Ethos is a regular column dedicated to discussing ethical challenges faced by entomologists. For more on the column's goals and structure, see Barrett M, Fischer B. 2023. Introducing Ethos: A Regular Forum for Interdisciplinary Conversations about Ethics in Entomology. American Entomologist. 69(1):40–44. https://doi.org/10.1093/ae/tmad016

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TO CRISPR OR NOT TO CRISPR?

Ethical Considerations in Gene-Editing Insects

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Genetically modified corn has helped feed the world (Hernandes-Lopes et al. 2023). Genetically modified mosquitoes could help eliminate devastating diseases like malaria (Hammond and Galizi 2017). Plainly, gene editing can serve some important human interests. Still, many people object to it. While some concerns have little scientific validity, there are valid ethical concerns that should be addressed.

A concern many people share is the potential impact of genetically edited insects on the environment. Gene drives are "selfish" genetic elements that are transmitted to progeny at unusually high rates and thus spread rapidly through populations. As a result, they are capable of modifying an entire population or species. The most widely discussed use of gene drives is in the prevention of malaria, the leading cause of human illness and death in many parts of the world (CDC 2021), where gene drives could be used to control mosquito populations.

At present, however, there are no surefire strategies to "recall" a gene drive once it has been released (Hammond and Galizi 2017). Given the many unintended environmental impacts of other technological advancements and our uncertainties about the impacts of using gene drives (Ahmad et al. 2022), it makes sense to have similar concerns about this form of gene editing. Granted, it is possible that the extraordinary benefits to human life of such a gene drive, if successful, outweigh the risks of any unintended environmental consequences. This is particularly likely to be true if convincing measures like "terminator genes" can be employed to control genetically edited insect populations in the wild (Hammond et al. 2021). Given the serious promise and ethical concerns of this technology, the National Academy of Sciences has published guidelines for responsible research that include self-governance and government regulation, evaluating gene drives on a case-by-case basis (NASEM 2016). So, while risks of environmental harm are important, we can now see how they might not be decisive: first, the corresponding benefits might

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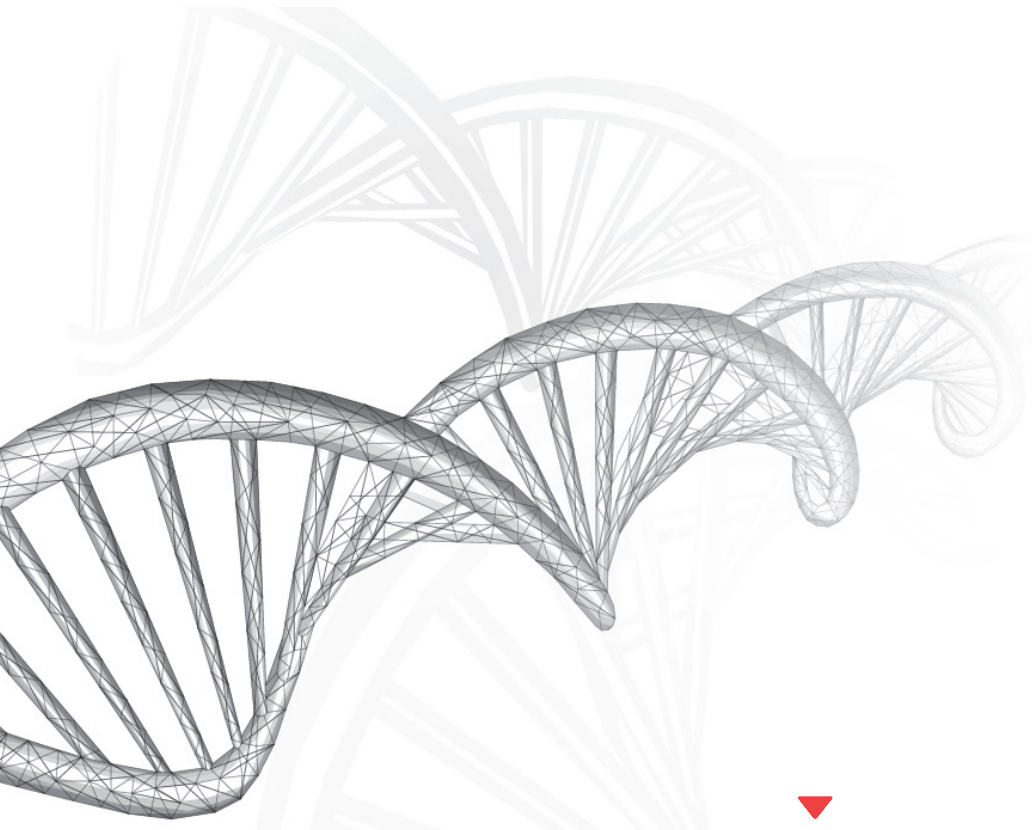

HOW SHOULD SUCH WELFARE RISKS BE FACTORED INTO DECISION-MAKING? ONE FUNDAMENTAL PRINCIPLE IN BIOETHICS IS NON-MALEFICENCE— A DUTY TO AVOID CAUSING HARM.

be very weighty; second, the risks might be mitigable.

