European Parliament

STOA workshop

The science and ethics of gene drive technology

Case study: Eradicating malaria

Participants' booklet

EPRS | European Parliamentary Research Service

Scientific Foresight Unit (STOA)

PE 634.426 – 19 March 2019

EN

The science and ethics of gene drive technology

Case study: Eradicating malaria

Participants' booklet

19 March 2019, 08:00-09:30

Paul-Henri Spaak Building, Room PHS 7-F387

European Parliament, Brussels

Prepared by Lieve Van Woensel and Jens Van Steerteghem, Scientific Foresight Unit (STOA)

Available at http://www.europarl.europa.eu/stoa/en/events/farming-without-agro-chemicals

Join the conversation on Twitter by using the hashtag **#GeneDriveSTOA** and by tweeting at **@EP_ScienceTech**

Table of contents

1. A debate on the case of using gene drive technology for eradicating malaria

Malaria is a terrible burden on humanity, causing suffering for approximately 200 million people per year globally and the death of more than 400 000, more than half of which are children aged under 5 years. It is troubling is that there seems to be no significant decrease in these numbers. The funds required to fight malaria have been predicted to rise from $5.1 billion per year in 2017 to $9 billion per year by 2030, whereas the funds actually available in 2017 reached only $3.1 billion. This makes it crucial that new tools will be developed.

'Gene drive' is such a tool. It drive is a genetic technology that can suppress mosquito populations that transmit malaria and therefore reduce the incidence of malaria. It can do this in several ways, but one way is through the manipulation of the sex ratio of the mosquito population. A genetic mechanism is introduced into a wild population by genetically engineering a group of starter-mosquitoes that will spread the genetic mechanism. The system causes all offspring to be males that carry that same mechanism, causing their offspring to be males as well. Soon, the whole population (or most of it) will be males and will consequently reduce in size.

While this technology has potential in fighting malaria, it is the subject of an often-polarised debate. Gene drive is not ready yet for deployment and it will take several years more before it is. This makes it an interesting subject for a scientific foresight study and STOA has performed a preliminary analysis in that direction, which is intended to serve as background for a debate in this event.

The event will start with a presentation of the results of the preliminary scientific foresight analysis of gene drive technology, so to be followed by a panel discussion on the technology and the concerns and opportunities linked to it, as well as on how risks could be assessed.

2. Programme

8:00 **Introduction**

- **Kay SWINBURNE**, MEP, STOA Panel member and workshop chair

8:10 **Project presentation**

- **Jens VAN STEERTEGHEM**, KU Leuven*

8:25 **Panel presentations**

- **Delphine THIZY,** Stakeholder Engagement Manager, Target Malaria
- **Philip Bob JUSU**, representing Ambassador Awad SAKINE, African Union (cancelled)
- **Sybille VAN DEN HOVE**, independent expert on the precautionary principle, Bridging for Sustainability SPRL

8:45 **Discussion**

9:20 **Closing remarks**

(*) Former trainee (until 28 February 2019) in Scientific Foresight Unit (STOA)

3. Speakers' biographies

3.1. Kay SWINBURNE, MEP, STOA Panel member and workshop chair

Kay SWINBURNE MEP is Vice-Chair of the European Parliament's Economic and Monetary Affairs Committee (ECON) and has shaped numerous pieces of European financial services legislation including the EMIR, MiFID II, CSDR and Banking Union files. In 2016, Kay was recognised as one of the most influential women in finance by Financial News.

Kay has been a rapporteur or shadow rapporteur on numerous legislative files covering market structure reform, reporting, settlement the recovery and resolution of CCPs, market abuse and OTC derivatives, and, through close US ties, provides a bridge for the ECON Committee to US regulators at the CFTC, SEC, and US Treasury.

Prior to her political career, she worked as an Investment Banker at a large global firm concentrating on corporate finance and M&A for the pharmaceutical and biotech sectors and as a Fund Manager advising on Biotechnology Investment.

3.2. Jens VAN STEERTEGHEM

Jens VAN STEERTEGHEM is currently a Master of Philosophy student at the University of Leuven (KU Leuven). Here, he previously obtained the degrees of Master of Biotechnology and Biochemistry and Bachelor of Philosophy, graduating summa cum laude for both. His interests are in the philosophy and history of science and technology in general, and physics in particular. In his spare time, he studies physics and reads on a wide range of topics. As former trainee at the Scientific Foresight Unit (STOA), Jens was in charge of coordinating and writing the technical part of the background note on the science and ethics of gene drive (case study: eradicating malaria).

3.3. Delphine THIZY

Delphine THIZY is the Stakeholder Engagement Manager of Target Malaria, a non-for-profit research consortium composed of 14 institutions across 3 continents aimed at developing and sharing an innovative vector control tool to save millions of lives from malaria in sub-Saharan Africa. She has over 10 years' experience in the field of stakeholder engagement in lower-income countries, with a particular attention to conflict drivers.

After receiving her Master's Degree in Economic development studies and project management from the Pierre Mendes University in Grenoble, France, she worked in advocacy for Palestinian farmers' rights before holding several positions within PlaNet Finance in the Middle East and South Asia. There she was responsible for technical assistance to microfinance institutions in post-conflict countries as well as leading a team for capacity strengthening of various civil society groups.

Afterwards she joined a consultancy company, Channel Research, specialising on social impact of projects. In that role she conducted a number of project evaluations in the field of humanitarian aid and development for a variety of donors and organisations – including the European Commission, members of the Red Cross and Red Crescent Movement and private foundations. After creating her own consultancy company, she specialised in social performance and stakeholder engagement for infrastructure and extractive industries. She led several teams for large social impact assessments across Africa.

In 2014, she joined Target Malaria as the Stakeholder Engagement Manager and works with teams in Burkina Faso, Ghana, Mali and Uganda, as well as, at the global level to engage stakeholders to co-develop and share an innovative long-term, sustainable and cost-effective vector control tool using genetic technologies to modify mosquitoes and reduce malaria transmission.

3.4. Sybille VAN DEN HOVE

Sybille VAN DEN HOVE is Executive Director of Bridging for Sustainability, a small research and consulting company in Belgium. She has B.A. in particle physics and a PhD in ecological economics. Her research focuses on environmental governance; science-policy interfaces; decision-making and policy formation under conditions of complexity; integration of natural and social sciences; environmental research strategies; and environmental strategies of corporations. Sybille mostly works in the areas of precaution and innovation, biodiversity governance at EU and international levels, and business sustainability. She is a former Chair of the Scientific Committee of the European Environment Agency (EEA). She is a member of the Board of Directors of Ion Beam Applications (IBA s.a.) and a member of several advisory committees in the field of sustainability. She was in the editorial team of the 2013 EEA report 'Late Lessons from Early Warnings: Science, Precaution, Innovation'. Since 2015, Sybille is the initiator and co-organiser, with EEA and Central European University, of a yearly Summer School on the Precautionary Principle in Budapest, Hungary

4. About STOA

4.1. Mission

The Panel for the Future of Science and Technology (STOA) forms an integral part of the structure of the European Parliament. Launched in 1987, STOA is tasked with identifying and independently assessing the impact of new and emerging science and technologies.

