http://www.who.int/news-room/fact-sheets/detail/malaria> [https://perma.cc/295A-UKPL].

21. *Dengue and Severe Dengue: Key Facts*, WORLD HEALTH ORG. (Sept. 13, 2018), <http://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue> [https://perma.cc/XEL3-83L8].

transmit the Zika virus.<sup>22</sup> As of 2018, eighty-six countries and territories have reported instances of mosquito-transmitted Zika infection.<sup>23</sup> Malaria is treatable, but the cost of eradication using conventional methods is prohibitive.<sup>24</sup> Treatments do not currently exist for dengue<sup>25</sup> or Zika.<sup>26</sup> The mosquitos are also increasingly resistant to pesticides, complicating population management.<sup>27</sup>

Controlling or eliminating disease vectors via CRISPR is the focus of much early-stage research and offers perhaps the most beneficial use of biotechnology to reduce or eliminate species populations.<sup>28</sup> Population management via gene editing may take different forms. Gene edits may cause sterility in the modified organisms, cause the modified organism to produce only male offspring, or prevent a modified organism's offspring from reaching sexual maturity.<sup>29</sup> Each of these options affect the targeted organisms, and perhaps their immediate offspring, but the genetic modifications do not spread throughout a population. For example, sterile insect techniques that prevent GE organisms or their offspring from reproducing depend upon repeated releases of the modified organism.<sup>30</sup> Such techniques may allow scientists to manage negative

22. *Mosquito Control: Can It Stop Zika at Source?*, WORLD HEALTH ORG., <https://www.who.int/emergencies/zika-virus/articles/mosquito-control/en/> [https://perma.cc/UD3U-LYW5] (last updated Feb. 17, 2019).

23. *Zika Virus: Key Facts*, WORLD HEALTH ORG. (July 20, 2018), <http://www.who.int/news-room/fact-sheets/detail/zika-virus> [https://perma.cc/M6EW-KA49].

24. See Danielle Renwick, *Can Malaria Be Eradicated?*, COUNCIL ON FOREIGN REL. (Oct. 5, 2016), <https://www.cfr.org/backgrounder/can-malaria-be-eradicated> [https://perma.cc/ACH3-HS5G] (citing a Gates Foundation estimate that malaria eradication “would cost between \$90 billion and \$120 billion”).

25. *Dengue and Severe Dengue: Key Facts*, *supra* note 21.

26. *Zika Virus: Key Facts*, *supra* note 23.

27. Zach N. Adelman & Zhijian Tu, *Control of Mosquito-Borne Infectious Diseases: Sex and Gene Drive*, 32 *TRENDS PARASITOLOGY* 219, 219 (2016).

28. GENE DRIVES ON THE HORIZON, *supra* note 11, at 5 (“Some of the fundamental reasons to conduct gene drive research include widely shared commitments to fighting human disease, promoting human welfare, and protecting and restoring the natural environment.”); Andrew Hammond et al., *A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector Anopheles Gambiae*, 34 *NATURE BIOTECHNOLOGY* 78, 78 (2016); see, e.g., Adelman & Tu, *supra* note 27, at 219 (“Given recent breakthroughs in the development of CRISPR-Cas9 reagents as a source of gene drive, more advanced technologies . . . may represent efficient and self-limiting methods to control mosquito populations.”).

29. Adelman & Tu, *supra* note 27, at 219, 222; Nikolay P. Kandul et al., *Transforming Insect Population Control with Precision Guided Sterile Males with Demonstration in Flies*, 10 *NATURE COMM.*, no. 84, Jan. 8, 2019, at 1, 1.

30. Conventional sterile insect techniques rely on radiation to sterilize male pest insects. *Diamondback Moth Project at Cornell University in 2015*, SHELTON LAB (Jun. 17, 2015), <http://shelton.entomology.cornell.edu/2015/06/17/cornell-dbm-project-2015/>

long-term impacts.<sup>31</sup> If the genetic modification is not effective or leads to unanticipated impacts, the next release could be canceled or altered.

Gene drives, by contrast, are genetic alterations intended to spread throughout a population of rapidly reproducing organisms after the initial release.<sup>32</sup> For example, scientists could use a gene drive to spread a genetic alteration through populations of *Aedes aegypti* and *Aedes albopictus* mosquitos (dengue vectors) to prevent generations of mosquitos from transmitting the dengue virus.<sup>33</sup> Gene drives could quickly affect populations far beyond the target area, thus magnifying concerns about irreversible impacts.<sup>34</sup> Research is underway to develop gene drive techniques that are reversible or that phase out over time, but these techniques are still in the experimental phase.<sup>35</sup>

The same gene-editing techniques that could target disease vectors may also control agricultural pests and invasive species.<sup>36</sup> Reducing pest insects could prevent billions of dollars in annual damage to crops and potentially lead to a dramatic reduction in the use of chemical pesticides.<sup>37</sup> Billions of dollars are also spent each

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[<https://perma.cc/8A6K-7VZR>]. The sterilized insects are then released to mate with local females of the same species, preventing offspring. *Id.* “[T]his reduces the pest population over time with multiple releases.” *Id.* Replacing radiation with advanced genetic engineering allows more precise modifications and thus could be more effective than conventional methods. *See id.*

31. *See, e.g.*, Kelly E. Ormond et al., *Human Germline Genome Editing*, 101 AM. J. HUM. ETHICS 167, 169 (2017).

32. *See, e.g.*, GENE DRIVES ON THE HORIZON, *supra* note 11, at 149; Douglas W. Drury et al., *CRISPR/Cas9 Gene Drives in Genetically Variable and Nonrandomly Mating Wild Populations*, 3 SCI. ADVANCES, no. e1601910, May 19, 2017, at 1, 1 (“Gene drives work by segregation distortion or ‘super Mendelian’ inheritance, wherein heterozygous individuals either transmit a desired gene in >90% of their gametes instead of the 50% Mendelian expectation or are transformed into homozygotes.”); Kyros Kyrou et al., *A CRISPR-Cas9 Gene Drive Targeting Doublesex Causes Complete Population Suppression in Caged Anopheles Gambiae Mosquitoes*, 36 NATURE BIOTECHNOLOGY 1062, 1062–66 (2018) (describing a gene drive experiment).

33. GENE DRIVES ON THE HORIZON, *supra* note 11, at 50–52.

34. Kevin M. Esvelt & Neil J. Gemmill, *Conservation Demands Safe Gene Drive*, 15 PLOS BIOLOGY, no. e2003850, Nov. 16, 2017, at 1, 2 (“[Gene] drive systems lack control mechanisms and are consequently highly invasive.”); Noble et al., *supra* note 10, at 1.

35. *See, e.g.*, John M. Marshall & Omar S. Akbari, *Can CRISPR-Based Gene Drive Be Confined in the Wild? A Question for Molecular and Population Biology*, 13 ACS CHEMICAL BIOLOGY 424, 424 (2018); Kevin M. Esvelt, *Daisy Drive Systems*, SCULPTING EVOLUTION, <http://www.sculptingevolution.org/daisydrives> [<https://perma.cc/327R-FSE2>] (describing daisy drive systems).

36. Raul F. Medina, *Gene Drives and the Management of Agricultural Pests*, 5 J. RESPONSIBLE INNOVATION S255, S256–57 (2017).

37. Brooke Borel, *When the Pesticides Run Out*, 543 NATURE 302, 303–04 (2017).

year to control invasive species in the United States.<sup>38</sup> An interagency effort is underway to evaluate the role of biotechnology in invasive species management.<sup>39</sup> A 2017 Invasive Species Advisory Committee report identified the following examples of advanced biotechnology applications for managing invasive species: utilizing the sterile insect technique to address insects such as a mosquito species endangering Hawaiian birds; releasing GE insects that are unable to carry diseases; modifying native species to make them more resistant to nonnative diseases; and enhancing crops to help them resist insect pests.<sup>40</sup>

Gene editing could also target a wide range of insects, plants, and animals that are not disease vectors, agricultural pests, or invasive species.<sup>41</sup> There is a lucrative pest control industry in the United States.<sup>42</sup> Without regulatory limitations, the same techniques used to control harmful organisms could also target pests that are nuisances to humans, livestock, or landscaping but do not pose infectious disease concerns. This potentially expansive use of gene editing highlights the need for deliberate, early, and effective guidance on the various potential uses of CRISPR.

