CONSERVATION

Deliberate extinction by genome modification: An ethical challenge

What circumstances might justify deliberate, full extinction of a species?

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mong the ways that genome modification could be used to modify wild populations of organisms, the deliberate outcome of fully eradicating a species has received little critical attention. The lack of discussion leaves a difficult ethical question unresolved: When so much attention is given to the value of biodiversity and the conservation of species, what circumstances, paradoxically, might justify the deliberate, full extinction of a species? At least one species is now a preliminary candidate for full extinction, and cases under consideration for temporary suppression and local extinction might pose a risk of full extinction. We discuss three cases in which genome modification might be used to eradicate a species. Together, we argue, these cases suggest that deliberate full extinction might occasionally be acceptable, but only extremely rarely. The cases also highlight tensions within some widely held views about the conservation of species and the governance of genome editing.

To encourage more critical attention to these tensions, all of the authors—environmental ethicists, bioethicists, conservation biologists, ecologists, social scientists, and scientists—participated in a May 2024 workshop to study the moral question posed by deliberate extinction through genome editing. The discussion that follows below draws upon that event.

PROSPECTIVE CASES

In principle, a spectrum of techniques for altering genomes could cause or facilitate full extinction of a species. The three cases on which we focus aim either at full extinction (global eradication outside of ex situ holding facilities) or at local extinction (eradication within a limited portion of a species' range) that carries a risk of full extinction.

New World screwworm

The New World screwworm (Cochliomyia hominivorax) is a leading, though little-discussed, candidate for full extinction, probably by means of a combination of genomic strategies now under development. Screwworm is a fly that in its larval stage is an obligate parasite of warm-blooded animals. The flies lay eggs on mucosal surfaces and wounds, and the larvae burrow into and consume the host's flesh, causing bacterial infections that can kill the host through sepsis. Screwworm is considered a severe threat to livestock and also infects wild animals and sometimes humans, as suggested by the species name hominivorax. Screwworm has already been eradicated from North America, some Caribbean islands, and (until recently) Central America using the sterile insect technique (SIT), in which mass-reared pupae are exposed to ionizing radiation that produces sterilizing genetic mutations. Flies are then allowed to emerge and are released in vast numbers, usually from planes, to saturate a release zone. The goal of the release is that wild-type females mate with sterilized males, preventing the wild population from reproducing.

Screwworm persists across most of South America, where the costs of SIT are likely prohibitively high. SIT can be greatly improved, however, by using a strain of screwworm genetically modified so that female larvae mature only in the presence of tetracycline and can therefore be eliminated from the populations raised for release (I). In business-as-usual SIT, both males and females are released. With females eliminated, the cost of rearing flies is reduced and, because females require a higher level of radiation than males, the radiation can be reduced, which means the males remain more fit and are likelier to mate. Additionally, because sterilized females are not among the released flies, the males can mate only with wild-type females, which maximizes their impact.

The modified strain also allows for alternatives to SIT that would be yet more effective. For example, releasing modified males without sterilization would transmit the female-killing modification to all off-spring and to residual numbers of a few subsequent generations—an example of the technique known as female-specific release of insect with a dominant lethal (fsRIDL) (1). Alternatively, the modification could be coupled with a gene drive so that the trait was transmitted to nearly all offspring through many generations (2). A combination of these techniques is sufficiently promising that full eradication of the species has emerged as a future possibility.

Use of SIT to eradicate the New World screwworm locally has been widely supported in North and Central America (3). There is also now interest in South America, starting in Uruguay (4, 5) and with the assistance of the International Atomic Energy Agency (IAEA) (which, given its expertise in radiation-based technologies, helps member countries develop and use SIT), the Food and Agriculture Organization of the United Nations, the US Department of Agriculture, and the Panama-United States Commission for the Eradication and Prevention of Screwworm, to continue the effort across the remainder of the screwworm's range. Although a plan published by IAEA envisions eradication solely through standard SIT (4), improved SIT and fs-RIDL approaches, which have already been developed, would greatly increase both cost-effectiveness and the odds of success, though approval has not yet been sought. A gene drive technique would require further research and approval, but, if successfully developed, would increase effectiveness and reduce costs still further.

The argument for moving forward is multipronged. Screwworm parasitism of animals causes substantial suffering, and parasitism of domestic animals, including livestock, is thought to diminish human food security (4) and raises special concerns about animal welfare, because humans arguably bear greater responsibility for animals under their care than for wild animals. Infections are difficult to treat, and, from reports of human cases, death from screwworm infection is painful and slow (6). The extent of the public health threat posed by

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screwworm is not certain, but any flesh-eating insect that caused occasional human mortality in the Global North would almost certainly be marked for suppression if not eradication.