The goal of its work is to assist, with independent information, the Members of the European Parliament (MEPs) in developing options for long-term, strategic policy-making.

The STOA Panel

The STOA Panel consists of 25 MEPs nominated from the nine permanent parliamentary committees: AGRI (Agriculture & Rural Development), CULT (Culture & Education), EMPL (Employment & Social Affairs), ENVI (Environment, Public Health & Food Safety), IMCO (Internal Market & Consumer Protection), ITRE (Industry, Research & Energy), JURI (Legal Affairs), LIBE (Civil Liberties, Justice and Home Affairs) and TRAN (Transport & Tourism).

Ramón Luis VALCÁRCEL SISO MEP is the European Parliament Vice-President responsible for STOA for the second half of the 8th legislature. The STOA Chair for the second half of the 8th legislature is Eva KAILI with Paul RÜBIG and Evžen TOŠENOVSKÝ elected as 1st and 2nd Vice-Chairs respectively.

The STOA approach

STOA fulfils its mission primarily by carrying out science-based projects. Whilst undertaking these projects, STOA assesses the widest possible range of options to support evidence-based policy decisions. A typical project investigates the impacts of both existing and emerging technology options and presents these in the form of studies and options briefs. These are publicly available for download via the STOA website: www.europarl.europa.eu/stoa/.

Some of STOA's projects explore the long-term impacts of future techno-scientific trends, with the aim to support MEPs in anticipating the consequences of developments in science. Alongside its production of 'hard information', STOA communicates its findings to the European Parliament by organising public events throughout the year. STOA also runs the MEP-Scientist Pairing Scheme aimed at promoting mutual understanding and facilitating the establishment of lasting links between the scientific and policy-making communities.

Focus areas

STOA activities and products are varied and are designed to cover as wide a range of scientific and technological topics as possible, such as nano-safety, e-Democracy, bio-engineering, assistive technologies for people with disabilities, waste management, cybersecurity, smart energy grids, responsible research & innovation, sustainable agriculture and health.

They are grouped in five broad focus areas: eco-efficient transport and modern energy solutions; sustainable management of natural resources; potential and challenges of the Internet; health and life sciences; science policy, communication and global networking.

ESMH

The European Science-Media Hub (ESMH), operating under the political responsibility of the STOA Panel, is a new platform to promote networking, training and knowledge sharing between the European Parliament, the scientific community and the media. The ESMH creates a network among policy-makers, scientists and media involving science, academia, educational and research entities, professional associations of journalists and scientists.

For journalists and media representatives, the ESMH organises training and workshops on current technological developments, both as subjects of their reporting and as means of facilitating their work. Via media monitoring and media intelligence tools, the ESMH follows the most popular topics in the field of science and technology on different platforms including magazines, newspapers and social media.

The ESMH will make information available to journalists, other media and citizens about new scientific developments, as well as about scientific topics that attract media attention and promote information based on evidence.

4.2. STOA Bureau

Ramón Luis VALCÁRCEL SISO
(EPP, ES)
EP Vice-President responsible for STOA

Eva KAILI (S&D, EL)
Chair of STOA

Committee on Industry, Research and Energy
(ITRE)

Paul RÜBIG (EPP, AT)
First Vice-Chair of STOA

Committee on Industry, Research and Energy
(ITRE)

Evžen TOŠENOVSKÝ (ECR, CZ)
Second Vice-Chair of STOA

Committee on Industry, Research and Energy
(ITRE)

4.3. STOA Panel members

Tiziana **BEGHIN**
(EFDD, IT)

EMPL Committee

Michał **BONI**
(EPP, PL)

LIBE *Committee*

*Renata **BRIANO***
(S&D, IT)

ENVI Committee

Carlos **COELHO**
(PPE, PT)

IMCO Committee

Mady **DELVAUX**
(S&D, LU)

JURI Committee

Christian **EHLER**
(EPP, DE)

ITRE Committee

Maria Teresa **GIMÉNEZ BARBAT**
(ADLE, ES)

CULT Committee

Andrzej **GRZYB**
(EPP, PL)

ENVI Committee

Danuta **JAZŁOWIECKA**
(EPP, PL)

EMPL Committee

Jan **KELLER**
(S&D, CZ)

EMPL Committee

Bogusław **LIBERADZKI**
(S&D, PL)

TRAN Committee

Anthea **McINTYRE**
(ECR, UK)

AGRI Committee

Momchil **NEKOV**
(S&D, BG)

AGRI Committee

Marijana **PETIR**
(EPP, HR)

AGRI Committee

Michèle **RIVASI**
(Greens/EFA, FR)

ITRE Committee

Virginie **ROZIERE**
(S&D, FR)

IMCO Committee

Claudia **SCHMIDT**
(EPP, AT)

TRAN Committee

Kay **SWINBURNE**
(ECR, UK)

ENVI Committee

Neoklis **SYLIKIOTIS**
(GUE/NGL, CY)

ITRE Committee

Anneleen **VAN BOSSUYT**
(ECR, BE)

IMCO Committee

Kosma **ZŁOTOWSKI**
(ECR, PL)

TRAN Committee

Parliamentary Committees:
AGRI: Agriculture and Rural Development
CULT: Culture and Education
EMPL: Employment and Social Affairs
ENVI: Environment, Public Health and Food Safety
IMCO: Internal Market and Consumer Protection
ITRE: Industry, Research and Energy
JURI: Legal Affairs
TRAN: Transport and Tourism

4.4. STOA Administration

Directorate-General for Parliamentary Research Services (DG EPRS)
European Parliament
Rue Wiertz 60
B-1047 Brussels
E-mail: stoa@europarl.europa.eu

Director-General
Anthony TEASDALE

Director
Wolfgang HILLER

Head of Unit - Scientific Foresight Unit (STOA)
Theo KARAPIPERIS

STOA Secretariat
Zsolt G. PATAKI, Head of Service
Mihalis KRITIKOS
Nera KULJANIĆ
Gianluca QUAGLIO

Scientific Foresight Service
Lieve VAN WOENSEL, Head of Service
Philip BOUCHER
Christian KURRER

European Science-Media Hub (ESMH)
Svetla TANOVA, Coordinator
Vitalba CRIVELLO
Eszter FAY
Silvia POLIDORI

Assistants
Emilia BANDEIRA MORAIS
Serge EVRARD
Rachel MANIRAMBONA
Vanda NOBRE DA SILVA
Damir PLEŠE

Trainee
Richelle BOONE

5. Background Note

The science and ethics of gene drive technology
A preliminary foresight analysis

Background Note

The science and ethics of gene drive technology

Case study: Eradicating malaria

A preliminary foresight analysis

In 2017, the World Health Organisation (WHO) reported 219 million malaria cases globally. A promising new tool in the fight against malaria is 'gene drive', a genetic technology with the capacity to suppress malaria by suppressing malaria-transmitting mosquito populations.