### B. Conservation

The Earth is in the midst of the sixth mass extinction and the first that is caused primarily by human activity.<sup>43</sup> The rapid pace of climate

38. U.S. FISH & WILDLIFE SERV., THE COST OF INVASIVE SPECIES 1 (2012), <https://www.fws.gov/verobeach/pythonpdf/costofinvasivesfactsheet.pdf> [<https://perma.cc/M7PU-92YB>]; see also R. ELIOT CRAFTON & SAHAR ANGADJIVAND, CONG. RES. SERV., IF11011, INVASIVE SPECIES: A BRIEF OVERVIEW 2 (2018).

39. Nat'l Invasive Species Council, *Technology Innovation*, U.S. DEP'T INTERIOR, <https://www.doi.gov/invasivespecies/technology-innovation> [<https://perma.cc/5CZD-UMVW>].

40. INVASIVE SPECIES ADVISORY COMM., U.S. DEP'T OF THE INTERIOR, ADVANCED BIOTECHNOLOGY TOOLS FOR INVASIVE SPECIES MANAGEMENT 1–2 (2017), [https://edit.doi.gov/sites/doi.gov/files/uploads/isac\\_advanced\\_biotechnology\\_white\\_paper.pdf](https://edit.doi.gov/sites/doi.gov/files/uploads/isac_advanced_biotechnology_white_paper.pdf) [<https://perma.cc/9522-ZQB7>].

41. Jonas J. Monast, *Editing Nature: Reconceptualizing Biotechnology Governance*, 59 B.C. L. REV. 2377, 2400 (2018).

42. *Id.*

43. Wolfgang Cramer et al., *Detection and Attribution of Observed Impacts*, in CLIMATE CHANGE 2014: IMPACTS, ADAPTATION, AND VULNERABILITY PART A: GLOBAL AND SECTORAL ASPECTS 979, 990 (Christopher B. Field et al. eds., 2014), [https://ipcc.ch/site/assets/uploads/2018/02/WGIIAR5-PartA\\_FINAL.pdf](https://ipcc.ch/site/assets/uploads/2018/02/WGIIAR5-PartA_FINAL.pdf) [<https://perma.cc/SWY2-5LK7>] (“Across the world, species extinctions are at or above the highest rates of species extinction in the fossil record.”); Gerardo Ceballos, Paul R. Ehrlich & Rodolfo Dirzo, *Biological Annihilation via the Ongoing Sixth Mass Extinction Signaled by Vertebrate Population Losses and Declines*, 114 PNAS E6089, E6095 (2017); Ian Johnston, *Humans are Ushering in the Sixth Mass Extinction of Life on Earth, Scientists Warn*, INDEPENDENT (May 31, 2017, 17:00),

change will likely exacerbate the pace of extinction by creating additional habitat pressures for some threatened species and placing many others at risk. Species most at risk are those that have limited range, require a unique habitat, and have a low population density.<sup>44</sup>

Biotechnology could provide a potential solution for some of these conservation challenges. In some instances, changing the genetic code of threatened or endangered species may expand suitable habitats by changing reactions to temperature or increasing resistance to diseases.<sup>45</sup> Gene editing may also bolster recovery efforts for species that experience a significant drop in population and thus have a limited genetic pool.<sup>46</sup>

Invasive species management also has implications for conservation.<sup>47</sup> Nonnative rodents, pigs, snakes, plants, and microbes have caused population collapses and forced displacement of native species.<sup>48</sup> However, the link between invasive species management and conservation is not cut and dry. For example, established invasive species may replace the ecological function of native species.<sup>49</sup> Climate change will further complicate the distinction between native and invasive species as habitats change and species migrate.

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extinction-humans-causing-earth-deaths-end-times-warning-a7765856.html [https://perma.cc/6RUB-LHK7].

44. Habiba Gitay et al., *Ecosystems and Their Goods and Services*, in CLIMATE CHANGE 2001: IMPACTS, ADAPTION, AND VULNERABILITY 235, 271 (James J. McCarthy et al. eds., 2001), [https://ipcc.ch/site/assets/uploads/2018/03/WGII\\_TAR\\_full\\_report-2.pdf](https://ipcc.ch/site/assets/uploads/2018/03/WGII_TAR_full_report-2.pdf) [https://perma.cc/B9VZ-UKAB].

45. Megan A. Supple & Beth Shapiro, *Conservation of Biodiversity in the Genomics Era*, 19 GENOME BIOLOGY, no. 131, Sept. 11, 2018, 1, 9–10.

46. Jeff A. Johnson et al., *Is There a Future for Genome-Editing Technologies in Conservation?*, 19 ANIMAL CONSERVATION 97, 98 (2016). For example, scientists are exploring the use of CRISPR to make cacao trees more resistant to fungi and viruses. Laura Geggel, *Can Gene Editing Save the World's Chocolate?*, SCI. AM. (Jan. 5, 2018), <https://www.scientificamerican.com/article/can-gene-editing-save-the-worlds-chocolate/> [https://perma.cc/3L5K-FWJ4].

47. Karl J. Campbell et al., *The Next Generation of Rodent Eradications: Innovative Technologies and Tools to Improve Species Specificity and Increase Their Feasibility on Islands*, 185 BIOLOGICAL CONSERVATION 47, 51 (2015) (noting the potential for CRISPR-enabled gene drives to control invasive rodents); Antonio Regalado, *First Gene Drive in Mammals Could Aid Vast New Zealand Eradication Plan*, MIT TECH. REV. (Feb. 10, 2017), <https://www.technologyreview.com/s/603533/first-gene-drive-in-mammals-could-aid-vast-new-zealand-eradication-plan/> [https://perma.cc/X463-5K7F].

48. Jessica Gurevitch & Dianna K. Padilla, *Are Invasive Species a Major Cause of Extinctions?*, 19 TRENDS ECOLOGY & EVOLUTION 470, 470 (2004); see also *Invasive Species: Endangered Species Program*, U.S. FISH & WILDLIFE SERV., <https://www.fws.gov/invasives/endangered-species.html> [https://perma.cc/DER3-E2EQ].

49. Medina, *supra* note 36, at S257.

De-extinction is another conservation-focused use for gene-editing technologies.<sup>50</sup> CRISPR allows scientists to alter the DNA of living organisms to give their offspring traits of extinct species. For example, efforts are underway to alter the DNA of band-tailed pigeons to create offspring resembling extinct passenger pigeons.<sup>51</sup> The result is a hybrid species rather than an exact replica of the extinct species, and the process raises a host of ethical questions regarding the purpose of de-extinction, obligations to reintroduced organisms, and implications for species conservation generally.<sup>52</sup> As Professor Alejandro Camacho notes, reintroducing extinct species could bolster ecosystem health by restoring an organism that plays a particularly important role in the local ecosystem, or the process could hamper conservation efforts by imposing new costs and risks.<sup>53</sup>

### C. *Broader Ecosystem Impacts*

The previous two sections discuss changes targeted at particular organisms and locations. Gene editing may also foster broader ecosystem impacts since altering individual organisms may also alter the ecosystems in which they live.<sup>54</sup> Some ecosystem changes may be deliberate, such as increasing a species's resilience to climate change.<sup>55</sup> Gene editing could also lead to unintentional ecosystem impacts, such as allowing new species to outcompete native organisms.<sup>56</sup> Gene editing could therefore cause invasive species

50. Alejandro E. Camacho, *Going the Way of the Dodo: De-Extinction, Dualisms, and Reframing Conservation*, 92 WASH. U. L. REV. 849, 858 (2015).

51. *De-Extinction Defined*, REVIVE & RESTORE, <https://reviverestore.org/passenger-pigeon-de-extinction/> [<https://perma.cc/N763-N5HJ>].

52. See Gregory E. Kaebnick & Bruce Jennings, *De-extinction and Conservation*, HASTINGS CTR. REP., July–Aug. 2017, at S2, S3–S4 (discussing the ethical considerations presented by de-extinction).

53. Camacho, *supra* note 50, at 856–59; see also Norman C. Ellstrand et al., *Got Hybridization? A Multidisciplinary Approach for Informing Science Policy*, 60 BIOSCIENCE 384, 385 (2010) (“[H]ybridization with the introduced mallard is the major conservation problem facing the endangered Hawaiian duck, and has led to its probable extirpation on the islands of Oahu and Hawaii.”).