The case against extinction consists of the species' intrinsic value (that is, any value the species possesses in and of itself—for what it is, rather than for what it provides or does for others) plus the value of any environmental benefits it confers, such as by holding deer populations in check or by providing food for predators. But these claims are limited. Screwworm is considered among the worst of pests in the cultures where it is present. Whatever intrinsic value it possesses must therefore be a value that a species possesses just by virtue of being a species, but claims about that kind of intrinsic value are highly contested. Although the environmental role of screwworm is not well studied, some research suggests that the fly is not ecologically vital (7), and its eradication is not known to have had substantial environmental impacts in North and Central America.

The broad support for use of SIT to achieve a series of local extinctions of screwworm suggests that the argument in favor of fully eradicating screwworm is likely to be compelling for many people—especially in light of a recent resurgence of screwworm in Central America, because the resurgence suggests that a permanent solution may be possible only with complete eradication. Most of our own author group agree that it is compelling.

Anopheles gambiae mosquitoes

Possible cases of temporary suppression or local extinction of species through genome editing also raise questions about full extinction, insofar as a risk of inadvertent full extinction should be taken into account in those cases. Mosquito species in the Anopheles gambiae complex, which are vectors for Plasmodium species that cause human malaria, are possible targets for temporary suppression and, at least in principle, full extinction. Malaria kills upward of half a million people annually and imposes a considerable economic toll on many countries in sub-Saharan Africa (8). Elimination of malaria might be facilitated through vector control strategies such as a gene drive that prevents development of one of the sexes, biasing the sex ratio and leading to a population crash (9). This strategy poses a possible though very slight risk of full extinction of anopheline vectors of malaria and perhaps, through interbreeding, of nonvector anopheline mosquitoes. Given the enormous human burden of malaria, which has been growing in recent years, the argument for extinction of An. gambiae is arguably even stronger than the argument for extinction of screwworm. Nor does the overall value of mosquitoes seem likely to outweigh the harm they cause humans. The ecological role of any one An. gambiae species would likely be filled by another (9). However, we can avoid deciding in favor of extinction in this case. Eliminating malaria requires eradication only of Plasmodium, not of the vectors, and Plasmodium can be eliminated with a combination of measures that interrupt its life cycle without necessarily wiping out its vector. Such measures could include bed nets, health care infrastructure that brings infected people indoors and prevents reuptake of Plasmodium into mosquitoes, the recently approved malaria vaccine, and perhaps a gene drive that modifies mosquitoes in ways that prevent them from being vectors for *Plasmodium*. In many places, *Plasmodium* has been eliminated in part by attacking the mosquito directly, through insecticides or habitat modification. In Africa, gene drives that cause temporary and local population suppression might prove to be necessary, but most commentators do not call for full extinction of the vector (9). Eliminating *Plasmodium* in this way would also be deliberate species extinction through genome modification, but one more easily justified.

House mouse, black rat, Norway rat

Several mammalian species are potential targets for sex-biasing gene drives meant to achieve local extinction in places where they are non-



New World screwworm larvae use tusklike mandibles to consume the flesh of warm-blooded animals, causing infections that can be fatal to the host.

native and pose a severe threat to native species. Foremost among these species are the house mouse (Mus musculus), the black rat (Rattus rattus), and the Norway rat (Rattus norvegicus), which threaten endangered bird species on islands across Oceania (10). Such a drive would be more humane, more targeted, and less environmentally damaging than population control by means of traps and poisons, but it might also present a very slight risk of global extinction of the target species, if individuals modified with the drive escaped the geographical containment of the island and if genes targeted by the drive were conserved across the species. Moreover, these species are widely viewed as pests, and they threaten global extinction of a large number of endemic species on islands where they are invasive. Nonetheless, neither we nor any other commentators, even among those who advocate use of such a drive, hold that local extinction of invasive rats or mice is permissible if there is a nonnegligible risk of global extinction (11). To help head off such risks, research on gene drives has focused on developing drives that are temporally limited or can be targeted at particular subpopulations of the species in question.

IMPLICATIONS FOR CONSERVATION

As tools for species population control, genomic technologies such as SIT, RIDL, and gene drive are designed to target a species precisely, in contrast to alternative strategies such as habitat modification, poisoning, or trapping, which typically have effects beyond the targeted species. Because these technologies can affect only the target species, avoiding unnecessary collateral effects, the prospect of using them to eradicate a species is a lens for examining the value of species themselves. That value—a combination of any intrinsic value and any benefit it provides others—has been paramount in conservation philosophy and policy, as the Endangered Species Act in the US attests. We believe that the cases above, taken together, illustrate that high value. They show that even decisions to eliminate parasites and vectors of disease require extremely compelling arguments as well as confidence that the eradication poses low risk to other species.