This background note looks at this technology and its possible impacts, including unintended ones, using a foresight approach within a very short time frame. It concludes that a foresight process is an appropriate tool to unravel the complexity of a complicated technology with inherent uncertainties. Despite these uncertainties, continued research into gene drive, as applied to malaria, was deemed important by study participants.

An overall outcome of this note regarding future scientific advice on a specific biotechnology is that there is a need for a general framework for risk assessment of technology.

AUTHORS

Jens Van Steerteghem, KULeuven[1], Lieve Van Woensel, Scientific Foresight Unit (STOA)

ACKNOWLEDMENTS

The experts that contributed to the scientific briefing: Austin Burt, Andrea Crisanti, Delphine Clotilde Thizy, Camilla Beech, Fabio Niespolo, Piet van der Meer, Anna-Pia, René Custers, Suresh Subramani, Karen Tountas, Stephanie James. Also all participants to the Foresight brainstorming.

[1] Former trainee at the Scientific Foresight Unit, until 28 February 2019

Executive summary

Foresight is a valuable approach for the European Parliament to anticipate the impact of disruptive and uncertain technological changes, such as biotechnology, on society. This background note has been conducted as a preliminary analysis for a future foresight project on a technology that holds promise for the fight against malaria and is the subject of an often-polarised debate – gene drive. This is a genetic technology that can reduce the population of malaria-transmitting mosquitoes, thereby decreasing malaria incidence.

A technical briefing paper was first prepared in a very short time frame compared to other scientific advisory studies. To be able to do so, the scope of the topic had to be narrowed down from 'gene drive technology' to a specific case for which sufficient scientific evidence is available. The case that we selected is gene drive for the eradication of malaria. The briefing was prepared by an author with a background in biotechnology and was peer reviewed in a 'crowd-review' process with eleven experts from various related disciplines. As such, the short briefing paper was considered to be of a sufficiently high quality to support the foresight intervention.

For the foresight approach, a group of participants was brought together to gather their reflections about gene drive technology applied to the suppression of malaria from a wide range of perspectives by following the STEEPED approach, which helps to explore a topic from seven viewpoints (social, technological, economic, environmental, political, ethical and demographic). Even though not all identified stakeholders could be represented, the outcomes led to a wide-ranging list of concerns and opportunities regarding the case as well as to identifications of gaps in the process, background information, and deficiencies in the approach. The main limitation of the study is its short time frame. From this situation several deficiencies which include the lack of a comparison case, insufficient information on international agreements on biosafety (the Cartagena Protocol), and the absence of a viewpoint from an environmentalist organisation opposed to gene drive. To remedy the limitations, additional information was collected and inserted in this report. A main concern was the ethical need to continue conducting research for the eradication of malaria. Still, there is also a need for a specific risk assessment of gene drive for eradicating malaria.

A main and more generalised outcome of this background note regarding future scientific advice on a specific biotechnology is that there is a need for a framework for risk assessment of technology.

The outcomes on the technology and its concerns and opportunities are planned to be the subject of a panel discussion during a breakfast event at the European Parliament (planned for 19 March 2019).

Table of contents

1. Aim of the project

1.1. Context

In the two-page EPRS publication "What if we genetically engineered an entire species?"[2], it is explained that gene drive is best known for its capacity to suppress malaria by eradicating mosquito populations. However, its applications reach much further, including its potential to erase herbicide and pesticide resistance in weeds and pests, and remove invasive species from ecosystems. This is a type of technology that is still in development and could potentially be quite disruptive, as it can interfere with the entire ecosystem.

1.2. Two-fold aim

The present project has two aims.

First, it is a test of the way one could approach an assessment of a biotechnology by applying a foresight approach in a very short time-frame. Not necessarily in order to provide a basis for decisions, but for providing a good basis for a further, more in-depth study. Foresight has been used in STOA's work since 2015. Furthermore, it is considered to be most useful for technologies with inherent associated uncertainties, and/or whose application can have a high impact on society.

Second, it is an assessment of the science and ethics of gene drive to exterminate mosquitoes that transmit malaria. Malaria is the most common disease transmitted by an infected female Anopheles mosquito. Moreover, it is the most important parasitic infection that occurs in people and accounts for more than 400,000 deaths per year. This disease is commonly associated with poverty and has a major negative impact on economic development in Africa, due to increased healthcare costs and lost ability to work.

[2] What if we genetically engineered an entire species? (2018), Lieve Van Woensel & Jens Van Steerteghem, European Parliamentary Research Service. PE 624.270 – December 2018

2. The methodology

Since 2015, studies for the European Parliament can be conducted by following the scientific foresight process in parallel with standard Technology Assessment studies. At present, this is applied for emerging technologies that are in full development and for which the implications of their applications are not well known yet.

Central in this project are a background document (technical briefing) and two meetings – one of experts and one of individuals who could be associated with relevant societal groups or stakeholders. Experts from various fields and organisations proofread the background document to ensure that it is of sufficiently high quality. Achieving consensus among experts was a prerequisite for finalising the document.

The second meeting was a brainstorming session that mapped the participants' envisioned "hopes" and "fears" with regard to gene drive technology as applied by Target Malaria[3]. We chose the participants so as to achieving a varied mix of expertise and perspectives. Here, we did not aim for consensus but only for evoking thoughts and feelings. The whole project was done in approximately 3 months' time.

2.1. Preparing the scientific briefing: Collecting the 'scientific evidence'

The project expert, who has a background in biotechnology though no specific expertise in gene drive, prepared an initial technical briefing paper. This document was reviewed by a group of eleven experts from technical as well as regulatory backgrounds. These experts from various fields and organisations proofread this technical document to ensure that it is of high quality. Achieving consensus among experts was a prerequisite for finalising the document. This initial briefing was critiqued for being too broad and, as a result of this, for being of insufficient quality. The peer-reviewing experts emphasised the need to carry out a comparison study with specific cases instead of gene drive in general. Subsequently, the author rewrote the document basing it on the case of Target Malaria but did not include a comparison case due to the time constraints. The same group of scientific experts reviewed the new scientific briefing as prepared thereafter. This resulted in a scientific briefing that provides a neutral, evidence-based overview of the status of malaria in the world and Target Malaria's gene drive with regard to the way it works, the benefits and risks it brings and the regulatory regimens that are applicable. This briefing was provided as preparatory input for the participants of the said foresight session, i.e., the second phase of the STOA project.

The experts included:

- Four experts from Target Malaria, including top researchers in the field.
- One manager from the Outreach Network for Gene Drive Research.
- A professor in biotechnology law.
- One policy analyst from the European Commission (EC) who follows developments in gene drive technology.
- A regulatory and responsible research manager from a biotechnology institute.
- One lead researcher from an American university working on gene drive in a different context.
- Two experts from the American Foundation for the National Institutes of Health (FNIH).