54. James E. DiCarlo et al., *Safeguarding CRISPR-Cas9 Gene Drives in Yeast*, 33 NATURE BIOTECHNOLOGY 1250, 1250 (2015) (noting that gene drives create the risk that “unintended genome editing occurring through the escape of strains from laboratories, coupled with the prospect of unanticipated ecological change, demands caution”).

55. See, e.g., Rachel A. Levin et al., *Engineering Strategies to Decode and Enhance the Genomes of Coral Symbionts*, 8 FRONTIERS MICROBIOLOGY, no. 1220, June 30, 2017, at 1, 2.

56. GENE DRIVES ON THE HORIZON, *supra* note 11, at 5 (“[U]sing a gene drive to suppress a non-native weed population may lead to unexpected consequences, such as the loss of habitat for native species or even the establishment of a second, more resilient invasive species.”); Kent H. Redford, William Adams & Georgina M. Mace, *Synthetic*

challenges in some areas, even as the technique helps eradicate invasive species in others.<sup>57</sup>

The extent to which gene drives would have lasting impacts on target populations or ecosystems remains unclear. For example, a 2018 study evaluating the potential ecosystem impacts of eradicating the *Anopheles gambiae* mosquito—one of the primary vectors responsible for spreading malaria in Africa—concluded that there are no ecosystem functions that are unique to the species.<sup>58</sup> According to one of the authors of the study, there are traits of the species that limit its role in ecosystem viability.<sup>59</sup>

These results are encouraging for infectious disease control, but they also point to the importance of rigorous analysis for each potential use of gene drives. Other mosquito species may play more important roles in their respective ecosystems, but U.S. law does not limit gene drives to mosquito species that carry critical infectious diseases.<sup>60</sup> There is a lucrative pest control industry in the United States.<sup>61</sup> Without regulatory limitations, the temptation may be too great to deploy gene drives to manage pests that are nuisances to humans, livestock, or landscaping but do not pose infectious disease concerns. This result may not be a cause of concern, and may even be desirable, but actions where extinction is a likely outcome should not be governed by the market alone. Lawmakers should establish safeguards requiring rigorous studies of potential impacts, similar to the work currently underway to assess the use of gene drives to target mosquito-borne diseases.<sup>62</sup> Society needs access to information that allows informed opinions about the technology and meaningful opportunities to influence governance choices.

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*Biology and Conservation of Nature: Wicked Problems and Wicked Solutions*, 11 PLOS BIOLOGY, no. e1001530, Apr. 2, 2013, at 1, 2 tbl.1.

57. Redford et al., *supra* note 56, at 2 tbl.1 (noting that genetically modified organisms “may promote invasive capabilities (or novel organisms may be invasive)”).

58. C. M. Collins et al., *Effects of the Removal or Reduction in Density of the Malaria Mosquito, Anopheles gambiae s.l., on Interacting Predators and Competitors in Local Ecosystems*, 33 MED. & VETERINARY ENTOMOLOGY 1, 10–11 (2018).

59. Hayley Dunning, *Removing Malaria-Carrying Mosquitoes Unlikely to Affect Ecosystems, Says Report*, IMPERIAL C. LONDON (July 26, 2018), <https://www.imperial.ac.uk/news/187427/removing-malariacarrying-mosquitoes-unlikely-affect-ecosystems/> [https://perma.cc/9R6M-66NB] (“As adults, *An. gambiae* mosquitoes are small, hard to catch, most mobile at night and not very juicy, so they are not a rewarding prey for both insect and vertebrate predators. Many do eat them -- sometimes accidentally -- but there is no evidence that they are a big or vital part of the diet of any other animal.”).

60. *See infra* Section II.B.

61. *Pest Management Industry Fact Sheet*, NAT’L PEST MGMT. ASS’N, <https://npmapestworld.org/newsroom/industry-fact-sheet/> [https://perma.cc/J562-GA7K].

62. *See* Noble et al., *supra* note 10, at 2.

Researchers are utilizing computer models to evaluate the likelihood of a gene drive spreading throughout a population.<sup>63</sup> Perhaps predictably at the early stage of CRISPR-enabled gene drives, the models are producing conflicting projections. For example, recent analysis by leading scientists involved in developing gene drive techniques suggests that gene drives released into wild populations could quickly spread well beyond the target area.<sup>64</sup> Another study released around the same time reaches a starkly different conclusion, projecting that resistance to the gene drive would “evolve almost inevitably in most natural populations” unless there are further interventions.<sup>65</sup>

The rapid spread of gene drives could be beneficial or harmful depending on the goals of the biotechnology efforts. Rapid spread could also contribute to disease eradication efforts, for example. Alternatively, it could undermine efforts to control invasive species in some areas without affecting the target species’s viability. The divergent potential outcomes are a fundamental challenge for scientists developing gene drive mechanisms and government officials considering whether to approve the use of gene drives. The actual impacts of a gene drive will not be certain until field trials take place, a point at which it may be difficult or impossible to reverse unintended results.<sup>66</sup>

## II. GOVERNING THE ECOLOGICAL IMPACTS OF GENE EDITING

Current U.S. law governing biotechnology generally focuses on risk to humans and agriculture rather than broader ecosystem

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63. See, e.g., *id.* (presenting results of a mathematical model exploring the potential spread of gene drives); see also Philip A. Eckhoff et al., *Impact of Mosquito Gene Drive on Malaria Elimination in a Computational Model with Explicit Spatial and Temporal Dynamics*, 114 PNAS E255, E255 (2017) (presenting results of a “mathematical model to simulate . . . gene drive approach[es] in a variety of sub-Saharan African settings”).

64. Noble et al., *supra* note 10, at 2.

65. Robert L. Unckless, Andrew G. Clark & Philipp W. Messer, *Evolution of Resistance Against CRISPR/Cas9 Gene Drive*, 205 GENETICS 827, 827 (2017). There are additional risks beyond the potential for rapid population collapse of the targeted species. Gene drives could impact nontargeted organisms via cross-breeding or lateral gene transfer. Kenneth A. Oye et al., *Regulating Gene Drives*, 345 SCIENCE 626, 626–27 (2014). Lateral gene transfer refers to “transmission of DNA . . . between different genomes.” Kara Rogers, *Horizontal Gene Transfer*, ENCYCLOPAEDIA BRITANNICA, <https://www.britannica.com/science/horizontal-gene-transfer> [https://perma.cc/QJ7Q-X726] (last updated Nov. 30, 2018).

66. See, e.g., Borel & Quanta, *supra* note 15 (noting that scientists are relying on computer modeling to assess gene drive impacts because they “have no experience engineering systems that are going to evolve outside of our control”).

impacts.<sup>67</sup> CRISPR, however, requires a broader approach to address the scope of potential uses for the technology.<sup>68</sup> The technology is a relatively recent breakthrough, and scientists are still discovering its expansive possibilities.<sup>69</sup> The technology promises profound societal benefits, including the disease eradication and conservation efforts described in Part I. It also places tremendous power in the hands of the scientists working with CRISPR.<sup>70</sup> Whether or not the technology delivers upon its promise, however, is up in the air. Current laws were not designed to address the fundamental questions regarding when and how humans should use genetics to redesign ecosystems.

The uncertainty about CRISPR's impacts, combined with the relatively low cost, simplicity, and precision of the technology, bring biotechnology governance questions into sharp relief. For example, when is it appropriate to use gene editing to reduce species populations or foster extinction? When is de-extinction or species enhancement appropriate? What governance standards apply? How do distinctions between native versus nonnative or natural versus nonnatural apply to gene-edited organisms? What is the proper role of government regulation versus nonbinding soft law governance?

The United States does not have a consistent approach when it comes to species preservation and eradication. On the one hand, Congress has enacted numerous laws aimed at preventing extinction domestically and internationally.<sup>71</sup> On the other hand, federal and state policies encourage management of disease-carrying insects, invasive species, and insects and animals that harm crops and

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67. See *infra* Section II.B.

68. Monast, *supra* note 41, at 2381–82 (advocating for a broader approach to biotechnology governance that balances competing societal values).

69. Jennifer Doudna and Emmanuelle Charpentier coauthored a seminal paper in 2012 about CRISPR and gene editing. For a review of that paper, see generally Martin Jinek et al., *A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 *SCIENCE* 816 (2012).

