## Issue Brief<sup>1</sup>

Issue Title	Development of engineered gene drives to control vector-
	borne diseases and invasive species
Description	Engineered open drives are angineered melopular machanisme
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	that are transmitted to progeny at super-Mendelian ( $>50\%$ )
	frequencies. There are various types of engineered gene drives,
	but many utilize CRISPR-Cas. Other mechanisms can include
	toxin-antidote systems and endonucleases, among others.
	Applications of engineered gene drives can be designed to
	suppress vectors of human and animal disease and to control
	invasive species. These are designed as alternative vector-
	control measures to conventional insecticide or rodenticide
	applications. Specific applications include:
	• Living modified Anopheles gambiae containing an engineered
	gene drive designed to target <i>doublesex</i> to reduce malaria
	transmission
	• Living modified Aedes aegyptii to reduce malaria transmission
	• Living modified <i>Culex sp.</i> mosquitoes to control West Nile
	virus transmission
	• Engineered gene drive rodents to control invasive rodents
	on islands
Timeline (<5 years, 5-10	Field trials within 5 years, or between 5 and 10 years. Releases
years, >10 years) to	for vector control suggested to be within 3 to 5 years, and
environmental release	within 5 to 10 years for controlling invasive species.

<sup>&</sup>lt;sup>1</sup> Information gathered from the members of the multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology. Descriptions complemented with publications published by the Secretariat of the Convention on Biological Diversity.

Potential impacts on the	Potential positive impacts could include:
objectives of the	• Controlling invasive species (reduced damage to native
Convention	biodiversity)
	• Reduced disease transmission, particularly for vulnerable,
	disproportionately affected communities
	• Increased access to resources and opportunities through a
	reduction in disease burden
	Potential negative impacts could include:
	• Disruption of ecosystems (e.g., food webs) due to removal
	or suppression of a species from the environment
	• Elimination of an endogenous species if the living modified
	organism containing an engineered gene drive spreads to
	native range of the host organism
	• Elimination or suppression of non-target organisms due to
	gene flow
	• Unintended persistence in the environment
	Off-target impacts within host organism
	• Transboundary movements
	• Reduction in genetic diversity (e.g., potential increased
	disease susceptibility, decreased ability of target organism to
	adapt to environment)
	• Niche replacement could bring new pathogens
	Potential points of consideration that may lead to a high level
	of uncertainty for the risk assessment of these applications:
	• Complexity of ecological systems, particularly when released
	into unmanaged or wild environments
	• Spatio-temporal scale of release of engineered gene (e.g.,
	reproduction rate, genotypic replacement, design to spread)

<ul> <li>Long term stability and evolution of the molecular system         <ul> <li>(e.g., mutation rate)</li> <li>Evolutionary response to deployment of engineered gene drive</li> <li>Host-pathogen response</li> <li>Next-generation effects</li> <li>Unforeseen impacts</li> <li>Potential extrapolation error of experimental data to environmental conditions in models</li> </ul> </li> <li>Other considerations         <ul> <li>Precautionary principle</li> <li>Monitoring for the potential emergence of unintended consequences</li> <li>Access to and sharing the benefits of the technology</li> <li>Improved human sustainable development and quality of life through a reduction in disease and economic burden</li> </ul> </li> </ul>
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• Changes to local economies due to reduced presence of an
invasive pest or disease vector
Reduction in economic loss due to pest outbreaks
• Intellectual property of the technology and access to its use
Concentration of the market to few biotechnological
organizations
• Free, prior and informed consent of indigenous peoples and
local communities
• Potential changes to traditional methods and communities
managing biological resources
• Impacts to traditional knowledge and spiritual beliefs of
indigenous peoples and local communities
• Ethics related to human intervention in nature
• Public outreach, engagement and inclusion
• Transparency in research, development and decision-making,
including declarations of conflict of interest

Consideration of alternative interventions
Precautionary approach
• Need for effective regulation and risk assessment
• Potential lack of available risk management and containment
measures (e.g., potential irreversibility of release)
• Need for monitoring
• Improved capacity-building for the regulation and potential
use of the technology
• Technology transfer
• Transboundary movements and the likely need for
international cooperation
Dual-use potential
• Consideration of the social, political and commercial
determinant of disease with respect to the potential costs and
benefits