Gene Drives

A report on their science, applications, social aspects, ethics and regulation.

The full report can be downloaded at https://genedrives.ch/report

Brief summary

Synthetic gene drives are a new form of genetic engineering intended to permanently modify, replace or even eradicate populations or whole species in the wild. In contrast to previous GMOs, gene drive organisms (GDOs) are meant to spread their genetic modifications far and wide; in other words they are meant to be invasive unlike previous GMOs. If this technology fulfils the ambitions of its developers, it will have major implications not just for biodiversity and ecosystems, but also for humanity's relationship with the natural world. Debate about if and how GDOs could be safely employed is proceeding, alongside work on the underlying technology and plans for its deployment, but the international regulatory framework, technology assessment and the inclusion of wide public deliberations lag behind. In this context we have published this report on Gene Drives – their science, applications, social aspects, ethics and regulation – to meet an urgent need for independent and informed analysis of gene drive technology and its implications.

The term 'gene drive' is currently defined as a system where genetic elements or traits have more than the usual 50% chance of being inherited, irrespective of whether they benefit or harm the organism inheriting them. There are many ways in which this 'biased inheritance' can be genetically engineered, and whilst the emergence of genome editing techniques based on the CRISPR-Cas9 system has accelerated developments, numerous issues remain unresolved and problematic. **Chapter 1** considers the basic science of gene drives and looks at the many different forms of engineered gene drives being suggested or developed so as to help the reader understand the action, risks and limitations of each one. Even the most technically advanced drives, which are currently the CRISPR/Cas9-based gene drives, reveal serious limitations in their functioning and important uncertainties at scientific, technical and practical levels. These include the potential for drives to spread uncontrollably and the likelihood of causing irreversible genetic changes. The chapter concludes that no gene drive technologies are currently fit for application.

Irrespective of whether the technology is ready or not, numerous species are now targets for modification, suppression or elimination with gene drives, as explored in **Chapter 2**. An overview is given of all potential applications currently under consideration, their state of research and development and the institutions involved. To date, species being considered as targets include insects, small mammals, fish, birds, plants, molluscs, nematodes, flatworms and fungi, including yeasts, and in many cases laboratory work on constructing gene drives in these organisms is well under way. Before any release of a gene drive organism into the environment, many questions would first need to be addressed. These include for example the biology and genetics of a species, its ecological role and interaction with other species, the niches it occupies and the consequences of creating a void in its absense, as extended over time and space. Thus, the identification and assessment of the risks of GDOs must be done on the basis of organisms and ecosystems, instead of starting from or being influenced by the claimed benefits. To better understand the risks of gene drive deployment, the chapter discusses three possible case studies in detail: mosquitoes, house mice, and the plant Palmer amaranth. In each of these case studies, routes

are identified through which unintended harm could occur, and it emerges that there is at present no solid scientific basis for performing the robust risk assessment that is essential to safeguard biodiversity and human health.

However, as discussed in specific examples in chapter 2 and expanded in **Chapters 3 and 4** (covering social aspects and ethics), discussions about gene drives must not be restricted to technical assessments of feasibility and risks. Chapter 3 looks at how the research is funded and patented and how the desire for funding can lead to unrealistic claims about what researchers and technologies can deliver. In the case of gene drives, the role of hype in the public discourse on this technology is important and may negatively impact alternative problem framings and solutions. As pointed out in chapter 4, ethical governance of gene drives goes beyond openly and inclusively considering gene drives; such governance also requires the consideration of the many alternative ways of formulating, framing and addressing the problems that the technology claims to solve. Many of these alternatives may carry fewer risks, may be more actionable in the short term, more sensitive to local needs and resources and/or may better align with a diverse range of worldviews. Crucially, many such alternatives emerge from a systems approach that considers the root of a problem, rather than simply addressing the current symptoms.

Therefore, as further detailed in Chapter 3 and 4, public engagement has to take place at the very beginning of the process, when funders, innovation stakeholders and researchers define what a problem is and set priorities for research and development. In the light of the many uncertainties regarding the "technological fix" of releasing GDOs into the environment, and its different levels of potential impact, free prior and informed consent of the peoples affected is indispensable. In this context "information" must not be reduced to promotion (see also Ch. 5). Good governance demands that actors reflect on how their values, interests and assumptions shape and inform their work. This enables divergent worldviews to be brought into the open, rather than being obscured by an overly narrow debate about human and environmental risk. Public debate on gene drives is needed, but it should not be framed by unsubstantiated and unrealistic claims about gene drives, nor by the assumption that gene drive technology will be accepted.

As addressed in various chapters, military funding is currently one of the largest resources for gene drive research, indicating that gene drives are being considered for use as offensive or defensive weapons. Due to the fact that they are intended to modify or eradicate species or populations, synthetic gene drives are inherently a dual-use technology, so gene drive research and development for civilian and military purposes cannot be separated. This dimension is crucial.

Chapter 5 explains the urgent need for effective international and legally binding regulation of GDOs. Offering a review of existing instruments and processes relevant to GDOs, it points out that current biosafety rules were established for previous GMOs and are therefore not fully equipped to manage the additional and unique risks of GDOs. The scope of the Convention on Biological Diversity (CBD) and its Protocols includes GDOs and its/these bodies have begun substantive work on the issue. Therefore the CBD and its Protocols are currently the best home for the international governance of GDOs. Legally binding governance arrangements at the international level are essential, but not yet in place. Therefore, in the interim, there should be no deliberate releases into the environment of GDOs. This must apply to field trials as well. Strict containment standards need to be applied to existing laboratory research. Monitoring and detection for unintentional releases and unintentional transboundary movements of GDOs have to be conducted. International rules for this period of constraint, as well as for liability and redress should there nevertheless be damage, must be operational and effective, including at national levels.

Concluding: In the current situation, strict application of the Precautionary Principle is the best guide when facing this new and potent technology. Given the high level of unpredictability, the lack of knowledge and the potentially severe negative impacts on biodiversity, ecosystems and agroecosystems, any release of GDOs must be placed on hold. Nor can it be assumed that it may be able to proceed in the future. Any eventual move towards deployment of this technology should only proceed once genuinely inclusive decision-making processes – including consideration of the ethics as well as alternative options - have been completed. It is also vital that technology assessment, additional risk assessment guidance and legally-binding governance structures are in place and that free, prior and informed consent for release has been obtained.