Let's compare this case with another: namely, insect farming, which currently rears several trillion insects a year in an effort to provide more sustainable protein to the world (van Huis and Tomberlin 2017, Barrett and Fischer 2023). Gene editing could be used to make insect rearing more efficient (Eriksson and Picard 2021), with the ultimate goal of improving human health, survival, and security. However, insects are notoriously small and hard to contain. The many invasive insects we struggle to control suggest that there can sometimes be devastating consequences on our ecosystems when they can and do escape from facilities unintentionally (such as with the spongy moth; UWM Extension 2023). These have had especially significant impacts for the environment and human health following selective breeding efforts, as with the the so-called 'Africanized honey bee' (Visscher 2024). If we are concerned about the consequences of intentionally releasing gene-edited insects, such as in the case of gene drive mosquitoes, we should probably also be concerned about the consequences of unintentionally releasing gene-edited insects from farms.

Again, the ethical concerns of environmental and human health impacts don't necessarily preclude gene-editing farmed insects. Instead, we may simply want to consider applying the lessons from the malaria example more broadly, requiring clear human benefits and the effective management of any risks in *all* gene-editing contexts. Importantly, gene drives may be especially risky technologies when they are *designed* to spread throughout wild populations; gene edits that occur in other contexts may pose a much smaller risk. Still, careful evaluation of risks and oversight of gene editing such as registering the use of the technology in animals (Taitingfong et al. 2023) may be the best ways to ensure that benefits are maximized and environmental risks are minimized wherever these technologies are used.

However, there are other concerns to which we might need to respond. Consider another example: gene-editing technologies may reduce the welfare of animals in service of human goals. For instance, CRISPR/Cas-9 gene editing has generated flightless adult black soldier flies (in the lab), where natural behaviors like flight are restricted in service of reducing rearing space (Zhan 2020). Plainly, then, there are welfare reasons to be concerned about gene-editing technology for insect livestock (Barrett et al. 2023). Although little is written on the ethics of gene-editing insects as mini-livestock and entomologists have reported little training on the ethical issues surrounding the use of these methods (Trout et al. 2010), we may have some precedent to rely on from parallel cases in vertebrate livestock farming.

How should such welfare risks be factored into decision-making? One fundamental principle in bioethics is *non-maleficence*—a duty to avoid causing harm (Beauchamp 2019). This creates a presumption against intentionally manipulating animals in ways that might be harmful to them—a point that applies equally to gene drives for mosquitoes and flightless flies. Again, though, there are questions about the importance of the human concerns that drive these modifications; there are also questions about the severity of risks and the degree of possible mitigation. Preventing life-threatening illnesses is clearly a weighty human concern, as is food production. In this case, however, there are bound to be pressing questions about whether there are relevant alternatives.

Supposing these are our best options, the issue will come down to the severity of the welfare risks and our ability to mitigate them. Importantly, not all genetic modifications are likely to harm insects. So, conducting more research now, before these gene-edited strains exist, on the normal behaviors and experiences of insects would

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allow us to better understand when and whether welfare is negatively impacted through genetic intervention. Further, such concerns might be assuaged if the use of welfare assessments steered us toward adopting genetic modifications that are either neutral or even enhance welfare, as has been suggested for vertebrate livestock (Shriver 2009, Croney et al. 2018). Indeed, relative to vertebrate livestock, piloting welfare enhancement edits may even be easier in insects (Eriksson and Picard 2021).

Given all these possible public concerns (and more we don't have time to cover, but see de Graeff et al. 2019, Bovenkerk 2020), entomologists developing gene-editing technologies in any context have a broader ambit of responsibilities than current training and regulatory environments suggest. As yet another example, many recommend that regulatory oversight should include community participation, ensuring democratic governance in the use of gene-editing technologies (though this is not currently practiced in the United States; West et al. 2022). Any ethical concerns can thus be subject to review by the broader community's values prior to developing or deploying these technologies. Further, as these technologies and the ethical challenges associated with them will continue to advance, mentors working on gene editing have a responsibility to provide educational opportunities on ethics to their graduate students as part of ethical and responsible conduct of research for their research area. Current research suggests that entomology students are currently underprepared to satisfy this unique professional responsibility (Trout et al. 2010).

If there is one lesson to glean from all these considerations, it is this: while our intended goals are undoubtedly admirable, the ends alone do not justify the means. Entomologists engaged in gene-editing research should proactively consider what the "means" mean—for humans, for the environment, and for the insects themselves.

Acknowledgments

Thanks to Bob Fischer for helpful comments on this article.

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DOI: https://doi.org/10.1093/ae/tmae058

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