Briefing for CBD Delegates:

Synthetic Gene Drives – Genetic Engineering Gone Wild

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Building International Capacity in Synthetic Biology Assessment and Governance

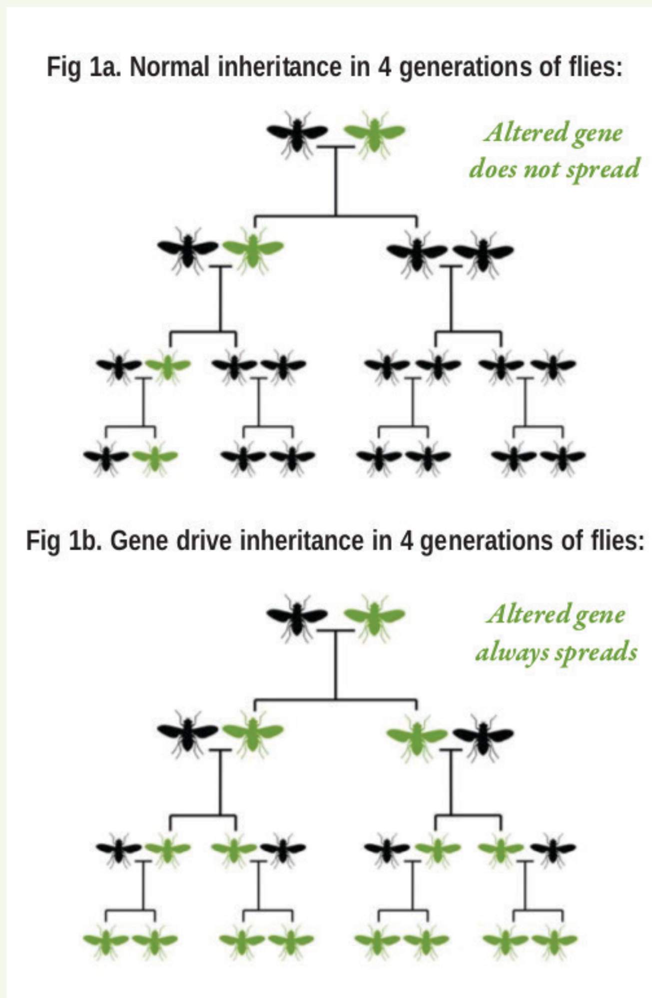
Briefing for CBD Delegates: Synthetic Gene Drives – Genetic Engineering Gone Wild

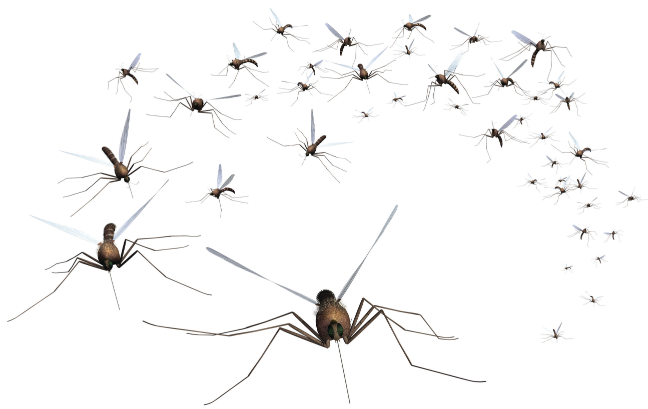
What are gene drives?

Gene Drives are a technique to engineer the genetics of entire populations. A gene drive is a genetic sequence that is meant to advantageously force itself (via sexual reproduction) through a population of organisms, passing on a particular trait to all or most offspring. This contrasts with the normal rules of inheritance where a new trait would ordinarily be diluted over time (see figure 1).

Mechanisms similar to gene drives may exist in nature. However, the advent of gene editing makes it possible to build human-designed, synthetic gene drives where a novel genetically engineered trait can be deliberately spread through an entire population by releasing only a handful of engineered organisms. There are now rapidly-advancing proposals to use synthetic gene drives to alter wild and domestic populations of insects, mammals, nematodes, fish and other species, which may impact ecosystems and biodiversity as well as agriculture, human security and conservation practice.

FIGURE 1: If a gene drive is designed to turn fruit flies yellow, after it is injected into one fruit fly the gene drive will force all of that fly's offspring to inherit and express this 'yellow' gene and reliably pass it on to their offspring. In time, the gene drive with the yellow fly trait will likely spread to the full population of fruit flies.





Introduction:

As the Convention on Biological Diversity (CBD) grapples with the implications of synthetic biology (next-generation genetic engineering), one of the most controversial and rapidly-developing areas of concern has been gene drives. To date, no working synthetic gene drive has been knowingly deployed in the environment. However, a series of successful 'proof of principle' experiments suggest that geneticists may have the tools to deliberately alter entire natural populations.[1] The near-term prospect of using gene drives shifts the practice of genetic engineering across significant ethical lines: it is now theoretically possible to bioengineer (or even drive to extinction) an entire natural population, and doing so involves genetically engineering species in the wild, not just in a laboratory.

Many researchers and policymakers have reacted to these new capabilities with caution, calling for strict controls and moratoria to be placed on the technology because of the ecological and social disruption a gene drive could unleash.[2] Others regard synthetic gene drives as a potential technological fix for long standing challenges in public health, conservation and agriculture. Military planners, too, are keen to understand this technology and potentially harness it for military uses.[3]

Today, the still-nascent gene drive technology already receives hundreds of millions of dollars of investment and its potential to be applied in the near-term is already influencing corporations, philanthropic organizations and governments. In the current cycle of negotiations at the Convention on Biological Diversity (CBD), governments of the world must address how to govern the technology of synthetic gene drives to best protect the natural world and ensure the conservation, sustainable use and equitable sharing of biodiversity.

A brief history of gene drives

For fifty years, a small community of researchers has been discussing how it may be theoretically possible to deliberately 'drive' a beneficial genetic trait into a natural population as a way to address problems of disease and invasive species.[4] In 2003, evolutionary geneticist Austin Burt first proposed using 'selfish' genetic elements called 'homing endonucleases' to create an engineered gene drive.[5]

However, it wasn't until the end of 2014 that two US-based teams of geneticists (from Boston and San Diego) separately managed to create working, self-sustaining gene drives using the newly-developed CRISPR-Cas9 gene editing platform.[6] These teams designed a system where the CRISPR-Cas9 system would copy itself into the genome of an organism to ensure that it was always inherited and expressed by the next generation, smuggling additional engineered traits along with it so that the trait cascaded from one generation to the next.