70. See, e.g., Michael Specter, *Rewriting the Code of Life*, *NEW YORKER*, Jan. 2, 2017, at 34 (quoting MIT professor Kevin Esvelt as telling an audience that “as a single scientist, I can alter an organism in a laboratory that will have more of an effect on all your lives than anything the [Massachusetts] legislature . . . can do”).

71. See, e.g., Migratory Bird Treaty Act, 16 U.S.C. § 703(a) (2012); Endangered Species Act, 16 U.S.C. § 1531(a)(3) (2012) (recognizing that threatened or endangered “species of fish, wildlife, and plants are of esthetic, ecological, educational, historical, recreational, and scientific value to the Nation and its people”); African Elephant Conservation Act, 16 U.S.C. §§ 4201–4203 (2012) (supporting elephant conservation programs); Wild Exotic Bird Conservation Act, 16 U.S.C. § 4902 (2012) (restricting international trade of exotic birds and encouraging conservation programs); Rhinoceros and Tiger Conservation Act, 16 U.S.C. § 5302 (2012) (supporting conservation of rhinoceros and tigers).

livestock.<sup>72</sup> Although this approach endorses efforts to eradicate harmful organisms, it does not endorse species extinction. The laws were enacted long before the development of modern gene-editing techniques.<sup>73</sup> The prospect of widescale impacts and the conflicting approaches to species eradication leave federal regulators without proper guidance for forthcoming proposals to release gene-edited organisms.<sup>74</sup>

This part describes two key sources of biotechnology and conservation governance: the ESA and the Coordinated Framework. Together, this collection of law and implementing regulations create the default approach for overseeing the intersection of gene editing and species viability in the United States.

#### A. *Endangered Species Act*

The ESA is the cornerstone of U.S. legal measures to prevent extinction and establishes the principle that plant and animal species have “esthetic, ecological, educational, historical, recreational, and scientific value to the Nation and its people.”<sup>75</sup> With the exception of pest insects and invasive species, the statute creates a legal regime to protect individual members of a vulnerable species and includes an expansive list of prohibited actions involving a member of a protected species.<sup>76</sup> Private landowners may face restrictions on the use of property that is designated as a “critical habitat” for a protected species.<sup>77</sup> Federal agencies whose actions may impact listed species

72. See, e.g., Plant Protection Act, 7 U.S.C. § 7701 (2012).

73. For example, the ESA was first enacted by Congress in 1973. Endangered Species Act of 1973, Pub. L. No. 93-205, 87 Stat. 884 (codified as amended at 16 U.S.C. §§ 1531–1544 (2012)).

74. See, e.g., INVASIVE SPECIES ADVISORY COMM., *supra* note 40, at 3 (“[I]nvasive species applications represent a divergence from the types of products and private sector applicants with which the regulatory agencies have traditionally dealt.”).

75. § 1531(a)(3); U.S. DEP’T OF AGRIC., PROPOSAL TO PERMIT THE FIELD RELEASE OF GENETICALLY ENGINEERED DIAMONDBACK MOTH IN NEW YORK: ENVIRONMENTAL ASSESSMENT, JUNE 2017, at 69 (2017) (“[The ESA] is one of the most far-reaching wildlife conservation laws ever enacted by any nation.”).

76. 16 U.S.C. § 1538(a) (2012) (prohibiting the “tak[ing]” of an endangered species). The ESA defines “take” as including the following actions: “harass, harm, pursue, hunt, shoot, wound, kill, trap, capture, or collect, or to attempt to engage in any such conduct.” *Id.* § 1532(19); see also *id.* § 1532(6) (exempting from the definition of “endangered species” any “species of the Class Insecta determined by the Secretary to constitute a pest whose protection under the provisions of this [Act] would present an overwhelming and overriding risk to man”). The law defines “endangered species” as one “in danger of extinction throughout all or a significant portion of its range.” *Id.* A “threatened species” is “likely to become an endangered species within the foreseeable future throughout all or a significant portion of its range.” *Id.* § 1532(20).

77. See *id.* § 1533(a)(3)(A)(i).

must consult with the United States Fish and Wildlife Service (“FWS”) or National Marine Fisheries Service (“NMFS”) to determine whether the actions may proceed.<sup>78</sup> Violations of the ESA may result in civil and criminal penalties.<sup>79</sup>

At this stage, it is unclear the extent to which the ESA will influence the deployment of gene editing. Some of the uncertainty rests with questions about the viability of the ESA itself. The ESA is perennially controversial due primarily to land use restrictions necessary to protect critical habitats and the costs associated with limiting economic activity when a protected species is present.<sup>80</sup> To date, the ESA has weathered repeated congressional efforts to repeal or weaken the law,<sup>81</sup> but the Trump administration may succeed in restricting the reach of the ESA where past efforts have failed.<sup>82</sup> In July 2018, the Department of Commerce proposed regulatory changes to allow agencies to consider the economic impacts of listing a species as threatened or endangered.<sup>83</sup> If implemented, the new regulations would significantly restrict the reach of the ESA and could potentially favor the use of genetic engineering for population management if doing so were more cost effective than other measures.<sup>84</sup>

Challenges to the ESA extend beyond current regulatory proposals. The FWS and NMFS consistently face long backlogs of

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78. *See id.* § 1536(a)(2); *see also* Nat. Res. Def. Council v. Houston, 146 F.3d 1118, 1125 (9th Cir. 1998) (noting that the NMFS is, along with the FWS, a service that an agency may be required to coordinate with under § 1536(a)(2)).

79. 16 U.S.C. § 1540(a)–(b) (2012).

80. *See, e.g.*, PERVAZE A. SHEIKH ET AL., CONG. RESEARCH SERV., RL33309, REAUTHORIZATION OF THE ENDANGERED SPECIES ACT (ESA): A COMPARISON OF PENDING BILLS AND A PROPOSED AMENDMENT WITH CURRENT LAW 1 (2006).

81. *See, e.g., id.* at 3–4 (describing three bills introduced in 2006 to amend ESA implementation); *see also* M. LYNNE CORN & KRISTINA ALEXANDER, CONG. RESEARCH SERV., R42945, THE ENDANGERED SPECIES ACT (ESA) IN THE 113TH CONGRESS: NEW AND RECURRING ISSUES 17–18 (2014) (describing proposed amendments to the ESA during the 113th Congress).

82. Lisa Friedman, Kendra Pierre-Louis & Livia Albeck-Ripka, *Law That Saved the Bald Eagle Could Be Vastly Reworked*, N.Y. TIMES (July 19, 2018), <https://www.nytimes.com/2018/07/19/climate/endangered-species-act-changes.html> [<https://perma.cc/H6UM-RCL5> (dark archive)] (referring to the Trump administration’s proposal as “the most sweeping set of changes in decades to the Endangered Species Act”).

83. Endangered and Threatened Wildlife and Plants; Revision of the Regulations for Listing Species and Designating Critical Habitat, 83 Fed. Reg. 35,193, 35,194–95 (proposed July 25, 2018) (to be codified at 50 C.F.R. pt. 424).

84. *See id.*; *see also* *ESA Implementation: Regulation Revisions*, U.S. FISH & WILDLIFE SERV., [https://www.fws.gov/endangered/improving\\_ESA/regulation-revisions.html](https://www.fws.gov/endangered/improving_ESA/regulation-revisions.html) [<https://perma.cc/XX8A-R3SA>] (last updated Aug. 14, 2018).

species awaiting a listing determination.<sup>85</sup> Furthermore, ESA protections are not automatic. In order for the ESA to apply, the FWS or NMFS must determine whether the species is threatened or endangered and, if so, how to respond.<sup>86</sup> The agencies have discretion when deciding whether listing is appropriate.<sup>87</sup> Government officials may also conclude that listing is warranted but delay the decision if listing would interfere with the agency's ability to protect other priority species.<sup>88</sup>

It is not clear how federal agencies will apply this discretion when considering a genetically modified organism. The statute does not specify how similar genetic codes of protected and modified species must be in order for protections to apply to both.<sup>89</sup> It does, however, allow protections to extend to species that “closely resemble[] in appearance, at the point in question, a species which has been listed pursuant to such section that enforcement personnel would have substantial difficulty in attempting to differentiate between the listed and unlisted species.”<sup>90</sup> The law also includes provisions for protecting “experimental populations,” such as a species that has recovered via captive breeding and is subsequently released into the wild.<sup>91</sup>

Other questions about the ESA's application to GE organisms arise because Congress implemented the ESA before the recent advances in biotechnology and thus did not contemplate the use of genetic engineering to drive species to extinction. First, the law does not apply prospectively. The listing process only becomes an option after the population collapse is underway.<sup>92</sup> Deliberate steps to initiate population collapse via a gene drive, therefore, would not trigger ESA protections until the gene drive spread throughout a population.