[3] Target Malaria is a not-for-profit research consortium that aims to develop and share technology for malaria control. It started as an university-based research programme and has grown to include scientists, stakeholder engagement teams, risk assessment specialists and regulatory experts from Africa, North America and Europe.

2.2. Running the foresight intervention: Collecting the 'societal evidence'

The foresight brainstorming is central in the process. This brainstorming is a discussion session that maps participant's envisioned "hopes" and "fears" with regard to gene drive technology as applied by Target Malaria.

We chose the participants with regard so as to achieve a varied mix of expertise and perspective, covering as many areas as possible from the range detected via the analysis at the very start of the project. The short time period for the project was the main constraint for involving the broadest possible group of stakeholder representatives. As said, the participants received the scientific briefing in advance, though it was also explained to them at the beginning of their brainstorming session.

Contrary to the peer review process of the scientific briefing, during a foresight brainstorming one focuses on collecting views, i.e. hopes and fears related to the topic (gene drive for eradicating malaria), where consensus between the participants is not required. Here we did not aim for consensus, only for evoking thoughts and feelings. All 'concerns' and 'opportunities' by participants are valid, and summarised as outcomes of the meeting.

2.3. Collecting complementary information

As the study was conducted over a very short period of time, the preparation was focused on the most pertinent evidence. During the foresight brainstorming, some gaps in background research have been spotted, for which additional information was collected. This covered information on the international regulatory framework for gene drive technology, information by the World Health Organisation (WHO) and the viewpoints of environmentalist organisations with a record of opposition to gene drive.

2.4. Analysing the overall outcomes

The outcomes were analysed according to the topic of the study and the methodology used. The overall views regarding the advantages as well as the disadvantages about gene drive technology for eradicating malaria have been listed. Due to the small scope of the project and the partial stakeholder participation combined with the development stage of the research, these conclusions are restricted to indications of expressed concerns and opportunities. Taking into account further input that has been collected based on the suggestion is of the participants in the foresight meeting, the conclusions could be somewhat framed and translated into some guidelines on the possible use of foresight approaches for assessing new biotechnologies.

3. Gene drive and malaria – the scientific briefing paper

The science and ethics of gene drive

'Gene drive' is a phenomenon that causes the biased inheritance of a genetic element in a sexually reproducing organism. The changed inheritance pattern can be such that the genetic element spreads through populations, even if the element negatively impacts the survival and reproduction of the organism.[2,6] Instead of the normal Mendelian 50% ratio of transmitting a gene (more specifically, an allele) to offspring, gene drive systems can increase the chance to nearly 100%. These effects are seen in naturally occurring genetic distortion mechanisms as well, and were the original inspiration of the technology. Gene drives are potentially useful in controlling or modifying populations of undesirable organisms, such as disease-transmitting insects, invasive alien species, or agricultural pests.[1,5,9,11,13] Scientists are therefore working on engineered gene drives in laboratory settings for different possible applications. There are distinct differences from a technological, ecological, and ethical point of view between these applications. This will affect the way we will evaluate them from a societal point of view and makes it difficult to present an overall opinion on gene drives. That is why we have chosen to focus in this paper on one particular application developed by the non-profit research consortium Target Malaria. We have chosen this application because it is one of the more advanced projects in a field where other approaches to suppress disease-transmitting insects are already applied.

Target Malaria serves as a case study of current research in controlling insect-borne diseases, which is the focus of much gene drive research. We would like to emphasise that what is relevant for the current case is not necessarily relevant for other cases.

Malaria

Malaria is a mosquito-borne infectious disease caused by a single-celled organism from the *Plasmodium* group. The *Anopheles* mosquito transmits the parasite from one person to another when taking a blood meal. So far, research has not delivered a vaccine that effectively immunises humans against *Plasmodium*. There is a vaccine being tested but one that provides only partial protection. For 2017, the World Health Organisation (WHO) reported 219 million malaria cases globally and 435 000 deaths, 266 000 of which were children aged under 5 years. 92% of cases and 93% of deaths occurred in Africa. Drug treatments, bed nets, and insecticide spraying are reaching their limits in reducing the burden of disease, and mainly have effects in-house, whereas the risks of attracting malaria outside remain high. WHO reports during the period of 2015-2017 show that there is no significant progress in reducing the number of malaria cases. The funds required to fight malaria with these approaches have been predicted to rise from $5.1 billion in 2017 to $9 billion per year by 2030, whereas the funds actually available in 2017 reached only $3.1 billion. The consensus is that eliminating malaria requires new tools in addition to the existing ones.

Case study: Target Malaria

Target Malaria is one prominent consortium working on the application of gene drives in malaria control and may be the first to apply for field trials. Their timeline currently foresees a request for regulatory review of field trials in 2024. The consortium receives the core of its funding from the Bill & Melinda Gates Foundation and the Open Philanthropy Project Fund. The aim of Target Malaria is to develop a gene drive that is capable of reducing three of the sub-Saharan mosquito species that transmit the malaria parasite: *Anopheles gambiae, Anopheles coluzzii,* and *Anopheles arabiensis*. Their broader objective is to develop a long-term, cost-effective, and sustainable solution that is complementary to conventional mosquito control methods.

The method Target Malaria uses, called 'population suppression', reduces the number of female malaria mosquitoes by manipulating the sex-defining biology of mosquitoes. Since only females bite and lay eggs, a population with primarily males will be less harmful and will reduce in size. Like in humans, mosquito males have both X and Y sex chromosomes while females have two X-

chromosomes. When the X-bearing egg cell receives an additional X-chromosome from the male parent, it will develop into a female mosquito, when a Y-chromosome is received, male development will ensue. The ratio at which this happens under normal conditions is 50/50. As is the case with gene drive, if one can change this ratio towards favouring Y-chromosome transmission in males, every generation will see an increase in the proportion of males.

To achieve this, researchers introduce a gene into the genome of the mosquito that codes for a DNA-cutting enzyme called a nuclease. These enzymes can be programmed to cut specific DNA sequences. When the nuclease gene is placed on the Y-chromosome of a male mosquito and programmed to cut key sequences on the X-chromosome during sperm formation, it will leave that chromosome fragmented. The sperm that contains this fragmented X-chromosome is unable to generate female offspring. This means that males carrying this nuclease-gene will produce sperm with functional Y-chromosomes only. When mating with a non-engineered female in the wild, the offspring will receive one X-chromosome from the mother and the engineered Y-chromosome from the father. Thus, the next generation will consist largely of males - all carrying the engineered gene on the Y-chromosome and unable to transmit X-chromosomes (see figure 16). Over time, the lack of females will cause the overall population to reduce in size and therefore less likely to transmit the malaria parasite.[7]

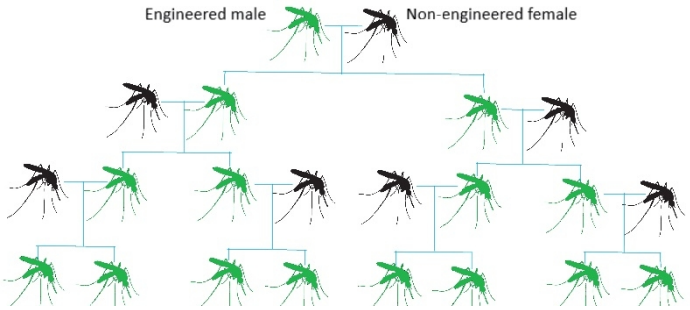

Figure 1: Engineered male mosquitoes (green) mate with wild females (black), producing male offspring carrying the engineered sequence. In time, these will dominate the population, causing it to reduce in size.