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The screwworm case, however, shows that the value is not absolute and overriding. Most of our group agree that, under extremely rare and compelling circumstances, deliberate extinction through genome editing is permissible.

The cases may also have repercussions for how species are valued. Western conservation ethicists and biologists often argue that the intrinsic value of species should be equal across species and should not track subjective human preferences (12). However, the willingness to eradicate screwworm and risk extinction of anopheline mosquitoes, though justified in terms of the harms these species pose, might be influenced by a dislike of parasitism or a disregard for species perceived as being lower on some understanding of a phylogenetic tree. These views need clarifying and assessment. Similar views are tacitly present elsewhere, such as in the conservation biology practice of eradicating parasitic mites and insects (the condor louse is an example) from endangered fauna on which those parasites depend. The idea that species can be ordered by moral status resembles the ancient Greek and medieval European concept of the scala naturae, or "great chain of being."

Western scholars now widely reject the scala naturae (13), but other philosophical traditions sometimes uphold similar orderings. Some lines of sub-Saharan African environmental thought, for example, recognize a "hierarchy of existence" on the ground that different species have different ontological and teleological characteristics (14). Even many in the West may not regard a Plasmodium species as equal in value to the mosquitoes that carry it, much less to humanity. A final set of questions that the cases raise for conservation is about the widely shared view that genome modification is particularly unappealing, compared to other ways of intervening in nature, because of a special moral status possessed by genomes or by genetic and evolutionary processes that are closely connected to organisms' identity. In contrast to genome modification, the use of SIT has historically aroused little to no public resistance. Yet, because both genome modification and SIT work by making genetic changes, they appear to be on par with each other in terms of their goals: They alter genomes in ways that lead to population suppression. Perhaps genome modification, which allows for more precise alterations, is more troubling because it seems to impose human design on the genome; because SIT is less precise, it appears to involve less control. Yet the irradiation in SIT is timed and titrated to accomplish exactly enough genomic scrambling to sterilize insects without disabling them. Variance in the genetic effects of radiation is not a lack of control; rather, it's the chosen method to achieve sterilization. The potential improvements in SIT blur the lines further. If SIT already is genetic modification of an organism, then why not carry out SIT on a genetically modified strain of the organism? And if using a genetic modification is acceptable in SIT, then why is it unacceptable to use that same modification in fsRIDL, or coupled with a gene drive, to achieve the same results more efficiently?

IMPLICATIONS FOR GOVERNANCE

Even if there were greater clarity on substantive moral issues such as the value of species or the disvalue of genome modification, there can be no simple, universally applicable criteria for handling decisions about when species extinction through genome editing should be pursued and when the effort should not be made. Both action and inaction have consequences and require justification. Ultimately, these decisions depend on value trade-offs—a weighing of competing fundamental moral commitments—that will be different in each case and will be seen differently in different cultures and communities.

Partly because the trade-offs depend on stakeholders' input, and partly to uphold basic principles of democratic legitimacy, decisions about extinction through genome modification should be made through appropriate collective decision-making processes. A key governance issue for these decision-making processes is the balance of local and

wider publics. For most decisions about releasing genetically modified organisms into the shared environment, local publics should have primacy in the decision-making (15). Their interests are most clearly at stake, and they likely have specific knowledge of many of the possible social and ecological consequences of the release. Indigenous Peoples, in particular, should have a primary role, as they hold distinct rights to determine the use of their lands and resources. Giving local publics a primary role in the decision can also help prevent the perpetuation of historical injustices that have prevented marginalized people from participating in environmental policy decisions, particularly in postcolonial contexts. Because both technology development and technology governance are dominated by the Global North, care must be taken to ensure that voices from the Global North are not overly influential in decisions about release, especially in the Global South.

In decisions to move forward with local extinction, especially of invasive and nonnative organisms, the preferences of local publics should therefore be weighted most heavily, if the risk of effects outside the local area is very low. Decisions to move forward with full extinction, however, may challenge the priority of local preferences (though on this question, too, there will be no one strategy that can be applied across cases). People who live distant from a species' range have asserted a stake in the planet's shared ecological heritage and have supported international efforts to preserve species. The argument for recognizing that publics in the Global South should have the same freedoms to make decisions about their environment that have long been claimed in the Global North is very powerful. So, too, is the need for a strong, collective approach to the decisions about species' existence. \square

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