Second, the law presumes that extinction is gradual, allowing federal regulators time to engage in a lengthy regulatory process of

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85. Oliver A. Houck, *The Endangered Species Act and Its Implementation by the U.S. Departments of Interior and Commerce*, 64 U. COLO. L. REV. 277, 280–81 (1993).

86. 16 U.S.C. § 1533(a)–(b) (2012).

87. *Id.* § 1533(a)(2)(A)–(C) (noting the agency discretion in the listing process).

88. *See id.* § 1533(b)(3)(B)(iii); *see also* 50 C.F.R. §§ 424.14(a)–(b), (c)(3), 424.10 (2018) (“The Secretary may . . . change the listed status of a species . . .”).

89. *See* Norman F. Carlin, Ilan Wurman & Tamara Zakim, *How to Permit Your Mammoth: Some Legal Implications of “De-Extinction,”* 33 STAN. ENVTL. L.J. 3, 22 (2013).

90. 16 U.S.C. § 1533(e)(A) (2012).

91. 50 C.F.R. § 17.81(a) (2018).

92. *See* 16 U.S.C. § 1533(a)(1)–(2) (2012) (listing factors for determining whether a species is threatened or endangered).

studying the threats to the species, formally listing the species as threatened or endangered, and implementing protections.<sup>93</sup> Gene drives could initiate rapid population collapses before the completion of the listing process. Not only would the ESA fail to prohibit the initial release of the gene drive, but federal officials may also be unable to respond, even if they are able to complete the listing process, if the threat to the species is a genetic trait explicitly designed to spread through the population.<sup>94</sup>

Third, the ESA presumes that habitat is static and that protected habitat should focus on a species's native range.<sup>95</sup> Habitat loss is the dominant threat for many vulnerable species,<sup>96</sup> and the problem will only get worse as the impacts of climate change take root. Some flora and fauna will migrate as temperatures rise.<sup>97</sup> Species that are unable to migrate, or that depend on a particular type of habitat that is no longer available, will perish unless there are new interventions.<sup>98</sup> Even in the absence of gene editing, dynamic habitat changes will exacerbate regulatory and political pressures on ESA habitat protections.<sup>99</sup> Genetically altering species could exacerbate the legal, ecological, and social challenges if the changes help a species migrate.

#### B. *The Coordinated Framework for Regulation of Biotechnology*

Due to the limited reach of the ESA, federal regulators depend on existing statutes focused on human health, pest management, and environmental impacts to address the intersection of conservation

93. *Id.* § 1533(b)(1)(A) (“The Secretary shall make [listing] determinations . . . solely on the basis of the best scientific and commercial data available to him after conducting a review of the status of the species and after taking into account those efforts, if any, being made by any State or foreign nation, or any political subdivision of a State or foreign nation, to protect such species, whether by predator control, protection of habitat and food supply, or other conservation practices, within any area under its jurisdiction; or on the high seas.”).

94. Monast, *supra* note 41, at 2409; *see also* Noble et al., *supra* note 10, at 2 (discussing the likelihood that gene drives would spread wild populations).

95. Camacho, *supra* note 50, at 870–71, 885. The native versus nonnative distinction frequently appears in wildlife management laws. *Id.* at 892.

96. Patrick Parenteau, *Rearranging the Deck Chairs: Endangered Species Act Reforms in an Era of Mass Extinction*, 22 WM. & MARY ENVTL. L. & POL’Y REV. 227, 233 (1998).

97. Craig Welch, *Half of All Species Are on the Move—And We’re Feeling It*, NAT’L GEOGRAPHIC (Apr. 27, 2017), <https://news.nationalgeographic.com/2017/04/climate-change-species-migration-disease/> [<https://perma.cc/B9WD-X4LC>]; *see also* Ben A. Minteer & James P. Collins, *Move It or Lose It? The Ecological Ethics of Relocating Species Under Climate Change*, 20 ECOLOGICAL APPLICATIONS 1801, 1801 (2010).

98. J.B. Ruhl, *Climate Change and the Endangered Species Act: Building Bridges to the No-Analog Future*, 88 B.U. L. REV. 1, 23–24 (2008).

99. *See id.* at 27–29.

and gene editing. The Coordinated Framework divides primary jurisdiction over nonhuman uses of biotechnology among three agencies: the Food and Drug Administration (“FDA”), the United States Department of Agriculture (“USDA”), and the Environmental Protection Agency (“EPA”).<sup>100</sup> The FDA regulates animal drugs and foods derived from plants and oversees genetic engineering aimed at controlling infectious diseases.<sup>101</sup> The USDA’s jurisdiction centers on animal and plant pests.<sup>102</sup> GE animals are subject to USDA regulation if they present a risk to livestock health.<sup>103</sup> GE insects may also be subject to USDA oversight if there is a risk the insects could spread livestock diseases, affect crops, or spread noxious weeds.<sup>104</sup> The EPA’s role in biotechnology governance focuses primarily on pesticides and toxic materials.<sup>105</sup>

The Coordinated Framework does not provide a comprehensive system for responding to potential ecological impacts of GE organisms.<sup>106</sup> Because the primary statutes informing biotechnology governance do not directly address ecological considerations, the agencies rely primarily on the National Environmental Policy Act (“NEPA”) to assess the environmental impacts of major federal actions.<sup>107</sup> NEPA serves an important function by requiring entities to

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100. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302, 23,302 (June 26, 1986); OFFICE OF SCI. & TECH. POL’Y, EXEC. OFFICE OF THE PRESIDENT, MODERNIZING THE REGULATORY SYSTEM FOR BIOTECHNOLOGY PRODUCTS: FINAL VERSION OF THE 2017 UPDATE TO THE COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY 1 (2017), [https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/2017\\_coordinated\\_framework\\_update.pdf](https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/2017_coordinated_framework_update.pdf) [https://perma.cc/B5W3-6WWY].

101. The Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 343(s)(2)(C), 360(b) (2012); The Public Health Service Act, 42 U.S.C. § 262(a), (i)(1) (2012 & Supp. 2017); OFFICE OF SCI. & TECH. POL’Y, *supra* note 100, at 9, tbl.1.

102. *See* The Plant Protection Act, 7 U.S.C. § 7701(2) (2012); The Animal Health Protection Act, 7 U.S.C. §§ 8302(14), 8304 (2012 & Supp. 2017). Other statutes granting the USDA jurisdiction over aspects of genetic engineering include the Federal Meat Inspection Act, 21 U.S.C. § 601(a) (2012) (defining secretary); *id.* § 602, and the Poultry Products Inspection Act, *id.* § 451.

103. *See* 7 U.S.C. § 8303 (2012).

104. *Id.* §§ 8302–8303, 8305 (2012 & Supp. 2017) (animal health protection); *see also id.* § 7701 (2012) (finding the “detection, control, eradication” and prevention of the “spread of plant pests or noxious weeds is necessary for the protection of the agriculture, environment, and economy of the United States”).

105. *See* The Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. § 136a (2012); The Toxic Substances Control Act, 15 U.S.C. §§ 2601–2629 (2012 & Supp. 2017).

106. Monast, *supra* note 41, at 2389–91, 2411.

107. *See* The National Environmental Policy Act, 42 U.S.C. § 4332(C) (2012); OFFICE OF SCI. & TECH. POL’Y, *supra* note 100, at 21–22 (stating that both the USDA and FDA still comply with NEPA requirements when they are applicable). NEPA only applies when

collect data, evaluate potential environmental impacts, and provide the public with an opportunity to submit comments prior to issuing a final decision.<sup>108</sup> The uncertainty presented by gene editing is precisely the type of question that calls for the thorough investigation required by NEPA. The statute, however, is procedural.<sup>109</sup> Agencies must evaluate the potential environmental impacts and justify why they choose a particular course of action, but NEPA does not require agencies to choose a particular course of action based on the environmental impacts identified by the analysis.<sup>110</sup>

In 2016, the FDA and USDA each approved field trials for GE insects designed to manage local populations.<sup>111</sup> The FDA considered the release of genetically modified *Aedes aegypti* mosquitoes—the subspecies that carry Zika and dengue—on the island of Key Haven, Florida.<sup>112</sup> The USDA considered the release of a genetically modified diamondback gypsy moth—a species that creates billion-dollar damages to crops—at a test site in New York.<sup>113</sup> In both instances, the genetic modification causes offspring of modified male insects to die before reaching sexual maturity.<sup>114</sup> This biological containment distinguishes the modified mosquitoes and moths at

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a “major Federal action[.]” has the potential to “significantly” impact the environment. 42 U.S.C. § 4332(C)(i)–(v) (2012).