When Dr. Ethan Bier of University of California San Diego and his student Valentino Gantz first successfully turned a population of fruit flies yellow using a synthetic CRISPR-Cas9 gene drive, he recognized how disruptive this was to ordinary patterns of inheritance: "We were stunned," said Bier, "It was like the sun rose in the west rather than east"[7] He called the technique "the mutagenic chain reaction": one genetic change in a generation starts a chain reaction through future generations.[8] He also dubbed the field 'active genetics'. Meanwhile, a patent on CRISPR-mediated gene drives was filed by Dr. Kevin Esvelt of Massachusetts Institute of Technology.[9] The patent covered a wide range of uses in agriculture, vector disease management and conservation, signaling the wide ranging implications of the technique. Since these patents became public in early 2015, dozens of teams worldwide are now developing genetic applications based on CRISPR gene drives.

Key concepts

CRISPR-Cas9 Molecule Structure

Trait: In biological development, a trait refers to a physical characteristic (e.g. size, colour, behaviour) that is thought to be controlled in part by a genetic sequence or by the environment.

Genetic Extinction and Genetic Biocontrol: Gene drives have been popularly dubbed a 'Genetic Extinction Technology' because it may be possible for a suppression or elimination gene drive to eliminate an entire species (whether intentionally or by accident).[10] Proponents of these techniques prefer call gene drive led elimination strategies 'genetic biocontrol.'[11]

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats): CRISPR is a popular 'gene editing' approach based on a naturally occurring system found in bacteria. It has been adapted to edit any strand of DNA. Using an RNA 'guide,' a DNA-cutting enzyme called Cas9 'edits' the DNA by causing a break in the DNA at that location. The cell machinery repairs this break and can deletes or removes genes, change the DNA sequence, or add new DNA sequences.

Local and Global Drives: Given that gene drives may spread aggressively across space, some gene drive developers have speculated that it may be possible to limit, control or direct the spread of gene drives, creating 'local' or 'limited-spread' gene drives – for example, Kevin Esvelt's 'Daisy Drive' proposal is intended to stop 'driving' after a certain number of generations.[12] These 'local drives' are currently still theoretical. By contrast, gene drives that are not limited in their spread have been termed 'global' or 'self-perpetuating' drives.[13]

Mendelian inheritance and biased inheritance: In Mendel's Law of Inheritance, or ordinary inheritance, there is a notional 50% chance that a trait will be passed onto offspring. In time, this means a trait would likely be diluted in a population (see Figure 1). Gene drives attempt to bias inheritance so that there is closer to 100% chance that a trait will be passed on. That means a trait passed on by sexual reproduction will increase in a population instead of decreasing.

Gene Drive Resistance: Since synthetic gene drives were developed, it has been observed that the successful spread of gene drives from generation to generation may be tempered or even stopped by a phenomenon of gene drive resistance.[14] While mechanisms of resistance are still unclear, it looks most likely that natural processes of mutation within an organism's genome can interrupt the proper function of the gene drive or its trait and cause the gene drive to stop 'driving.' Because of this resistance, gene drives are even less likely to live up to their claimed uses.

How does a CRISPR Gene Drive work?

A standard RNA-guided CRISPR synthetic gene drive works by building a copy of the CRISPR system itself directly into the genetic code. A sequence of added DNA generates the CRISPR enzymes and a "guide" RNA that tells the CRISPR enzymes exactly where to cut. The CRISPR enzymes cut DNA on both alleles of the organism chromosomes and then insert a copy of the DNA strand that encodes the CRISPR machinery – thereby establishing the gene drive on both alleles of the organism and ensuring that it will always get passed on. The desired sequence is then built into the sequence for the CRISPR machinery as a sort of 'payload' (cargo) gene that also gets passed forward to the next generation. The payload gene encodes the trait required to push through the generations. In this way the gene drive and its payload gene cascade from one generation to the next.

Other Synthetic Gene Drive Approaches

While CRISPR-Cas9 gene drives are most well-known, there is not one single gene drive technology. Below are some other different approaches to gene drive currently being developed:

Engineered Underdominance – an engineered system where homozygous offspring are made more fit than heterozygous offspring and then a trait is piggybacked through homozygous offspring to spread through a population.[15]

Meiotic drive – a process that interferes with meiosis (cell division) to ensure that a certain allele is overrepresented and therefore preferentially selected – thereby overcoming mendelian inheritance.[16]

X-shredder – A modification that disables an x chromosome during meiosis thereby ensuring that only XY (male) offspring will be produced.[17]

Current state of gene drive technology

It has been over three years since the first working synthetic CRISPR gene drives using yeast and fruit flies were disclosed in the scientific literature.[18] Since then, CRISPR gene drives have been successfully incorporated (in the lab) into other insects, particularly mosquitos,[19] and teams are also building gene drive systems for mice,[20] rats and nematode worms (Caenorhabditis elegans).[21] Other approaches similar to gene drives are being tested in fish,[22] and teams are working on gene drives for agricultural pests.[23] All this is occurring long before oversight mechanisms have been developed.

An important characteristic of a successful gene drive system is that it can only work in host organisms that uses sexual reproduction and that have a rapid reproductive cycle. Humans and other mammals who only reproduce after about 20 years have too slow a reproductive cycle to spread a gene drive in the population in a practical way, although researchers could attempt to use gene drives to 'correct' inherited traits. To date, no working gene drives have been reported in plants, reptiles or mammals although these are theoretically possible.

Proposed applications of gene drives

Interest and funding for gene drives has so far been academic, philanthropic and military and has focused on applications intended for combatting vector-borne diseases and speculative conservation approaches. However, it is widely recognised that gene drives' most significant future uses may be in agriculture, fisheries, forestry and other economic sectors that rely on managing the natural world.[24]

Agriculture

Agriculture is the field where gene drives are most likely to end up being applied and although agribusiness companies are not publicly admitting to funding gene drive development, they are actively involved in discussions about the technology.[25] Current efforts to use synthetic gene drives in agriculture focus on pest eradication. The California Cherry Board is funding research on gene drives to eliminate Drosophila Suzukii, a fruit fly that attacks ripe soft fruit.[26] Teams at Texas A&M university

are developing gene drive mice as an attempt to avoid stored grains spoilage.[27] Others have proposed using a gene drive to prevent locusts from swarming,[28] red flour beetles from attacking grains, diamondback moths from attacking brassica crops[29] and honey bees to enhance pollination.[30]

A key patent on RNA-guided gene drives[31] extensively describes some of the ways that the use of gene drives in crop plants could be commercially harnessed:

Gene drives could be pushed into weed species to make those weeds more susceptible to common herbicides, attempting to overcome widespread herbicide resistance in monoculture systems – e.g. in Palmer Amaranth (pigweed) which is becoming resistant to Monsanto's glyphosate (RoundUp) weedkiller across North America.[32]