Another type of gene drive under investigation by Target Malaria works by disrupting a gene essential for female fertility, effectively reaching the same results by reducing mosquito reproduction.[12] A still different take on the problem of malaria, pursued by the University of California, Irvine Malaria Initiative (UCI MI), is called 'population replacement' and involves driving genes through the population of mosquitoes that confer resistance to the malaria parasite.[8] As mentioned earlier, these different approaches bring along different dynamics that require their own assessment.

Risks and Safeguards

Gene drive technology has stirred much discussion on potential risks associated with research and implementation. One often-raised concern is the potential impact of suppressing the target population on the wider ecosystem. In the case of population reduction drives such as that being pursued by Target Malaria, concern has been raised about the potential impact of reduced mosquito numbers on, for example, fish that feed on their eggs and larvae. Research from Imperial College London finds little evidence for such negative impacts on African ecosystems by removing the dominant malaria-carrying mosquitoes.[4] It should likewise be kept in mind that current insecticide-based mosquito control methods also aim to reduce mosquito numbers and have other environmental and health effects.

Another potential risk relates to transfer of the gene drive to different but related mosquito species. This would not be a problem if these other species are malaria-carrying mosquitoes themselves, but it might be if they were benign. Mating and producing viable offspring between the species must be physiologically, anatomically and ecologically possible for this to happen.

Considering that the research into these risks is still young, more investigation is required. A 2016 report by the U.S. National Academies of Science, Engineering and Medicine stated there is not enough information to decide on the use of gene drive technologies and recommends a phased testing pathway with risk assessments in every phase to uncover the extent of the risks. The WHO also recommended such a pathway for genetically modified mosquitoes.

The risk of accidental release of gene drive mosquitoes from research labs is minimised by conducting research in areas of the world where the mosquito species is not endemic and does not have the ability to establish itself, at least until field-testing. Gene drive research is also always under regulatory oversight by national authorities, ensuring it complies with safety requirements.

As with other pest control strategies, resistance to gene drive may arise after several generations or may already be present in wild populations. This is one of the challenges that researchers developing functioning gene drives need to overcome.[3,10,14]

Regulation

Organisms with engineered gene drives are genetically modified organisms that fall under national and international law-provisions, thereby making the release of such organisms subject to prior authorisation and case-by-case prior risk assessment.

Populations of organisms do not respect national boundaries and gene drives do not either. This makes international cooperation in gene drive development and implementation crucial. On the global level, the UN Cartagena Protocol on Biosafety to the Convention on Biological Diversity details procedures for intentional and unintentional transboundary movements of Living Modified Organisms, under which gene drive organisms are classified. In November 2018, the Convention of the Parties emphasised the need for a precautionary approach in terms of research and release. Case-by-case risk assessments are required and risk management measures need to be in place. Additionally, "free, prior and informed consent" of potentially affected indigenous peoples and local communities is to be sought or obtained where appropriate, in accordance with national circumstances and legislation.

Risk assessment frameworks for genetically modified organisms exist and are applied to organisms with gene drives, but may need to be assessed for their suitability to address aspects particular to gene drive technology. Several national authorities have already reviewed their regulation and the European Food Safety Authority (EFSA) is in the process of reviewing the current environmental risk assessment framework for GMO. It will take several more years for an application for the release of organisms with gene drives to be ready for evaluation, which gives time to regulatory agencies to prepare themselves. In any case, the release of any genetically modified organism is subject to prior authorisation and case-by-case prior risk assessment.

Reviews by national authorities

- Australian Academy of Science: "Synthetic Gene Drives in Australia: Implications of Emerging Technologies" (May 2017)
- European Academies Science Advisory Council: "Genome editing: scientific opportunities, public interests and policy options in the European Union" (March 2017)
- American Academy of Sciences, Engineering and Medicine: "Gene Drives on the Horizon" (June 2016)
- German Central Committee on Biological Safety "Position statement of the on the classification of genetic engineering operations for the production and use of higher organisms using recombinant drive systems" (February 2016)
- Dutch National Institution for Health and Environment (RIVM) "Gene drives: Policy Report" (2016)
- United States Environmental Protection Agency "2017 Update to the Coordinated Framework for the Regulation of Biotechnology" (2017)

References

(1) Burt, A., Coulibaly, M., Crisanti, A., Diabate, A., & Kayondo, J. K. (2018a). Gene drive to reduce malaria transmission in sub-Saharan Africa. *Journal of Responsible Innovation*, *5*(sup1), S66–S80. https://doi.org/10.1080/23299460.2017.1419410

(2) Burt, A., & Crisanti, A. (2018b). Gene Drive: Evolved and Synthetic. *ACS Chemical Biology*, *13*(2), 343–346. https://doi.org/10.1021/acschembio.7b01031

(3) Champer, J., Reeves, R., Oh, S. Y., Liu, C., Liu, J., Clark, A. G., & Messer, P. W. (2017). Novel CRISPR/Cas9 gene drive constructs reveal insights into mechanisms of resistance allele formation and drive efficiency in genetically diverse populations. *PLOS Genetics*, *13*(7), e1006796. https://doi.org/10.1371/journal.pgen.1006796

(4) Collins, C. M., Bonds, J. A.S., Quinlan, M. M., Mumford, J. D. (2018). Effects of the removal or reduction in density of the malaria mosquito, Anopheles gambiae s.l., on interacting predators and competitors in local ecosystems. *Medical and Veterinary Entomology*, (2018), doi: 10.1111/mve.12327

(5) Courtier-Orgogozo, V., Morizot, B., & Boëte, C. (2017). Agricultural pest control with CRISPR-based gene drive: time for public debate: Should we use gene drive for pest control? *EMBO Reports*, *18*(6), 878–880. https://doi.org/10.15252/embr.201744205

(6) Esvelt, K. M., Smidler, A. L., Catteruccia, F., & Church, G. M. (2014). Concerning RNA-guided gene drives for the alteration of wild populations. *ELife*, *3*. https://doi.org/10.7554/eLife.03401

(7) Galizi, R., Doyle, L. A., Menichelli, M., Bernardini, F., Deredec, A., Burt, A., … Crisanti, A. (2014). A synthetic sex ratio distortion system for the control of the human malaria mosquito. *Nature Communications*, *5*(1), 3977. https://doi.org/10.1038/ncomms4977