108. See OFFICE OF SCI. & TECH. POL’Y, *supra* note 100, at 22–23; see also Victor B. Flatt, *The “Worst Case” May Be the Best: Rethinking NEPA Law to Avoid Future Environmental Disasters*, 6 ENVTL. & ENERGY L. & POL’Y J. 25, 32–36 (2011) (describing the requirements of an environmental impact study under NEPA).

109. See 42 U.S.C. § 4332(C); Flatt, *supra* note 108, at 32.

110. 42 U.S.C. § 4332(C).

111. See FDA, FINDING OF NO SIGNIFICANT IMPACT (FONSI) IN SUPPORT OF A PROPOSED FIELD TRIAL OF GENETICALLY ENGINEERED (GE) MALE *Aedes aegypti* MOSQUITOES OF THE LINE OX513A IN KEY HAVEN, MONROE COUNTY, FLORIDA UNDER AN INVESTIGATIONAL NEW ANIMAL DRUG EXEMPTION 8 (2016) [hereinafter FDA FONSI], <https://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM514699.pdf> [https://perma.cc/W9DT-Q7Z6]; U.S. DEPT. OF AGRIC., PROPOSAL TO PERMIT THE FIELD RELEASE OF GENETICALLY-ENGINEERED DIAMONDBACK MOTH IN NEW YORK: ENVIRONMENTAL ASSESSMENT, DECEMBER 2016, at 1 (2016) [hereinafter DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT], [https://www.aphis.usda.gov/brs/aphisdocs/16\\_076101r\\_pea.pdf](https://www.aphis.usda.gov/brs/aphisdocs/16_076101r_pea.pdf) [https://perma.cc/4K9L-C2W5].

112. FDA, ENVIRONMENTAL ASSESSMENT FOR INVESTIGATIONAL USE OF *Aedes aegypti* OX513A, at 18–19 (2016) [hereinafter FDA MOSQUITO ENVIRONMENTAL ASSESSMENT], <https://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM514698.pdf> [https://perma.cc/B5FC-LFA8].

113. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 10.

114. See *id.* at 64; FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 112, at 21–22.

issue from gene drives designed to spread through multiple generations.

The respective agencies conducted environmental assessments (“EAs”) as required by NEPA. The EAs were limited to the impacts of the field trials themselves rather than the broader implications if the insects were eventually approved for commercial release.<sup>115</sup> In each instance, the agency concluded that there likely were no significant environmental impacts that would result from the trials, and thus in-depth environmental impact statements were unnecessary.<sup>116</sup> The conclusion that the release would not have a significant impact rested on comparisons between the release of the genetically modified insects and the use of conventional chemical pesticides to control the insects, the geographic containment of the modified insects, and the biological containment built into the trial since the modified insects die without passing on the genetic modifications to other members of the species.<sup>117</sup> Because the trials did not include gene drives, the agencies considering the proposed field trials did not have to consider the prospect of uncontrolled spread beyond the initial generation of released GE insects.

Both agencies identified endangered species and habitats that the GE organism could potentially impact.<sup>118</sup> The FDA concluded that there would be minimal interaction and that genetic modifications would not create a risk of harm from ingestion.<sup>119</sup> The USDA concluded that no endangered species were located near the test site; that prevailing winds would not allow the modified insects to travel to areas with endangered plants that may suffer harm from the moths;

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115. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 65 (“[A]t the conclusion of the experimental release, the release site will be treated with a pesticide” to “eliminate any remaining diamondback moths.”); FDA, FDA RELEASES FINAL ENVIRONMENTAL ASSESSMENT FOR GENETICALLY ENGINEERED MOSQUITO, AUGUST 5, 2016 UPDATE (2016), <https://www.fda.gov/animalveterinary/newsevents/cvmupdates/ucm490246.htm> [<https://perma.cc/XL9D-5JSJ>] (“FDA’s finalization of the EA and FONSI does not mean that Oxitec’s GE mosquitoes are approved for commercial use.”).

116. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 11; FDA FONSI, *supra* note 111, at 85.

117. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 64 (“[The] sterile insect technology in the GE diamondback moth strain . . . mitigates many of the possible theoretical hazards and risks associated with insect genetic engineering.”); FDA FONSI, *supra* note 111, at 8 (finding that after studying “[t]he consequences of escape, survival, and establishment” the proposed field study “is not expected to cause any significant adverse impacts on the environment”).

118. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 57–64; FDA MOSQUITO ENVIRONMENTAL ASSESSMENT, *supra* note 112, at 45–46, 91.

119. FDA FONSI, *supra* note 111, at 6–7.

and, even if the insects did spread, the effects would not be different from the nonmodified diamondback moths that already exist across the country.<sup>120</sup> The agency also determined that releasing the moths may lead to environmental benefits by reducing the amount of insecticides applied during the growing season.<sup>121</sup> Harm to species that prey on the insects was unlikely because the populations would otherwise be controlled with pesticides and the preying species consume other insects.<sup>122</sup>

The EAs for the GE moth and mosquito field trials considered circumstances with a high level of confidence in geographic and biological containment measures. Similar approaches for NEPA analysis may not work in the gene drive context or when agencies consider proposals for releasing multiple GE organisms in the same ecosystems. Comparing the release of genetically modified organisms with conventional pest management strategies, for example, will be incomplete when the risks of spreading gene drives are unknown or there are greater interactions between GE organisms. The focus on listed or proposed endangered species may be insufficient in some cases if the release of the gene drive could result in population collapses in nonlisted species. Limiting the scope of an EA to consider only field trials, as opposed to national or international impacts, may also be insufficient if gene drives could potentially spread to nontarget populations. NEPA requires consideration of worst-case scenarios and thus allows agencies to conduct more expansive analyses for field trials, but agencies have discretion to determine which scenarios to consider.<sup>123</sup>

### C. *Nonregulatory Governance*

The limitations of the ESA and the statutes forming the basis of the Coordinated Framework leave many of the crucial decisions regarding the intersection of gene editing and species viability to nonregulatory forms of governance such as standards, codes of

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120. DIAMONDBACK MOTH ENVIRONMENTAL ASSESSMENT, *supra* note 111, at 65–67.

121. *Id.* at 58.

122. *Id.* at 57–58.

123. Flatt, *supra* note 108, at 32–33; Richard Lazarus, *The National Environmental Policy Act in the U.S. Supreme Court: A Reappraisal and a Peek Behind the Curtains*, 100 GEO. L.J. 1507, 1519 (2012) (“[A]gencies can seek to avoid preparing an EIS by agreeing to mitigate environmental impacts as necessary to reduce the impact of the proposed action below the ‘significant’ threshold.”); *see also* COUNCIL ON ENVTL. QUALITY, EXEC. OFFICE OF THE PRESIDENT, *THE NATIONAL ENVIRONMENTAL POLICY ACT: A STUDY OF ITS EFFECTIVENESS AFTER TWENTY-FIVE YEARS*, 19–20 (1997), <https://ceq.doe.gov/docs/ceq-publications/nepa25fn.pdf> [<https://perma.cc/XSL9-FT23>].

conduct, and guidelines.<sup>124</sup> Scientists may develop their own ethical codes.<sup>125</sup> Government agencies and foundations funding research may impose their own requirements.<sup>126</sup> Universities and other research institutions appoint committees to oversee research on human and animal subjects.<sup>127</sup> Research projects may create their own standards, such as the international Target Malaria project that established its own ethics advisory committee, research transparency requirements, and stakeholder engagement strategies.<sup>128</sup>

A growing body of scholarship points to these “soft law” mechanisms as critical components of a governance system for emerging technologies.<sup>129</sup> Rigid restrictions on research and experimentation may hamper scientists’ ability to explore new technologies that could have profound social impacts.<sup>130</sup> Soft law measures provide oversight for research and development phases. Because they are not regulatory, they can evolve more quickly than formal regulation, particularly where existing statutes do not adequately address issues presented by the new technology.<sup>131</sup> Nonbinding governance measures already guide gene-editing research, including species management and de-extinction, and others are proposed by academics and stakeholders.<sup>132</sup>

124. See, e.g., GENE DRIVES ON THE HORIZON, *supra* note 11, at 148 (identifying three types of governance for gene drives: self-governance by scientists involved in the research, formal regulation by national or state authorities, and a “middle ground in which governments create guidelines that shape the behavior of scientists and research institutions by creating norms and expectations of good practice”).