- Gene drives could be used to engineer new traits into crops more quickly – e.g. crops could be engineered to grow in new suboptimal environments by rapidly introducing 'climate ready,' stress-tolerant or virus-resistant genes.[33]
- Theoretically, weed and pest species could also be made susceptible to less toxic or biologically inert substances as future pesticides.
- Theoretically, pests may be 'reprogrammed' to avoid human crops or, in the case of pollinators, to be drawn towards crops to enhance pollination services on farmers fields.[34]
- Gene drives may also be used as a shortcut in animal breeding to more rapidly add new traits to agricultural species such as livestock.[35]
- It has been claimed that gene drives could theoretically be used to eradicate animals' ability to feel pain – presented as enabling pain-free, cruelty-free meat production.[36]

"In the future, gene drive could become a commonplace management technique for agribusiness, big or small, to edit the genome of the livings beings that hamper productivity. Given the lack of reliable modeling, it is safe to assume that normalizing the use of CRISPR-based gene drive could lead to an ecological cacophony: every interest group in the agro-food industry editing the genome of those they call pests, spreading various mutations through gene drive, and causing long-term effects on the ecological dynamics of ecosystems – and on the human populations depending on them.[37]

Vector-borne disease

The most high-profile promises made for synthetic gene drive systems involve proposals to suppress or eliminate species that carry human and animal diseases. Vector-borne diseases such as Malaria, Dengue, Zika , sleeping sickness, Lymes Disease or Schistosomiasis are typically carried by biting insects, mites or animal pests – e.g. mosquitoes, ticks and rats. Geneticists are experimenting with gene drives that will engineer these host organisms to disrupt the disease transmission cycle. Some gene drive projects, for example those run by Target Malaria of Imperial College in the UK, attempt to suppress or eradicate natural mosquito populations that carry malaria.[38] Others, such as work by Dr Anthony James of UC Riverside, attempt to engineer mosquitos so they are unable to carry the malaria parasite.[39] Others hope to make vector insects become repelled by human scent.[40] Gene drives may potentially be used not only to combat human vector-borne diseases but also zoonotic diseases affecting wild or domesticated animals (e.g. eliminating the New World Screwworm which afflicts cattle).[41]

Conservation

Some conservation organizations aggressively promote the speculative uses of gene drives for conservation purposes. Proponents claim that synthetic gene drives might be used to eliminate or suppress populations of invasive species or could be added to species close to extinction to help them survive environmental and disease stresses. One high profile project, GBIRd (Genetic Biocontrol of Invasive Rodents) is planning to release 'daughterless' gene drive mice onto islands in order to crash invasive mouse populations that are eating birds eggs or hunting other native fauna.[42] In Hawai'i, work is underway to explore using gene drives against culex mosquitoes that carry a parasite responsible for avian flu, a disease that is wiping out the culturally important and rare honeycreeper bird.[43] Other potential targets for gene drive-led eradication include brown tree snakes in Guam and Asian carp and other invasive fish in Australia and the US Great Lakes.[44]

Types of gene drives

Gene drive developers have imagined several types of gene drive applications. It is important to note that almost all of these are only theoretical.[45]

Global Drive: continues spreading until it affects a species globally.

Local Drive: only works for a limited time, geography or number of generations.

Reversal Drive: is released to undo the effects of a previous gene drive.

Sensitizing drive: renders an organism more sensitive to an external chemical or stress.

Suppression drive: reduces the numbers of an overall population.

Threshold drive: is effective when a certain number of gene drive organisms are released into a population.

Precision Drive: targets populations that display a specific genetic variation

'Daughterless' or sex-limiting gene drives: cause only male offspring to be born in order to tip the sex ratio of a population and cause it to collapse.

Who is driving (and funding) Gene Drives?:

Recently released emails from gene drive researchers at Texas A&M and North Carolina State University reveal that currently, the field of gene drive development is financially driven and structured by two major players: The Bill and Melinda Gates Foundation and the US Military's Defence Advanced Research Project Agency (DARPA).[46] Additionally, significant philanthropic bodies driving and shaping gene drive developments include The Tata Trusts,[47] Open Philanthropy Project (founded by Facebook co-founder Dustin Moskovitz) and the Foundation for the National Institutes of Health (FNIH).[48] Microsoft co-founder Paul Allen is also a significant funder.[49] The funders are mostly concentrated in the United States (with the exception of Tata Trusts who nonetheless spend their funds on US research). Funding for gene drive development currently exceeds a quarter of a billion US dollars.[50]

Funder	Recipient	Value (US $)
DARPA	Various projects including 'Safe Genes'	65-100 million
Gates Foundation	Target Malaria	75 million
Tata Trusts	Center for Active Genetics	70 million
Open Philanthropy Project	Target Malaria	17.5 million
Gates Foundation	Foundation for the National Institutes of Health	9.43 million
Gates Foundation	Massachusetts General Hospital Corporation	2.587 million
Open Philanthropy Project	NEPAD/African Union	2.35 million
Gates Foundation	Emerging Ag	1.6 million
Paul G Allen Frontiers Group	Center for Active Genetics	1.5 million
California Cherry Board	UC Riverside	500,000 so far (approx)
Maxmind	MIT and GW Univ (for Schistosomiasis)	100,000

Funding for gene drives research, in order of value

Thorny issues raised by gene drives

Biosafety threat and ecological risk: Significant threats to biodiversity

As novel organisms deliberately intended for environmental release, gene drives carry the same biosafety risks as other genetically engineered organisms (e.g. potential for unanticipated behaviours, traits and effects), and more. Previously, GMO developers have claimed that their novel organisms would not persist and spread beyond controlled use or cause significant change to wild ecosystems. By contrast, synthetic gene drives are designed expressly to spread and create large-scale changes in wild populations and to intentionally impact entire ecosystems. A high-profile study by leading gene drive developer Kevin Esvelt surveyed results from existing gene drive projects and concluded that gene drive organisms are likely to become invasive in wild populations: "The bottom line is that making a standard, self-propagating CRISPR-based gene drive system is likely equivalent to creating a new, highly invasive species," wrote Esvelt and his co-author. "Both will likely spread to any ecosystem in which they are viable, possibly causing ecological change.[51]"

Unlike agricultural GMOs where a farmer acquires new seed from season to season, gene drive organisms are expected to persist and pass on their modifications over several generations of wild species and would operate in poorly understood ecosystems with potentially wide geographical and ecological differences. It is not possible to assess the potential impacts gene drives may have on these different 'receiving environments' or to foresee how mutations might create unexpected traits that also emerge and spread.