(8) Gantz, V. M., Jasinskiene, N., Tatarenkova, O., Fazekas, A., Macias, V. M., Bier, E., & James, A. A. (2015). Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(49), E6736-43. https://doi.org/10.1073/pnas.1521077112

(9) Hammond, A. M., & Galizi, R. (2017). Gene drives to fight malaria: current state and future directions. *Pathogens and Global Health*, *111*(8), 412–423. https://doi.org/10.1080/20477724.2018.1438880

(10) Hammond, A. M., Kyrou, K., Bruttini, M., North, A., Galizi, R., Karlsson, X., … Nolan, T. (2017). The creation and selection of mutations resistant to a gene drive over multiple generations in the malaria mosquito. *PLOS Genetics*, *13*(10), e1007039. https://doi.org/10.1371/journal.pgen.1007039

(11) Johnson, J. A., Altwegg, R., Evans, D. M., Ewen, J. G., Gordon, I. J., Pettorelli, N., & Young, J. K. (2016). Is there a future for genome-editing technologies in conservation? *Animal Conservation*, *19*(2), 97–101. https://doi.org/10.1111/acv.12273

(12) Kyrou, K., Hammond, A. M., Galizi, R., Kranjc, N., Burt, A., Beaghton, A. K., … Crisanti, A. (2018). A CRISPR–Cas9 gene drive targeting doublesex causes complete population suppression in caged Anopheles gambiae mosquitoes. *Nature Biotechnology*, *36*(11), 1062–1066. https://doi.org/10.1038/nbt.4245

(13) Medina, R. F. (2018). Gene drives and the management of agricultural pests. *Journal of Responsible Innovation*, *5*(sup1), S255–S262. https://doi.org/10.1080/23299460.2017.1407913

(14) Unckless, R. L., Clark, A. G., & Messer, P. W. (2017). Evolution of Resistance Against CRISPR/Cas9 Gene Drive. *Genetics*, *205*(2), 827–841. https://doi.org/10.1534/genetics.116.197285

4. Foresight for exploring the societal perspective

4.1. Foresight methodology

For the future assessment of technologies of a disruptive nature or encompassing many uncertainties, STOA applies foresight practices[4] that focus on the exploration of how technologies could affect society in the future. Foresight helps in surpassing the limits of scientific evidence in these cases by balancing scientific evidence with public acceptance, possible impacts of scientific and technical developments, economic consequences, etc.

The key elements in a foresight intervention are:

- to compose a group of individuals who mirror a variety of societal groups or stakeholders involved in the technology or its application field or are possibly impacted by the topic (malaria, gene drive or wider genetic technologies);
- to ensure the participants can interact in an interdisciplinary way without the need to reach a consensus on their opinions (in contrast to the process of obtaining scientific evidence);
- to envision possible impacts, covering both the intended ones (*in casu* the eradication of malaria) and the unintended ones (such as unforeseen damages to the ecosystem);
- to list hopes and fears by systematically scanning the 360 degree approach via STEEPED. This is a checklist that specifies seven lenses through which we perceive the impacts of techno-scientific developments, thereby ensuring that we cover all the areas of interest or concern, including their national differences. The seven perspectives are social, technological, economic, environmental, political/legal, ethical and demographic aspects.

In addition, to guide this exploration, the participants were handed the following three simple 'what if' questions: 'What if gene drive eradicated malaria?', 'What if one or more countries opposed application of gene drive for eradicating malaria?' and 'What if gene drive interfered in the ecosystem?'. Some participants critiqued these 'what if' questions for their accuracy, however, the goal was to elicit discussion. A takeaway for future foresight interventions when using 'what if' questions is that 'what if' questions are to be carefully prepared and that their purpose is to be clarified at the beginning of the meeting.

[4] *Towards Scientific Foresight in the European Parliament* (2015). European Parliamentary Research Service. Brussels.

4.2. Participants

The choice of participants was constrained from the start by the limited time frame of the project. This means that we worked with volunteers rather than real stakeholders. We reached out to volunteering colleagues and professional and personal acquaintances with relevant backgrounds and were contacted by others who were interested to participate. The Outreach Network for Gene Drive Research put us in contact with experts in the field of gene drive research. Prominent organisations and institutions of relevance were contacted as well but without success.

Throughout the project, we were aware of the biases of our participants and experts and ourselves. Target Malaria has a stake in this project and was closely involved in reviewing the background document and in the discussion meeting. However, we included multiple independent experts for the different stages of the project, which minimised possible bias. Our own bias shows itself by our choice in participants, most of whom come from our immediate surroundings. The lack of a sceptical opinion among the participants can be partly attributed to this. It must also be noted that the sample size of 16 participants means that the outcomes of the discussion session are also likely to be skewed statistically.

We now provide a description of our participants that shows their relevance to the study. No names are mentioned due to rules regarding privacy.

Potential participants were convened in the preparatory phase, after identifying the stakeholders. The participants present during the actual brainstorming included:

- Two associates of Target Malaria involved in stakeholder management.
- A professor in biotechnology law.
- Two participants from different departments in the EC who follow developments in gene drive technology.
- A bioethicist from the European Commission.
- A regulatory and responsible research manager from a biotechnology institute.
- A PhD student in ecology.
- A PhD student in European Studies.
- A science communicator.
- Seven employees from the European Parliament with: a legal and political science background, a historical and foresight background, a policy analyst background, a natural science background, a medical background.
- One person in the group has a history of being a malaria patient, four are from countries burdened by malaria.

4.3. Outcomes of the foresight brainstorming

This section documents the outcomes of the discussion session under the STEEPED headings. Naturally, this section is our interpreted summary of the discussion, edited in bullet points, which we then categorised under the STEEPED headings. There was no requirement for reaching a consensus among participants and we censored nothing in writing these comments here.

The actual proceedings of the meeting involved first an explanation of the foresight methodology we would be using during the meeting, with an emphasis on the STEEPED scheme, a short presentation of some key elements of the background paper with room for questions or comments from participants, and then the discussion. We made clear that during this discussion we welcomed comments of all sorts. We divided the participants in two groups with an eye to achieving a balance in perspectives and shifted some participants from one group to another midway through the discussion so that both groups got input from most perspectives. We provided lunch for the participants and the duration of the meeting was twice 45 minutes.

The ideas expressed by the participants of the foresight brainstorming are listed below, structured according to the STEEPED scheme.

Social

- Reduction in malaria cases increases wellbeing.
- Local communities will profit from gene drive without monetary cost. This means it is more accessible than other methods.
- Research into gene drive does not take away resources from research into vaccines and drugs, or from conventional control methods.
- Gene drive makes no distinction based on creed, colour or economic status.
- Wellbeing does not solely consist of health - it has more components.
- Pressure groups may influence locals to act against their own interests.
- If a lot of money is involved, then special interest groups will try to influence the debate.
- Public resistance can be camouflaged vested interests.
- Among local communities the fear exists that a gene drive mosquito could introduce a new disease. For many, the term 'genetically modified' mosquito is associated with cancer.