125. *Id.* at 148, tbl.8-1.

126. *Id.*

127. See, e.g., *Institutional Animal Care and Use Committee*, UNC: RESEARCH, <https://research.unc.edu/iacuc/> [<https://perma.cc/63VN-N6GP>]; *Introduction to Human Research Subject Protection*, UNC: RESEARCH, <https://research.unc.edu/human-research-ethics/introduction-human-research-subject-protection-unc/> [<https://perma.cc/X3J7-ZXUQ>] (noting that the University of North Carolina has institutional review boards that review each research study project).

128. *Ethics Advisory Committee*, TARGET MALARIA, <https://targetmalaria.org/ethics-advisory-committee/> [<https://perma.cc/8Y5V-DXM2>].

129. GENE DRIVES ON THE HORIZON, *supra* note 11, at 167; see also Timothy F. Malloy, *Soft Law and Nanotechnology: A Functional Perspective*, 52 JURIMETRICS 347, 349 (2012); Ana Nordberg et al., *Cutting Edges and Weaving Threads in the Gene Editing (R)evolution: Reconciling Scientific Progress with Legal, Ethical, and Social Concerns*, 5 J.L. & BIOSCIENCES 35, 82 (2018) (noting the “important role” of soft law mechanisms).

130. See, e.g., Mandel & Marchant, *supra* note 12, at 158–59. Genetically modified organisms may also pose significant risks to public health and ecosystems. *Id.* at 159.

131. *Id.* at 158–59.

132. GENE DRIVES ON THE HORIZON, *supra* note 11, at 7–8; Claudia Emerson et al., *Principles for Gene Drive Research*, 358 SCIENCE 1135, 1135–36 (2017); INT’L UNION FOR CONSERVATION OF NATURE, IUCN SSC GUIDING PRINCIPLES ON CREATING PROXIES OF EXTINCT SPECIES FOR CONSERVATION BENEFIT 10–12 (2016),

While soft law measures are crucial components to a governance system, they are not well suited for questions regarding voluntary extinction or de-extinction and do not replace the need for democratic decisionmaking to determine the proper balance between public health, environmental, and economic considerations. The technical experts who develop and oversee professional standards and guidelines may prioritize risk management and safety over conservation goals and other societal values.<sup>133</sup> Stakeholder engagement, while increasingly recognized as an important element in technology governance, may not be a priority or may not be feasible due to limited resources.<sup>134</sup>

Furthermore, disagreement among scientists regarding the proper use of gene editing highlights the problems with relying on soft law to fill in where regulation does not provide clear signals regarding value choices and acceptable levels of risk. Thus far, key figures in the development of CRISPR and the use of CRISPR to facilitate gene drives have called for major limitations on the use of techniques soon after publishing papers describing the techniques.<sup>135</sup> Scholars debate these proposals in academic journals. In the meantime, experiments with CRISPR and gene drives continue unabated.

### III. ALIGNING BIOTECHNOLOGY AND CONSERVATION GOVERNANCE: A PROPOSAL

The prospect of voluntary extinction, combined with the pace and scale of CRISPR developments, calls for a consistent set of standards to guide formal regulatory activity as well as the range of soft law measures that guide the trajectory of gene-editing research. Although the ESA and other conservation statutes may not be directly applicable, they are a compelling indication of societal values. Biotechnology governance should incorporate reasonable

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<https://portals.iucn.org/library/sites/library/files/documents/Rep-2016-009.pdf> [<https://perma.cc/R7JE-FCGD>]; Douglas J. McCauley et al., *A Mammoth Undertaking: Harnessing Insight from Functional Ecology to Shape De-Extinction Priority Setting*, 31 FUNCTIONAL ECOLOGY 1003, 1003 (2016) (proposing that de-extinction efforts “(i) select target species from guilds with low functional redundancy; (ii) concentrate on species that went extinct recently rather than older extinctions; and (iii) only work with species that can be restored to levels of abundance that meaningfully restore ecological function”).

133. Monast, *supra* note 41, at 2381–82.

134. Natalie Kofler et al., *Editing Nature: Local Roots of Global Governance*, 362 SCIENCE 527, 527, 529 (2018) (stating that community engagement is “largely missing” from the process of gene-editing research and development).

135. Esvelt et al., *supra* note 6, at 1; *see also* David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCIENCE 36, 36 (2015); Oye et al., *supra* note 65, at 626.

presumptions about the appropriate use of new technologies based on conservation efforts already in place.

The ESA, in particular, is an enduring policy statement about the intrinsic value of species and the importance of conservation. The principles that form the foundation of the ESA can, and should, guide the use of gene editing. Boiling the ESA down to its core elements, the law recognizes that humans generally have an obligation to prevent extinction, that protecting threatened species requires protecting individual members of species, and that federal agencies must avoid exacerbating threats to endangered species.<sup>136</sup> This structure—creating broad protections for threatened or endangered species, exempting certain species, and providing limited exemptions for activity that may harm protected species—provides a template for aligning biotechnology and conservation. Incorporating these elements into gene-editing governance would provide clear policy guidance regarding acceptable uses of gene editing.

The remainder of this Article recommends three revisions to biotechnology governance as an initial step to align gene-editing research and conservation goals. The first two recommendations apply the ESA framework to biotechnology governance generally: (1) federal agencies should indicate that they will not generally allow the release of GE organisms that could threaten species viability; and (2) the agencies should allow for exemptions to the general ban and specify criteria for qualifying for exemptions. The third recommendation identifies initial updates to ESA regulations to clarify how the statute applies to genetically modified organisms.

*A. Establish a Presumption Against Release of Genetically Modified Organisms that Could Foster Species Extinction*

As a threshold matter, federal agencies should establish a presumption against releasing modified organisms that present a risk of extinction for the target species or other nontarget species. This step would provide clarity for regulators, researchers, and investors. This step would also inform soft law governance measures.

Implementation could take different forms, some of which could occur via existing statutory authority and some of which would require new legislation. One option includes directing the Council on Environmental Quality, or the lead permitting agency, to revise NEPA procedures to specify that agencies should reject proposed releases of GE organisms if the NEPA process identifies a reasonable

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136. See *supra* notes 75–91 and accompanying text.

risk to species viability, including to nontarget species.<sup>137</sup> While such a step would place limits on some near-term applications of gene editing, extinction and the potential for major irreversible ecological impacts are the quintessential examples where clear guidance is important. This move would not bar future developments that would either achieve desired outcomes without threatening species viability or fall within a specified exemption. Revised NEPA guidelines could also require agencies to specify, in a transparent manner, the acceptable and unacceptable levels of potential risk to the ecosystem and nontarget species. Finally, NEPA revisions could also focus gene-editing research efforts on nonlethal strategies, such as targeting a virus rather than its carrier or gene drive techniques that phase out over generations.<sup>138</sup>

Federal agencies funding gene-editing research should also implement the presumption against extinction in their funding guidelines. Guidelines from the National Institutes of Health (“NIH”), for example, establish safety practices and containment procedures to protect researchers, the public, and the environment. The NIH Guidelines only apply to government funding and thus do not apply to research funded solely via private investment.<sup>139</sup> The Guidelines also focus solely on laboratory research and do not address prospective release of GE organisms into the environment.<sup>140</sup> The NIH Guidelines have a broad reach nonetheless.<sup>141</sup> Institutions receiving, or hoping to receive, NIH funding may require all researchers to comply with the guidelines, not just those that may qualify for the federal funding.<sup>142</sup>

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137. The Council on Environmental Quality “oversees NEPA implementation, principally through issuing guidance and interpreting regulations that implement NEPA’s procedural requirements” and “reviews and approves Federal agency NEPA procedures, approves alternative arrangements for compliance with NEPA for emergencies, [and] helps to resolve disputes between Federal agencies and with other governmental entities and members of the public . . . .” *Council on Environmental Quality*, WHITEHOUSE.GOV, <https://www.whitehouse.gov/ceq/> [<https://perma.cc/M2UC-DCC9>].