Because synthetic gene drives harness the CRISPR gene editing system which has been observed to create unexpected 'off-target' effects, there is good reason to be concerned about unanticipated changes and mutations – this risk will reoccur anew with every generation as the CRISPR system will be continually re-employed, not in the lab but in the wild.[52]

Many of the current gene drive projects aim to eradicate or remove species. Removing a pest may seem attractive, but even pests have their place in the food chain. Eradicating one species might unpredictably open up space for the expansion of another species which may carry diseases, affect pollination or otherwise threaten biodiversity. Even removing the vector of a disease (e.g. a mosquito species) can push the disease into different hosts with health and ecological ramifications. There are many cautionary ecological lessons from previous 'biocontrol' experimentation. Gene drive developers have noted that if a gene drive is too successful at spreading, it could likely become an invasive organism in its own right.[53]

Food Security implications

It is likely that gene drive technology, if left unchecked, will assume importance in agricultural systems, with implications for food security and nutrition, as well as land rights and farmer sovereignty. A gene drive organism that enters a farmer's production and spreads (intentionally or otherwise) could affect harvests, pollinators, predation, on-farm biodiversity or could even be intentionally designed to suppress food production with implications for hunger, human rights and the realisation of sustainable ecological agriculture. Changes to the food web (including removing or redirecting pollinators) can also impact agricultural productivity. There are indications that large and small agribusiness companies (including Monsanto, Dow and Cibus) are taking an active interest in the technology[54] as are livestock breeders.[55] Gene drives could foreseeably be used to strengthen monopolies in the agricultural sector with negative effects on small farmers and peasants.

False Solutions: techno-fixing conservation and health

The proposals for gene drives, especially as an application for conservation – e.g. eradicating invasive species – comes as part of a wider move to seek simplistic 'breakthrough' or 'silver bullet' technological fixes to problems that are often rooted in more complex social, cultural, legal and economic causes. For example, the introduction of invasive species may follow from trade policies, exclusion of traditional community stewards from ancestral lands and unsustainable use of biodiversity by industrial actors. Real solutions to biodiversity challenges often lie in community-led conservation and development efforts that harness traditional knowledge to build cultural and economic resilience while restoring ecosystems.[56] Gene drives are an example of short circuiting the systemic changes required while leaving power imbalances in place. Gene drives do not spring from traditional knowledge systems of ecological management but from knowledge systems (e.g. synthetic biology) backed by monopoly protections.

Dual use – militarization of gene drives

In 2017, a classified study on gene drives was undertaken by the secretive US Military JASON group to understand the "potential threats this technology might pose in the hands of an adversary,"[57] and the international Bioweapons Convention has also been exploring the dual use implications of this technology.[58] Potential biowarfare uses of gene drives range from attacking food sources to weaponizing flying insects. One of the major backers of gene drive development is the US Defence Advanced Research Projects Agency (DARPA) who contribute US$65-100 million to bankroll some of the most high profile gene drive developers under a project called 'Safe Genes.[59]' While DARPA insist that their 'Safe Genes' project is purely defensive (aiming to be able to identify and disable hostile or rogue gene drives), it is concerning that the technology is being developed and driven from a militarized context. Particularly concerning are proposals for 'precision drives' that target 'locally fixed alleles' (specific mutations) and 'local drives' since these could better be weaponized to target certain populations, agricultural systems or ecosystems.[60]

Gene drives and the ENMOD treaty

"Environmental modification techniques" refers to any technique for changing – through the deliberate manipulation of natural processes – the dynamics, composition or structure of the Earth, including its biota." – 1977 ENMOD convention against hostile uses of environmental modification techniques.[61]

Because of their ability to re-shape ecosystems, gene drives could potentially fall under the 1977 ENMOD (Environmental Modification) treaty. While the treaty only forbids 'hostile use' of Environmental Modification, there is no clear guidance on what constitutes hostile use – in particular whether releasing a gene drive against a population without consent and with potentially adverse social, economic, cultural or biodiversity impacts should be considered hostile.

Human rights: Indigenous and Sovereign territories

Gene drives may pose significant challenges to the rights of nations as well as of Indigenous Peoples and Local Communities to determine their own territories and biodiversity. Because gene drives are designed to spread in nature, they do not respect national or other territorial borders. Article 32.1 of the UN Declaration of the Rights of Indigenous Peoples declares that:

> "States shall consult and cooperate in good faith with the Indigenous Peoples concerned through their own representative institutions in order to obtain their free and informed consent prior to the approval of any project affecting their lands or territories and other resources"[62]

The release of a gene drive which may spread into and impact indigenous territories will therefore require free prior and informed consent by all Peoples whose territories may be affected or else their rights are being infringed.

Ethics: Equity in engineering evolution?

The case of gene drives raises significant issues of equity and justice between groups of people and between generations. Gene drives are a high leverage technology where a single deliberate or accidental release in one place by one individual or group may intentionally reshape ecosystems and biology across many geographies and across time. As such, it is an exercise in power and developers of ecosystems are claiming the authority to redirect evolutionary development. If the removal or alteration of a species by a gene drive should have significant negative ecological or other impacts after several generations, there may be no means for those who experience loss to claim damages and those responsible may lay beyond liability. A far more basic ethical question concerns whether any humans have the right to deliberately intervene with evolutionary processes. Many cultures and worldviews, especially among traditional and indigenous societies, have strong taboos against playing with nature and regard protecting the ecological balances as a sacred duty.

Urgent questions

The field of synthetic gene drive development is still very immature and even basic questions about the technology are not settled:

Can synthetic gene drives be recalled or stopped from 'driving' once released?

Because synthetic CRISPR gene drives may continue spreading from generation to generation, an urgent question is whether gene drive mechanisms can be 'turned off' in the wild. At present there are no proven methods of creating "local," controllable gene drives or disabling a gene drive in the wild. Speculative proposals include developing 'reversal drives' where a second gene drive is released to disable the first gene drive but this proposal has been met with concern.[63] One of the aims of DARPA's Safe Gene's project is to explore if there may be technical means to limit or disable gene drives but that work is in a very early stage.[64]

Can Synthetic gene drives be safely field-tested?

Some advocate that gene drive organisms currently under development can be field tested through a 'stepwise approach' where tests move through different levels of containment and scales of trials and can be stopped or recalled at any step if problems emerge.[65] Unfortunately, the stepwise approach may be severely challenged at the point of environmental release since a gene drive organism may be designed to spread in populations and so there may be no useful distinction between 'small' and 'large' scale open release (a small release may spread to a larger release).

Is containment of gene drives possible?

International protocols for containment of gene drive organisms do not currently exist, although some authorities (Netherlands,[66] Australia[67]) have begin to specify the need for biocontainment levels for for such organisms. Other gene drive research may be proceeding under lower levels of containment.

