The Prospect of Using Genome Editing for Deliberate Extinction

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Advancing genome editing technologies, prominent among them synthetic gene drive systems, may lead to methods for suppressing or locally exterminating some species, or even driving them extinct. How that prospect accords with the Endangered Species Act (ESA) is an emerging policy issue with potentially profound ramifications for environmental, public health, and agricultural policy.

Effects of a gene drive system would depend on the design of the system, e.g., alleles targeted for change, diversity of a species' gene pool, and a species' population structure.[1] For example, a drive that reduced female fertility in malaria-transmitting mosquitoes *Anopheles gambiae* could lead to substantial population decline on a regional scale, though modeling suggests that complete extinction is unlikely.[2] Gene drive systems are also in development to eliminate invasive rodent populations that threaten other species on oceanic islands.[3] Other candidate species include the New World screwworm, a blow fly causing considerable damage to livestock and posing a threat to humans, for which genes required for female development or fertility have been identified and could be targeted by gene drive.[4]

Eliminating disease-carrying mosquitoes and screwworm appears to be permissible under the ESA, which exempts insect pest species that present "an overwhelming and overriding risk" to humans. The law's applicability to a widespread population decline of invasive rodent populations due to a gene-drive system is more ambiguous. ESA protections apply only after a species is listed as endangered, which typically requires evidence that the species has already declined. The ESA, therefore, may not apply to the prospective threat of a gene drive.[5] Additionally, how genome editing would be considered in the listing process is not settled. The factors that trigger listing have generally been external threats to a species such as hunting and habitat change, not genetic alterations integrated into a species' gene pool.

But if the letter of the law needs clarification, the spirit of the ESA clearly places an extremely high value on species and rules out eradication in most cases. The exception made for insect pests shows, however, that some goals, such as preventing the enormous public health harms associated with some insects, might override that high value. Exactly which harms are overriding—and whether they are posed only by insects—are important questions. But, plainly, if the ESA is taken to heart, genetic interventions that could lead to a species' extinction should be evaluated very conservatively and would be acceptable only rarely

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[1] NASEM, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* NASEM Washington, DC, 2016.

[2] A. R. North, A. Burt, H. C. J. Godfray, Modelling the suppression of a malaria vector using a CRISPR-Cas9 gene drive to reduce female fertility. *BMC Biology* **18**, 98 (2020).

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