Technological

- Genetic resistance to gene drive cannot be stopped. This will act as a break on the spread of the drive. Researchers have to overcome it to make a successful gene drive.
- In implementing new tools we must be sure it does not compromise the efficacy of other tools - gene drive does not have this problem.
- If the targeted mosquito species is eradicated, it is possible to reintroduce it from lab populations free of malaria. However, this is likely to encounter strong opposition from local communities.
- Gene drive is not a silver bullet - it must be used in conjunction with conventional methods. Complete eradication is deemed impossible, not even smallpox is completely eradicated.
- The endonuclease used may increase mutations in the gene drive organisms - the so-called off-target effects. Others pointed out the endonucleases will be improved in the future and mutations happen naturally anyhow. One participant said that implementation of gene drive should wait until better endonucleases are in place.
- Hybridisation of gene drive mosquitoes with other species is possible in the Anopheles complex (a set of closely related species, some of which transmit the malaria parasite) but has never been observed outside of the complex. This kind of interbreeding is highly implausible since it pertains to wholly different species. The comment is made that this is analogous to humans interbreeding with chimpanzees.
- Once released, gene drive is irreversible.
- The point is made that in the long term a dependency on the technology may occur since continuous reduction of mosquito populations requires periodic releases of gene drive mosquitoes.
- Can the technology can be abused?

Economic

- If successful, local communities relieved from the burden of malaria will increase their economic output.
- If successful, international money flowing to Africa to fight malaria can be used for other things. The health personnel present in Africa will have to/can be redirected to other things.
- There will be an impact on the pharmaceutical industry if the profits from malaria drugs are lost.
- There could be resistance from producers of bed nets, drugs and pharmaceuticals.

Environmental

- There are no predators that feed specifically on Anopheles mosquitoes. Other mosquito species with more or less the same niche would fill the gap left open if Anopheles species went extinct. Anopheles eggs laid in stagnant, temporary pools have no ecological function; if these eggs were removed due to reduced populations, this would have little to no ecological impact.
- The absence of the malaria parasite should be considered ecologically as well: Parasites often induce behavioural changes in the organisms they infect - the removal of this behavioural change could alter the ecology of the system. Furthermore, there is the phenomenon of 'host switching' in parasitology - under high pressure, the malaria parasite might infect other mosquito species than Anopheles. This should be included in a risk analysis.
- If the three main mosquito species that spread malaria are eradicated, this might favour other species that spread other diseases.

Political/Legal

- With regard to patenting gene drive, one participant with expertise noted that there is not much of a business model behind gene drive. This means patents would not be very profitable. The comment was made that much depends on patent holder behaviour in the context of humanitarian applications. Furthermore, in the case of Target Malaria, all research is published, which means that the novelty criterion for patents is not fulfilled.
- Target Malaria has one patent for gene drive in its entirety in order to protect the technology and avoid any attempts to patent applications of it for commercial instead of humanitarian use.
- Risk assessment mechanisms need fine-tuning for gene drive technology.

Ethical

- It is an opportunity to generate public trust.
- If the U.S. and Europe decide on a moratorium, people in danger of getting malaria will likely be refused a (partial) solution. Would China or other countries fill this gap? What type of dependencies would that create? However, a full moratorium hardly ever materialises; usually the door to research is kept open.
- Perhaps it is unethical not to make use of gene drive in order to diminish/eradicate malaria.
- It is important that African countries can decide for themselves to implement gene drive or not. It should not be the West.
- Instrumentalising organisms by manipulating the DNA of a species goes against many people's values. This is analogous to the opposition to GMOs.
- There needs to be a discussion and debate among all those concerned before actual decisions on release take place.
- A suspicion was raised as to why Africa is still, after so long, suffering from malaria without much improvement. Could there be a political incentive to keep Africa underdeveloped to gain easy access to its resources? Considering the Western world is a relatively small part of the world population but consumes far more than its due, there could be a reason to keep other parts of the world from developing the same standards of living. The link is made to gene drive by pointing towards possible attempts to withhold its application and thereby keep malaria in Africa. Other participants counter this suspicion by saying everyone has much to gain from stability in Africa, e.g. for reducing emigration. Also, at the present moment the community of researchers agree that gene drive is not yet ready for implementation. There is no hidden political power that forces this consensus.

Demographic

- The increased welfare brought about by the reduction in malaria cases will start the demographic shift sooner and could limit population growth earlier than foreseen.
- Successful reduction of malaria incidence will have a strong positive effect on the survival of young children, which might put pressure on population growth and therefore perhaps migration too.

4.4. Closing remarks

The foresight phase disclosed some deficiencies in the study: The lack of an explicitly sceptical perspective from an environmentalist organisation and the lack of a second case study to compare and contrast the case of Target Malaria. The first one could be partly remedied by including a chapter with additional information, which could include a section that focuses on the main arguments of statements published by sceptical organisations. In that chapter, we could also follow up on other elements that were felt to be insufficiently treated in the background document and second meeting. The second deficiency is inherent to the short timeframe of the chosen approach.

5. Additional information collected as a follow-up of the foresight meeting

During the foresight discussion session, the following additional information was found to be necessary:

- Information on the international regulatory framework for gene drive technology. This was provided by Piet van der Meer, a professor of biotechnology law (University of Ghent).
- Input from the WHO regional office for Europe. This was in response to the scientific briefing.
- Viewpoint from environmentalist organisations with a record of opposition to gene drive.

5.1. International biosafety framework

Provided by Professor Piet van der Meer

Organisms with engineered gene drives are genetically modified organisms that fall under national and EU biosafety rules, thereby making the release of such organisms subject to prior authorisation, which is based on case by case scientifically sound risk assessment.

Organisms with engineered gene drives also fall under the Cartagena Protocol on Biosafety (CPB), which means that the import of such organisms into the territory of the Parties of the CPB is subject to the Advanced Informed Agreement procedure of the CPB (article 7 and following of the CPB). In addition, in the case of an event that results in a release of an LMO, which may lead to unintentional transboundary movement with possible significant adverse effects, the originating Party shall notify potentially affected States (article 17 CPB).

5.2. Input from the WHO regional office for Europe

The use of gene drive technology in controlling mosquito-borne diseases (not only malaria but also dengue, chikungunya, Zika) is a very interesting subject for the WHO.

During the Zika pandemic in 2016 there were a lot discussions around deploying new mosquito control methods (specifically against Aedes aegypti) but the Vector Control Advisory Group (VCAG) (https://www.who.int/vector-control/vcag/en/) recommended to conduct "carefully planned pilot deployment under operational conditions accompanied by rigorous independent monitoring and evaluation [...]".

In terms of using gene drive technologies in malaria control Target Malaria's vector control technology uses gene drive to reduce mosquito populations, with the aim of developing selective vector control, specific to the Anopheles gambiae s.l. vectors that transmit human malaria parasites in Africa. In 2018, at its 8th meeting, VCAG, considering the update from Target Malaria, came up with the following conclusion: "VCAG encourages further development of tools utilizing gene-drive based technologies while recognizing that these strategies are still in the early phases of development, and that important challenges lie ahead for their development and deployment. More evidence from laboratory-based studies is needed before semi-field or open field-testing should be undertaken."