Strict containment may need to fully isolate any individual gene drive organism from escaping to the environment and assume there is no 'threshold' for safe escape. Some gene drive advocates argue that geographic isolation is possible – e.g. on islands or in ecosystems where there are no species relatives in the wild that the gene drive trait could pass into. However, geographic isolation may not be secure for many species under consideration. For example, insects such as mosquitos can be carried thousands of miles by weather currents or human transport, while rats and mice move routinely between islands (e.g. by boat traffic) – indeed, that is how invasive species arrive in 'isolated' locations in the first place.

Can gene drives cross to other species?

It is possible that a gene drive construct could spread to closely related species through gene flow (interbreeding of neighbouring species)[68] – so, for example, a gene drive in an Asian carp may spread to other carp. It is less clear if gene drive constructs can jump between species by other means such as horizontal gene flow. This would require further investigation and may happen at too low a rate for detection. Whether and how gene drives would function in non-target species is a further question for investigation.

Will gene drives work? Will they breed resistance?

Gene drives may not work as effectively or precisely as proponents initially hoped. As with any living evolving organisms, gene drive organisms will mutate and change over time. Within barely a year of the invention of CRISPR gene drives, researchers working on mosquitos already witnessed the emergence of gene drive resistance as evolution selects mutations that disable or alter against the gene drive.[69] An early review in *Genetics* concluded that "resistance to standard CGD [CRISPR gene drive] approaches should evolve almost inevitably in most natural populations" unless specific strategies to overcome resistance were developed.[70] Researchers are now trying to design means to overcome resistance, rendering gene drives potentially more powerful and invasive.[71] gene drive mutations may potentially also change the nature of the trait that is driven through a population.

Governance of Synthetic gene drives – an accelerating controversy

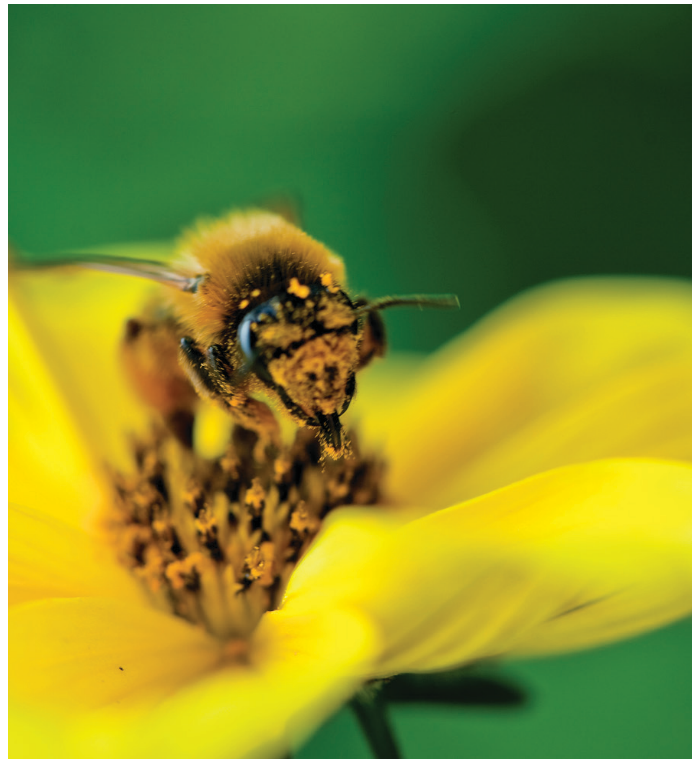
Given the significant impact that synthetic gene drives can have on biodiversity, food security and peace it is not surprising that the recent invention of this technology has been accompanied by fierce policy debate. In under three years from the first proof-of principle experiments the topic of gene drive governance has moved rapidly to the center of international biodiversity negotiations, with calls from over 170 organisations for a moratorium on gene drive release and experimentation.[72] Emails released under Freedom of Information laws show that key funders are now spending millions of dollars on a public relations and lobbying assault to prevent a moratorium.[73] A further $2.35 million have been awarded to the African Union's NEPAD for 'promoting the use of gene drives.'[74]

Governance gaps: the case for a moratorium

International Civil Society organisations are recommending that the UN Convention on Biological Diversity place an immediate moratorium on applied research, development and release of genetically engineered gene drives (including field trials).[75] They argue that some serious governance gaps must be addressed:

Inability to regulate the transboundary movement

There is no internationally agreed process for the effective governance of transboundary effects arising from the release of a gene drive. Since gene drives are likely to eventually spread across political boundaries, this is a very significant governance gap.[76] The CBD has previously recognised the environmental, cultural and human health risks posed by living organisms that are genetically modified (LMOs). Through the Cartagena Protocol on Biosafety,[77] the principle of prior informed consent has been established with respect to the transboundary movement of LMOs that are released into the environment. This puts a duty on a party exporting such an LMO to seek prior informed consent from the destination country. The procedures are designed to cover intended movement across the border of a single nation. They are clearly unsuited to the unrestricted flow of an gene drive organism, which is designed to spread in nature without respect for borders. As a



gene drive deliberately aims to change or remove species, and species range across political borders, transboundary effects will likely arise across multiple countries. If a gene drive was proposed for release in one country, it follows that all potentially affected countries would need to be taken into a process of advance joint consideration under new procedures that do not yet exist.

Containment

Gene drives are designed to persist and spread. While gene drive developers claim there may in the future be technical and geographical means to effectively contain gene drive organisms, these hypothetical claims and assumptions need to be rigorously examined and tested.[78] Strict laboratory handling and containment rules for all gene drive research should be internationally agreed upon and put into practice before further research can proceed even in the lab.

Monitoring, assessment and liability

Critical to any release proposal would be the development of internationally accepted procedures for not only monitoring and assessing impacts, but also tracking the spread of gene-drive constructs

in the wild. This would involve developing practical means to detect gene drive constructs in wild populations, obtaining agreement on the scope of effects that should be monitored and importantly, the methodologies to be used. Also verified means of removing and reversing gene drives in the wild would need to exist. Without detailed research into these topics, it is not practical to begin to frame agreements. Research is also needed into how responsibility for the costs of monitoring should be distributed and how liability rules would be framed including responsibility to remove and verify the removal of gene drives

Free, Prior and Informed consent

Besides the provisions of the Cartagena Protocol that requiring that parties should obtain prior informed consent before transboundary movement of a living modified organism that is released into the wild, there are additional duties placed upon states that could impact the invasion of gene drive organisms into the land and territories of Indigenous Peoples and local communities. The concept of free prior informed consent (FPIC) is one of the fundamental aspects enshrined in the UN Declaration on the Rights of Indigenous Peoples (see above).