138. See Yuemei Dong et al., *CRISPR/Cas9-Mediated Gene Knockout of Anopheles Gambiae FREP1 Suppresses Malaria Parasite Infection*, 14 PLOS PATHOGENS, no. e1006898, Mar. 8, 2018, at 1, 1; Marshall & Akbari, *supra* note 35, at 425–28 (discussing strategies to control gene drives after release).

139. Mandel & Marchant, *supra* note 12, at 192.

140. *Id.* at 193.

141. Jeffery D. Wolt, *Safety, Security, and Policy Considerations for Plant Genome Editing*, in 149 PROGRESS MOLECULAR BIOLOGY & TRANSLATIONAL SCI. 215, 232 (2017).

142. See David Rainer & Susan Cook, *Overcoming Regulatory Gaps in Biological Materials Oversight by Enhancing IBC Protocol Review*, in ENSURING NATIONAL BIOSECURITY 73, 86 (Carole R. Baskin & Alan P. Zelicoff eds., 2016); see also UNC

Federal funding and research guidance need not ban funding recipients from laboratory-scale research that could impact species viability. Such research may be necessary to develop new techniques that address social needs without eradicating species, techniques that can accomplish goals such as the eradication of malaria by modifying mosquitos so they cannot serve as a vector.<sup>143</sup> Guidance and funding restrictions could, however, prioritize strategies that do not rely on species eradication and potentially provide guidance on the release of genetically modified organisms developed through the use of federal funding.

*B. Allow Exemptions for Specific Public Health and Environmental Goals*

The presumption against the release of GE organisms that could trigger extinction need not be absolute. There are compelling health and governance justifications for utilizing CRISPR to control infectious diseases, particularly when conventional control strategies are ineffective or prohibitively expensive (e.g., malaria or Zika virus).<sup>144</sup>

In addition to health benefits, the focus on a small number of vectors of severe infectious diseases could serve as a testing ground for gene-editing techniques, allowing researchers to gather information on the implications of population management and species conservation via gene editing. Allowing limited uses of gene editing would not restrict laboratory-scale experiments, thus striking a balance between precaution and technology development. It would also allow opportunities for regulators and stakeholders to develop informed opinions about gene editing as information becomes available. Information from the early stage uses of gene editing could then guide regulatory decisions and stakeholder engagement involving other potential releases of GE organisms.

Other exemptions could also apply when species eradication is the goal. In the context of invasive rodents endangering the viability

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DEPT OF ENV'T, HEALTH & SAFETY, NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES 4 (2017), <https://ehs.unc.edu/files/2015/11/rdna.pdf> [<https://perma.cc/B359-3X3S>] (“NIH Guidelines are applicable to[] [r]esearch conducted at or sponsored by an institution that receives any support for recombinant or synthetic nucleic acid research from the NIH.”).

143. Dong et al., *supra* note 138, at 1–3.

144. See, e.g., Antonio Regalado, *Bill Gates Doubles His Bet on Wiping Out Mosquitoes with Gene Editing*, MIT TECH. REV. (Sept. 6, 2016), <https://www.technologyreview.com/s/602304/bill-gates-doubles-his-bet-on-wiping-out-mosquitoes-with-gene-editing/> [<https://perma.cc/5VSD-CRD7>].

of island bird populations, for example, the only viable option may be removing, as opposed to controlling, the rodent populations.<sup>145</sup> This type of exemption is potentially expansive and could include a wide range of agricultural pests. Specific criteria for the exemption would be necessary to ensure that the exception does not undermine efforts to impose meaningful limits on the use of biotechnology to eradicate species.

*C. Clarify the ESA's Application to Genetically Modified Organisms*

The first two recommendations provide guidance for gene-editing research, but they do not clarify broader questions regarding the ESA's applicability to genetically modified organisms. As noted above, addressing GE organisms is not the only area where the ESA needs to evolve to remain effective in a world with changing climates and migrating species. A detailed set of recommendations to prepare the ESA for current and emerging challenges is beyond the scope of this Article.<sup>146</sup> Instead, the remainder of this Article recommends initial steps that could occur via administrative rulemaking or legislation to align the ESA with the recent advancements in genomic sciences.

First, policymakers could resolve uncertainty regarding the ESA's reach over gene-edited organisms by clarifying that the definition of species includes GE organisms. The statute provides only a general definition of the term "species" that is broad enough to include species with genetic codes altered by humans.<sup>147</sup> Extending ESA protections to GE organisms could be particularly important if the purpose of the genetic modification is to preserve an existing species or reestablish viable populations of extinct species. Otherwise the genetic intervention could create the ironic effect of preventing the modified organism from qualifying for ESA protections.

Second, policymakers could adapt a 1996 proposed rule on hybrid species—species resulting from cross-breeding between protected and unprotected species in the wild or in captivity—to

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145. McGrath, *supra* note 4; *see also* Gurevitch & Padilla, *supra* note 48, at 470.

146. Other scholars have offered detailed recommendations for updating conservation statutes. *See, e.g.*, Camacho, *supra* note 50, at 897–902 (proposing a "risk-based adaptive ecosystem management" approach to address de-extinction); Ruhl, *supra* note 98, at 60–62 (recommending certain FWS steps to help threatened and endangered species survive threats posed by climate change).

147. *See* 16 U.S.C. § 1532(16) (2012) (defining "species" to include "any subspecies of fish or wildlife or plants, and any distinct population segment of any species of vertebrate fish or wildlife which interbreeds when mature").

address GE organisms. The proposed rule would have protected hybrid species that more closely resemble a protected species than a hybrid of a protected and an unprotected species.<sup>148</sup> The proposed rule did not protect cross-breeding in captivity or “the artificial transfer of genetic material from one taxonomic species into another (i.e., transgenics),” but it did make an exception for captive breeding conducted pursuant to an approved recovery plan.<sup>149</sup> The agencies never finalized a rule addressing hybridization, relying instead on case-by-case determinations.<sup>150</sup>

Applying the proposed hybrid species rule to GE organisms would strike a compromise that extends ESA protections to gene editing intended to support recovery efforts while excluding other GE organisms created in laboratories and those targeting species that are not listed as endangered or threatened. The approach could leave important gaps, particularly if recovery efforts are not first approved by the FWS or NMFS. It would, however, provide a pathway for conservation-focused gene editing, and the agencies could update the approach as biotechnology matures.

#### CONCLUSION

CRISPR may add to a suite of tools for conservation on the one hand and species eradication on the other. It may also change the equation on extinction itself, allowing scientists to reverse extinction in some circumstances and deliberately foster extinction in others. Gene editing, therefore, raises important questions for conservation and natural resource management. U.S. law does not currently address these questions and the gaps in U.S. regulation of biotechnology and endangered species leave regulators and researchers without clear policy guidance regarding acceptable uses of gene editing. Without updates that address the overlap between biotechnology and conservation governance, regulation will evolve based on case-by-case applications of existing laws that were not designed to address the biotechnology-conservation nexus.

Regulators and researchers have an opportunity to incorporate conservation goals into biotechnology governance, particularly while

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148. Endangered and Threatened Wildlife and Plants; Proposed Policy and Proposed Rule on the Treatment of Intercrosses and Intercross Progeny (the Issue of “Hybridization”); Request for Public Comment, 61 Fed. Reg. 4710, 4710–11 (proposed Feb. 7, 1996) (to be codified at 50 C.F.R. pt. 424).

149. *Id.* at 4712.

150. John A. Erwin, *Hybridizing Law: A Policy for Hybridization Under the Endangered Species Act*, 47 ENVTL. L. REP. 10615, 10615 (2017).

much CRISPR-related research remains at an early stage. The proposal outlined in this Article strikes a balance between scientific research, societal benefits, and a precautionary approach for genetic techniques that are still in developmental stages. It also recognizes that questions about species viability do not start with a blank slate. Society has made important value choices regarding species conservation that provide the foundation of the ESA and other conservation statutes. Gene-editing governance should incorporate these value choices to ensure that any gene-editing efforts deliver societal benefits without undermining conservation goals.