VCAG's general statement on gene-drive based technologies.

While the committee recognised the potential of new gene-drive based technologies to suppress vector-borne diseases, it cautioned that transgenic vector strains possessing forms of the gene drive currently in development may be difficult to recall if they are released intentionally or unintentionally. This characteristic of such genetic modification strategies calls for extremely thorough cage trials in the laboratory accompanied by ecological and epidemiological assessments

of relevance to target countries before conducting field trials where escape of strains into the environment is possible. Despite the need for more information on how to responsibly release gene-drive containing vector strains, VCAG supports continued efforts to develop this technology. The ultimate use of gene-drive based technology will require thorough assessment of the potential benefits and risks, including examination of ethical, legal and regulatory considerations, as well as, governance frameworks.

5.3. Environmentalist organisation's opposition to gene drive

We requested input from environmentalist organisations with a record of opposition to gene drive but, despite multiple attempts, ultimately received no feedback. We include here a summary of several points of a publication authored by the Civil Society Working Group on Gene Drives (composed of several organisations) called "Reckless Driving: Gene drives and the end of nature"[5].

What are the environmental dangers of gene drives?

Greater threat of unintended consequences

Gene drives carry the same biosafety risks that other genetically engineered organisms carry and more. We know the track record of genetically modified organisms (GMOs) acting in unexpected ways and causing a variety of environmental harms, while not delivering on their promised benefits. Gene drives are designed not only to spread rapidly but also to do it with exponential efficiency. There is nothing in the natural world to compare them to and that limits our capacity to predict their behaviour.

Severing a strand in the ecological web

Gene drives are designed to create large-scale changes in populations and intentionally impact entire ecosystems. We know so little about the web of life as it is, are we really ready to take such radical steps to alter the course of evolution? It's impossible to predict the ecological consequences of such a rapid, massive, unprecedented disruption. Removing a pest may seem attractive, but even pests have their place in the food chain. Additionally, eradicating one species might unpredictably open up space for the expansion of another species which may carry diseases, affect pollination or otherwise threaten biodiversity.

Could gene drives jump species?

Promoters of gene drives present them as precise mechanisms, just as GMO promoters did. But living systems and sexual reproduction processes are messy and unpredictable. We now know there is occasional horizontal gene transfer (movement of genes between different species) and that some genes do cross over into related species.

Dangers to society

The ethical, cultural and societal implications of gene drives are especially complex and challenging. Civil society groups, and even some gene drive researchers, are raising the alarm about the power of this technology. Such a powerful tool may be too tempting to military funding agencies and hi-tech agribusiness who see advantages to exploring this Pandora's box. This raises the basic question: who will this technology benefit and who decides how it will be used? The potential threat of weaponized gene drives can't be overstated. While a harmful gene drive could theoretically be engineered into a fast-spreading parasite to 'wipe out' a population or used to crash a food harvest, the bigger threat may come from the changing geopolitics and security requirements that the existence of gene drives may unleash.

[5] http://www.etcgroup.org/content/reckless-driving-gene-drives-and-end-nature

6. Conclusions

6.1. About gene drive targeting malaria

The overall sentiment of the participants with respect to Target Malaria's efforts were positive. No one of the participants advocated a moratorium, neither for implementation nor for research into this type of gene drive. A main outcome was the ethical need to continue conducting research for the eradication of malaria.

The concerns revolved around secondary effects that require attention but were not presented as counter arguments to application in most cases. Economic and demographic issues were touched upon rather infrequently - present authors believe more attention should be paid to effects of this sort.

Consensus was reached on the importance of self-determination of African countries subject to malaria and on gene drive technology being a supplementary control method rather than a silver bullet.

Although the most vocal opposition to gene drive takes this as central, during the foresight meeting, there was relatively little discussion about the uncertainties surrounding the ecological effects of gene drive. However, during the wrap-up after the brainstorming sessions, the need was expressed for a risk assessment framework for reviewing such possible unintended impacts.

6.2. About the value of a foresight approach in a very short time-frame

Of course, working in a short time-frame and with volunteers as participants we are far from the real foresight process. This means we cannot reach the level of depth of a usual foresight study. However, the basic principles were applied. These cover a foresight brainstorming guided by the STEEPED scheme with a group of people from different backgrounds relevant for the topic in an interdisciplinary context.

We find a foresight approach is useful in assessing biotechnologies, even in a short time-frame. For complex issues such as gene drive, it is important in a foresight intervention to ensure that an accessible scientific briefing is available at an early stage or to foresee that there is sufficient time to prepare one (internally or by outsourcing to external experts). The time constraints of the study made it challenging for us to organise a foresight brainstorming with participants representing a sufficiently wide range of stakeholders as well as from an adequate degree of interdisciplinarity. However, even if the short time frame for the foresight study has considerable limitations, it proves to be valuable for assessing the issue at stake: the concerns and opportunities flowing out of this foresight study could eventually serve as a basis for the specifications of an in-depth study. A study such as this one could be improved by collecting opinion papers from stakeholders before the brainstorming session. Taking into this type of information can prevent shortcomings in the case of gaps in the stakeholder representation.

Furthermore, as the foresight meeting started with the scientific briefing, the outcomes on the topic also offer a good insight into the technology and the societal consequences at stake for the policy-makers who might have to prepare policy in these complicated areas. Additionally, the use of the STEEPED scheme helped in obtaining a first assessment of the gene drive technology for eradicating a huge societal problem such as malaria from a wide range of perspectives.

Regarding the technical assessment of biotechnology, a conclusion is drawn that these technologies are complicated and need an in-depth assessment by highly specialised experts in order to describe all their possible scientific aspects. This would be the usual STOA process.

A main conclusion from the meeting with technical and legal experts and the foresight meeting is that biotechnology requires risk assessments per specific case, i.e. the specific technology as well as the application area.

6.3. Overall conclusions

An in-depth foresight approach cannot be conducted in a short time-frame, however, even with this constraint we find it is an appropriate tool for unravelling the complexity of a complicated technology and to set out specifications for a possible further in-depth study. Additionally, it can provide a proper insight into the areas of possible impact of the investigated technology from a wide variety of perspectives. Such insights could lead to a more focused and in-depth study that is backed by specific research questions.

The need for a risk assessment framework

In addition to the foresight approach that enhances the insights into the societal impacts of potentially high-impact technologies, a need for various ways of assessing the risks of biotechnologies and its specific cases of biotechnological applications was revealed. Furthermore, such a risk assessment approach should be available for the three main targets of biotechnology, i.e. the applications in plants, animals and humans.

A main and generalised outcome of this study regarding future scientific advice on biotechnology is that there is a need for a risk assessment framework for such technologies.

This is a publication of the Scientific Foresight Unit (STOA)
EPRS | European Parliamentary Research Service

PE 634.426