This need to obtain FPIC for gene drive projects was explicitly flagged by the recent AHTEG on Synthetic Biology:

> *Given the current uncertainties regarding engineered gene drives, a precautionary approach and cooperation with all countries and stakeholders that could be affected, taking into account the need for the free, prior and informed consent of indigenous peoples and local communities, might be warranted in the development and release of organisms containing engineered gene drives, including experimental releases, in order to avoid potential significant and irreversible adverse effects to biodiversity. (Paragraph 25)*[79]

A timeline of gene drive policy to date	
July 2014	Oye et al. (2014) paper on 'Regulating gene drives' in *Science* raises policy challenges half a year before first working gene drives are developed.[80]
March 2015	Gantz and Bier (2015) publish first paper demonstrating working CRISPR gene drive.[81]
March 2015	UN CBD Technical Series No. 82 on Synthetic Biology warns that "Potential undesired consequences could result from the use of 'gene drive' systems."[82]
July 2015	US National Academy of Sciences for Engineering and Medicine (NASEM) announces its study on gene drive research in non-human organisms.
September 2015	CBD Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology identifies gene drives as both a potential risk and benefit to biodiversity.[83]
February 2016	Dutch GMO Agency RIVM publishes policy report on gene drives, noting insufficient risk assessment, the need for an international approach to governance and new legislation to prevent accidental gene drives.[84]
June 2016	US NASEM report, "Gene Drives on the Horizon" published and concludes gene drives are not ready to be released into environment and sets out series of policy recommendations.[85]
September 2016	30 leading environmentalists and conservationists issue statement calling for 'No Gene Drives in Conservation.'[86]
September 2016	International Union for Conservation of Nature (IUCN) passes a resolution that asks it to explore the implications of gene grives and to refrain from supporting or endorsing research, including field trials, into the use of gene drives until this assessment has been undertaken.[87]
December 2016	170 Civil Society organisations author a call for a moratorium on gene drive releases.[88]
December 2016	CBD COP13 decision on Synthetic Biology includes precautionary language asserting that decisions on synthetic biology apply to gene drive organisms.[89]
February 2017	The Norwegian Biotechnology Advisory Board recommends a moratorium on the use of gene drives until international regulations for handling and risk assessment are in place. The board is split on appropriateness of field trials but agree on need for formal international oversight.[90]
May 2017	Australian Academy of Sciences releases discussion paper, "Synthetic gene drives in Australia: implications of emerging technologies," which emphasises need for "stringent, multiple containment measures" for gene drive research.[91]
December 2017	Gene Drive Funders network publish proposed principles for gene drive Research in *Science*.[92]
December 2017	CBD Ad Hoc Technical Expert Group on Synthetic Biology issues report with highly precautionary language on gene drives. Notes that additional research and guidance needed before engineered gene drives could be considered for release into the environment, including into lands and territories of indigenous peoples and local communities. Also emphasizes need for precaution, free prior and informed consent, consultation, containment guidelines and other aspects.[93]

Endnotes

1 Valentino M. Gantz and Ethan Bier, “The Mutagenic Chain Reaction: A Method for Converting Heterozygous to Homozygous Mutations.” Science, vol. 348, no. 6233, 24 April 2015, pp. 442-444., science.sciencemag.org/content/348/6233/442.

2 ETC Group, “170 Global Groups Call for Moratorium on New Genetic Extinction Technology at UN Convention,” News Release, 5 December 2016, http://www.etcgroup.org/content/160-global-groups-call-moratorium-new-genetic-extinction-technology-un-convention

3 DARPA, “Safe Genes,” https://www.darpa.mil/program/safe-genes

4 Christopher Curtis, “Possible use of translocations to fix desirable genes in insect populations,” Nature, Vol. 218, No. 5129, 1968, pp. 368-369.

5 Austin Burt, “Site-Specific Selfish Genes as Tools for the Control and Genetic Engineering of Natural Populations.” Proceedings of the Royal Society B: Biological Sciences vol. 270 no. 1518, 7 May 2003, pp. 921-928.

6 Valentino M Gantz, Nijole Jasinskiene, Olga Tatarenkova, Aniko Fazekas, Vanessa M. Macias, Ethan Bier, and Anthony A. James, “Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi” Proceedings of the National Academy of Sciences, vol. 49 no. 112, 8 December 2015, http://www.pnas.org/content/112/49/E6736.

7 John Bohannon, “‚ÄòChain reaction‚Äô spreads gene through insects,” Science, 19 March 2015, http://www.sciencemag.org/news/2015/03/chain-reaction-spreads-gene-through-insects

8 Valentino M. Gantz and Ethan Bier, “The Mutagenic Chain Reaction: A Method for Converting Heterozygous to Homozygous Mutations.” Science, vol. 348, no. 6233, 24 April 2015, pp. 442-444., science.sciencemag.org/content/348/6233/442.

9 Esvelt et al, “Concerning RNA-guided gene drives for the alteration of wild populations,” eLife, Vol 3, 2014, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4117217/

10 ETC Group, “170 Global Groups Call for Moratorium on New Genetic Extinction Technology at UN Convention,” News Release, 5 December 2016, http://www.etcgroup.org/content/160-global-groups-call-moratorium-new-genetic-extinction-technology-un-convention

11 See: http://www.geneticbiocontrol.org/

12 Kevin Esvelt, “Daisy Drives,” Sculpting Evolution, http://www.sculptingevolution.org/daisydrives

13 Kevin Esvalt, “Gene Drive FAQ,” Sculpting Evolution, http://www.sculptingevolution.org/genedrives/genedrivefaq

14 Tina Seay, “Resistance to CRISPR gene drives may arise easily,” Science News, 20 July 2017, https://www.sciencenews.org/article/resistance-crispr-gene-drives-may-arise-easily

15 R. Guy Reeves Bryk J, Altrock PM, Denton JA, Reed FA, “First Steps towards Underdominant Genetic Transformation of Insect Populations,” PLOS ONE, Vol. 9, No. 5, 20 May 2014, https://doi.org/10.1371/journal.pone.0097557

16 John M. Marshall, Anna Buchman, H√©ctor M. S√°nchez C. and Omar S. Akbari, “Overcoming evolved resistance to population-suppressing homing-based gene drives” Scientific Reports, Vol. 7, No. 3776, 2017, https://www.nature.com/articles/s41598-017-02744-7

17 Jackson Champer, Anna Buchman and Omar S. Akbari, “Cheating evolution: engineering gene drives to manipulate the fate of wild populations” Nature Reviews, 2016, https://www.gene-drives.com/cheating-evolution.pdf

18 Valentino M. Gantz and Ethan Bier, “The Mutagenic Chain Reaction: A Method for Converting Heterozygous to Homozygous Mutations.” Science, vol. 348, no. 6233, 24 April 2015, pp. 442-444., science.sciencemag.org/content/348/6233/442.

19 Heidi Ledford and Ewen Callaway, “‚ÄòGene drive‚Äô mosquitoes engineered to fight malaria,” Nature, November 23rd 2015, https://www.nature.com/news/gene-drive-mosquitoes-engineered-to-fight-malaria-1.18858

20 See: http://www.geneticbiocontrol.org/

21 Kevin M Esvelt, “Gene Drive Systems in Nematode Worms,” Sculpting Evolution, http://www.sculptingevolution.org/genedrives/current/nematodes

22 PestSmart, “Daughterless Carp” https://www.pestsmart.org.au/wp-content/uploads/2013/03/CPFS2_daughterless.pdf

23 Raul F. Medina, “Gene drives and the management of agricultural pests,” Journal of Responsible Innovation, Vol. 5, No. 1, 2017, https://www.tandfonline.com/doi/full/10.1080/23299460.2017.1407913

24 Virginie Courtier-Orgogozo, Baptiste Morizot, and Christophe Bo√´te, “Agricultural pest control with CRISPR-based gene drive: time for public debate,” Science and Society, June 2017, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452019/

25 ETC Group, “Gene Drive Files Expose Leading Role of US Military in Gene Drive Development,” December 2017, http://genedrivefiles.synbiowatch.org/2017/12/01/us-military-gene-drive-development/

26 Antonio Regalado , “Farmers Seek to Deploy Powerful Gene Drive,” MIT Review, December 2017, https://www.technologyreview.com/s/609619/farmers-seek-to-deploy-powerful-gene-drive/

27 Caroline M. Leitschuh, Dona Kanavy, Gregory A. Backus, Rene X. Valdez, Megan Serr, Elizabeth A. Pitts, David Threadgill & John Godwin, “Developing gene drive technologies to eradicate invasive rodents from islands,” Journal of Responsible Innovation, Vol 5, sup1, 2017, https://www.tandfonline.com/doi/full/10.1080/23299460.2017.1365232?scroll=top&needAccess=true

28 Ed Ryder, “Knocking out odour receptor genes in locusts to prevent swarming,” Gene Editing, 6 November 2016, https://www.gene-editing.org/single-post/2016/11/05/Knocking-out-odor-receptor-genes-in-locusts-to-prevent-swarming

29 Kate Kelland, “Genetically modified diamondback moth offers pest control hope,” Reuters, 15 July 2015, https://www.reuters.com/article/us-science-moths-gmo/genetically-modified-diamondback-moth-offers-pest-control-hope-idUSKCN0PQ00120150716,

30 Plan Bee, https://genedrive.wordpress.com/author/genedrivebees/

31 Justia Patents, https://patents.justia.com/patent/20160333376

32 National Academies of Sciences, Engineering, and Medicine, “Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values,” 2016, http://nas-sites.org/gene-drives/

33 ETC Group, “Outsmarting Nature?: Synthetic Biology and Climate Smart Agriculture,” Communique no. 114, 26 Novemeber 2015, http://www.etcgroup.org/content/outsmarting-nature/report

34 Plan Bee, https://genedrive.wordpress.com/author/genedrivebees/

35 Serap Gonen, Janez Jenko, Gregor Gorjanc, Alan J. Mileham, C. Bruce A. Whitelaw and John M. Hickey, “Potential of gene drives with genome editing to increase genetic gain in livestock breeding programs,” Genetics Selection Evolution, 2017, https://gsejournal.biomedcentral.com/articles/10.1186/s12711-016-0280-3

36 David Pearce, https://www.gene-drives.com/

37 Virginie Courtier-Orgogozo, Baptiste Morizot, and Christophe Bo√´te, “Agricultural pest control with CRISPR‚Äêbased gene drive: time for public debate,” Science and Society, June 2017, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452019/

38 See: https://targetmalaria.org/

39 J.D Warren, “UC Riverside-led Team Wins $14.9 Million to Battle Disease-carrying Mosquitoes,” UCR Today, July 2017, https://ucrtoday.ucr.edu/48303

40 Phys.org, “Genetic engineering alters mosquitoes‚Äô sense of smell” https://phys.org/news/2013-05-genetic-mosquitoes.html

41 John Min, Andrea L. Smidler, Devora Najjar & Kevin M. Esvelt, “ Harnessing gene drive,” Journal of Responsible Innovation, December 2017.

42 See: http://www.geneticbiocontrol.org/

43 Antonio Regalado, “The Plan to Rescue Hawaii‚Äôs Birds with Genetic Engineering,” MIT Review, May 2016, https://www.technologyreview.com/s/601383/the-plan-to-rescue-hawaiis-birds-with-genetic-engineering/

44 Revive and Restore, http://reviverestore.org/

45 Kevin Esvelt, Gene Drive Q&A, http://www.sculptingevolution.org/genedrives/genedrivefaq

46 ETC Group, “Gene Drive Files,” http://genedrivefiles.synbiowatch.org/

47 Garby Robbins and Bradley J. Kijes, “India‚Äôs Tata gives UCSD $70M in hot area of genetics,” San Diego Union Tribune, October 2016, http://www.sandiegouniontribune.com/news/science/sd-me-tata-gift-20161018-story.html

48 “Foundation for the National Institutes of Health ‚Äî Working Group on Malaria Gene Drive Testing Path,” July 2016

49 Sharon Begely, “Billionaire Paul Allen bets $100 million on risky scientific research,” March 2016, https://www.statnews.com/2016/03/23/paul-allen-scientific-research/

50 ETC Group, Gene Drive Files, http://genedrivefiles.synbiowatch.org/

51 Kevin M. Esvelt , Neil J. Gemmell, “Conservation demands safe gene drive,” PLOS Biology, November 2017, https://doi.org/10.1371/journal.pbio.2003850

52 European Network of Scientists for Social and Environmental Responsibility, “ENSSER Statement on New Genetic Modification Techniques: products of new genetic modification techniques should be strictly regulated as GMOs,” 27 September 2017, https://ensser.org/topics/increasing-public-information/ngmt-statement/

53 Kevin M. Esvelt , Neil J. Gemmell, “Conservation demands safe gene drive,” PLOS Biology, November 2017, https://doi.org/10.1371/journal.pbio.2003850

54 ETC Group, Gene Drive Files

55 Amy Harmon, “Open Season is seen in Gene Editing of Animals,” New York Times, https://www.nytimes.com/2015/11/27/us/2015-11-27-us-animal-gene-editing.html

56 ETC Group, “Who Will Feed Us?,” October 2017, http://www.etcgroup.org/whowillfeedus

57 “DARPA Safe Genes Press Release,” The Gene Drive Files, http://genedrivefiles.synbiowatch.org/

58 Kenneth A. Oye, “On Regulating Gene Drives: A New Technology for Engineering Populations in the Wild,” Presentation to UN Biological Weapons Convention Meeting of Experts Session 4 : Science and Technology Developments, August 2014, https://www.unog.ch/80256EDD006B8954/(httpAssets)/AF55C5956B5C771DC1257D2C00554383/$file/BWC+MX+2014+-+Presentation+-+Regulating+Gene+Drives.pdf

59 DARPA, “Safe Genes,” https://www.darpa.mil/program/safe-genes

60 ETC Group, Gene Drive Files, http://genedrivefiles.synbiowatch.org/page/2/?s=locally+fixed+alleles

61 “Convention on the Prohibition of Military or Any Other Hostile Use of Environmental Modification Techniques” http://www.un-documents.net/enmod.htm

62 UN Declaration on the Rights of Indigenous Peoples, p.15, http://www.un.org/esa/socdev/unpfii/documents/DRIPS_en.pdf

63 Michael Vella et al, “Evaluating Strategies for reversing CRISPR-Cas9 gene drives,” Scientific Reports, Vol. 7, No. 11038, 2017, https://www.nature.com/articles/s41598-017-10633-2

64 DARPA, “Building the Safe Genes Toolkit,” Web page, July 2017, https://www.darpa.mil/news-events/2017-07-19

65 National Academies of Sciences, Engineering, and Medicine, “Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values,” 2016, http://nas-sites.org/gene-drives/

66 J. Westra et al, “Gene Drives: Policy Report,” RIVM Letter report 2016-0023, National Institute for Public Health and the Environment, 2016, https://rivm.openrepository.com/rivm/bitstream/10029/596002/3/2016-0023.pdf

67 Australian Academy of Science, “Synthetic Gene Drives in Australia: Implications of Emerging Technologies,” Discussion Paper, May 2017, https://www.science.org.au/files/userfiles/support/documents/gene-drives-discussion-paper-june2017.pdf

68 National Academies of Sciences, Engineering, and Medicine, “Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values,” 2016, http://nas-sites.org/gene-drives/

69 Ewen Callaway, “Gene drives thwarted by emergence of resistance organisms,” Nature News, 31 January 2017, https://www.nature.com/news/gene-drives-thwarted-by-emergence-of-resistant-organisms-1.21397

70 RL Unckless et al, “Evolution of Resistance Against CRISPR/Cas9 Gene Drive, “ Genetics, Vol. 205, No. 2, February 2017, pp. 827-841. https://www.ncbi.nlm.nih.gov/m/pubmed/27941126/

71 John M. Marshall et al, “Overcoming evolved resistance to population-suppressing homing-based gene drives,” Scientific Reports, Vol. 7, 19 June 2017, https://www.nature.com/articles/s41598-017-02744-7

72 ETC Group, “170 Global Groups Call for Moratorium on New Genetic Extinction Technology at UN Convention” http://www.etcgroup.org/content/160-global-groups-call-moratorium-new-genetic-extinction-technology-un-convention

73 ETC Group, Gene Drive Files, http://genedrivefiles.synbiowatch.org/

74 “Towards Zero Malaria by 2030: Biological control of mosquitoes,” NEPAD, May 2017, http://www.nepad.org/content/towards-zero-malaria-2030-biological-control-mosquitoes

75 ETC Group, “170 Global Groups Call for Moratorium on New Genetic Extinction Technology at UN Convention” http://www.etcgroup.org/content/160-global-groups-call-moratorium-new-genetic-extinction-technology-un-convention

76 National Academies of Sciences, Engineering, and Medicine, “Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values,” 2016, http://nas-sites.org/gene-drives/

77 See: https://bch.cbd.int/protocol

78 Kevin Esvelt, “Daisy Drives,” Sculpting Evolution, http://www.sculptingevolution.org/daisydrives

79 Report of The Ad Hoc Technical Expert Group On Synthetic Biology Montreal, Canada, 5-8 December 2017, p. 5, https://www.cbd.int/doc/c/aa10/9160/6c3fcedf265dbee686715016/synbio-ahteg-2017-01-03-en.pdf

80 Oye et al, “Regulating Gene Drives,” Science, July 2014, http://science.sciencemag.org/content/early/2014/07/16/science.1254287/tab-pdf

81 Valentino M. Gantz and Ethan Bier, “The mutagenic chain reaction: a method for converting heterozygous to homozygous mutations.” Science, Vol. 348, No. 6233, December 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687737/

82 Secretariat of the Convention on Biological Diversity, Synthetic Biology, Montreal, Technical Series No. 82, 2015, https://www.cbd.int/doc/publications/cbd-ts-82-en.pdf

83 Ad Hoc Technical Expert Group on Synthetic Biology, “Report of the AHTEG,” Montreal, Canada, 21-25 September 2015, https://www.cbd.int/doc/meetings/synbio/synbioahteg-2015-01/official/synbioahteg-2015-01-03-en.pdf

84 J. Westra et al, “Gene Drives: Policy Report,” RIVM Letter report 2016-0023, National Institute for Public Health and the Environment, 2016, https://rivm.openrepository.com/rivm/bitstream/10029/596002/3/2016-0023.pdf

85 National Academies of Sciences, Engineering, and Medicine, "Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values," 2016, http://nas-sites.org/gene-drives/

86 ETC Group, "30 Environmental Leaders say ‚ÄòNo!‚Äô to Gene Drives in Conservation," News release, 1 September 2016, http://www.etcgroup.org/content/30-environmental-leaders-say-no-gene-drives-conservation

87 Synbiowatch.org, "Genetic Extinction Technology rejected by international group of scientists, conservationists and environmental advocates," News Release, 1 September 2016, http://www.synbiowatch.org/gene-drives-iucn-pr/

88 ETC Group, "170 Global Groups Call for Moratorium on New Genetic Extinction Technology at UN Convention," News Release, 5 December 2016, http://www.etcgroup.org/content/160-global-groups-call-moratorium-new-genetic-extinction-technology-un-convention

89 ETC Group, "Four Steps Forward, One Leap Back on Global Governance of Synthetic Biology," News release, 19 December 2016, http://www.etcgroup.org/content/four-steps-forward-one-leap-back-global-governance-synthetic-biology

90 The Norwegian Biotechnology Advisory Board, "Statement on Gene Drives," 14 February 2017, http://www.bioteknologiradet.no/filarkiv/2017/02/Statement-on-gene-drives.pdf

91 Australian Academy of Science, "Synthetic Gene Drives in Australia: Implications of Emerging Technologies," Discussion Paper, May 2017, https://www.science.org.au/files/userfiles/support/documents/gene-drives-discussion-paper-june2017.pdf

92 Claudia Emerson et al, "Principles for Gene Drive Research," Science, Vol. 358, No. 6367, 1 December 2017, http://science.sciencemag.org/content/358/6367/1135

93 The AHTEG report on Synthetic Biology is available here: https://www.cbd.int/doc/c/aa10/9160/6c3fcedf265dbee686715016/synbio-ahteg-2017-01-03-en.pdf?download.